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BOOK OF ABSRACTS

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ORAL PRESENTATIONS

200.4 - Serial Transverse Enteroplasty (STEP) for the Short Gut Syndrome (SGS) Patients with Gut Failure (GF)

Yasser Fouda, Masato Fujiki, Neha Parekh, Cassandra Pogatschnik, Lisa Moccia, Sandra Perdue, Guilherme Costa, Hirak Pahari, Koji Hashimoto, Mohammed Osman, Kareem Abu-Elmagd

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Introduction: With recent evolution of gut rehabilitation, bowel lengthening is increasingly utilized to restore nutritional autonomy in patients with GF. This is the first largest single center experience with STEP particularly among adults with different causes of SGS including Crohn's and allograft rejection.

Methods: Over 7 years, 65 SGS-GF-patients received a total of 79 STEP procedures. Sixty one(94%) patients were adults and 4(6%) were children with an age ranging from 2 to 79 years. All patients suffered loss of nutritional autonomy with the requirement for total parenteral nutrition (TPN), or IVF-micronutrient replacement. The leading causes were vascular occlusion (n=22), surgical adhesions (n=13), and Crohn's disease (n=12). Interestingly, the procedure was performed in an isolated intestinal allograft after partial recovery from acute rejection. The mean pre-STEP length of the residual bowel was 71 ± 13 cm with partially or fully preserved colon in 54(83%) and intact ileo-cecal valve in 14(22%) Reestablishment of gut continuity was accomplished preoperatively in 24(37%) and simultaneously performed in 41(63%). The procedure was reproducible in a total of 13(20%) patients. GLP2 was used as an adjunct therapy before and / or after the STEP procedure in 11(17%) patients.

Results: With a total of 79 STEP-procedures and overall total number of 2 to 36 cuts, there was an increment in the bowel length ranging from 2 cm to 50 cm. The increase in the bowel length was influenced by length of the residual bowel, intestine diameter and the cumulative number of the transverse cuts. With a mean follow up of 19 ± 7 months, a total of 28(43%) patients achieved full nutritional autonomy with discontinuation of TPN therapy. The remaining 37(57%) experienced partial reduction in the TPN and IVF support. Length of residual bowel, volume / caloric contents of initial TPN therapy, and presence of the ileo-cecal valve were significant predictors of successful outcome.

Conclusions: STEP along with autologous gut reconstruction is an effective bowel lengthening procedure for the management of SGS –GF patients. The operation is also technically feasible in Crohn's disease patients and recipients of intestinal allografts.

210.4 - Dynamic repopulation, phenotypic evolution and clonal distribution of recipient B cells and plasma cells in graft mucosa associated with rejection after human intestinal transplantation

Elizabeth Waffarn [1, 2], Jianing Fu [1, 2], Kristjana Frangaj [1, 2], Wenzhao Meng [3], Aaron Rosenfeld [3], Kortney Rogers [1, 2], Eline Luning Prak [3], Mercedes Martinez [4], Tomoaki Kato [5], Megan Sykes [1, 2, 5, 6]

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Introduction: Alloantibodies produced by recipient B cells and plasma cells (PC) are associated with rejection after intestinal transplantation (ITx). The dynamics of recipient B cell repopulation of intestinal allografts, phenotypic and clonotypic changes, and roles in mediating rejection have not been defined.

Methods: Prospective collection of immunosurveillance samples was performed for 24 ITx recipients. We serially analyzed chimerism, phenotype, and clonotype (by BCR sequencing) of recipient B cells (CD19+) and PC (CD138+) in allografts and peripheral blood using multicolor flow cytometry and BCR IgH V region sequencing.

Results: Flow cytometric analysis demonstrated eventual (months to >1 year) replacement of graft donor lamina propria B cells by recipient (Fig.1). In patients with donor T cell blood macrochimerism (>4%), who demonstrated reduced rejection, replacement of B cells occurred over several months, while replacement was more rapid in patients without T cell macrochimerism (p=0.057). In the first 200 days post ITx, recipient PCs (>1% of CD45+ cells) appeared in 2 / 2 patients with DSA+ mixed rejection, but in 0 / 5 patients without both DSA and rejection. (p=0.06). Surface IgG+ recipient B cells appeared in grafts of 4 / 5 patients with early rejection (DSA+ or -) compared to 0 / 2 patients free of rejection (p=0.04). BCR sequencing of sorted recipient B cells and PCs from 4 patients showed overlapping clones distributing across time and tissue-space. In one patient, dominant BCR clones were identified in ileal biopsies during persistent mixed rejection (POD16 vs POD37+44), and these were largely different than dominant clones identified during infection (POD68), suggesting the initially dominant clones are rejection-related (Fig.2). These clones were expanded in the intestinal allograft compared to the circulation or pre-transplant lymphoid tissues. Dominant overlapping clones were not detected in ileal samples from 3 patients free of rejection or DSA.

Conclusion: Graft recipient B cell repopulation is delayed in patients with circulating T cell macrochimerism, who have less DSA and rejection. Graft repopulating recipient B cells may acquire IgG expression and plasma cell phenotypes in association with rejection. Recipient B cell clones distribute throughout the graft and further identification of potentially alloreactive clones may facilitate understanding of how B cells participate in organ-specific alloimmunity in intestinal transplantation.

Figure 1. Multicolor flow cytometry analysis showing replacement of graft donor B cells by recipient cells after transplant (A) in patients with or without blood donor T cell macrochimerism (B), time to >50% occupation by recipient B cells (C), and frequency of recipient plasma cells and IgG+ B cells in the graft(D).

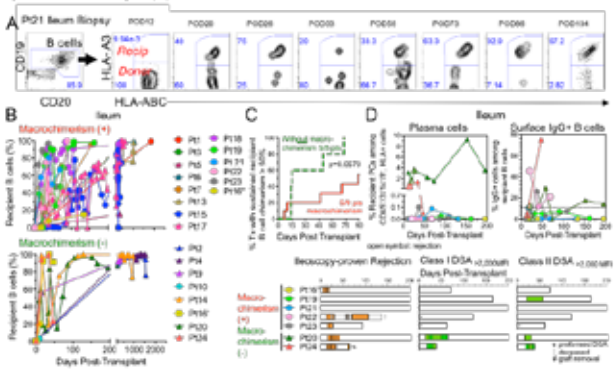
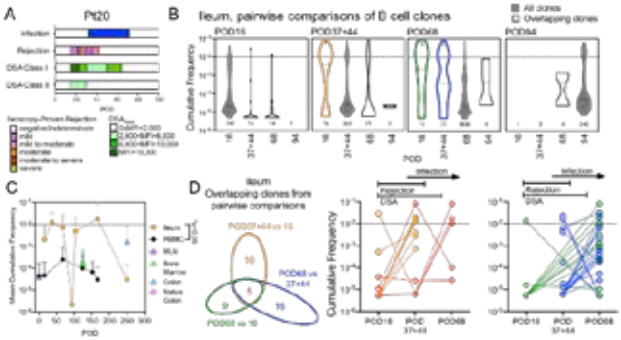


Figure 2. In a patient with rejection, DSA, and cryptosporidium infection (A), sorted recipient B cells from repeat ileal biopsies identify overlapping dominant BCR clones in pairwise comparisons during rejection (B, orange), which were maintained in the gut at higher frequency than PBMC (C). Different overlapping clones increased during infection (B green and blue, D). POD: Post-operative day.



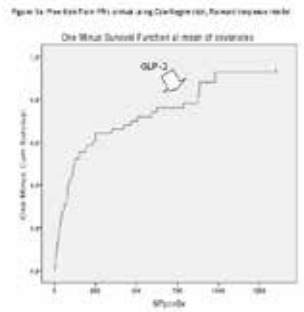
220.4 - Results of Medical and Surgical Rehabilitation of Adult Patients with Type III Intestinal Failure in a comprehensive unit: Is it possible to predict intestinal rehabilitation?

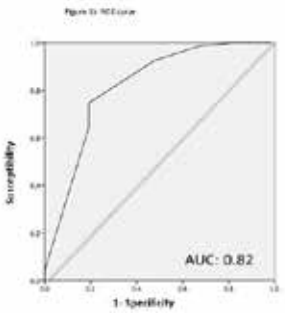
Hector Solar, Mariana Doeyo, Fernando Lobos, Santiago Rubio, Carolina Rumbo, Diego Ramish, Adriana Crivelli, Pablo Barros Schellotto, Gabriel Gondolesi

Hospital Universitario Fundacion Favaloro

Introduction: Short bowel syndrome (SBS) remains the main cause of Intestinal Failure (IF). The management at a comprehensive unit assures an adequate evaluation, maximizing opportunities to achieve intestinal autonomy.

We aim to report the long term results of medical and surgical rehabilitation of patients (pts) with type III IF (III-IF) and to develop a formula to predict PN independency based on anatomical and clinical variables.



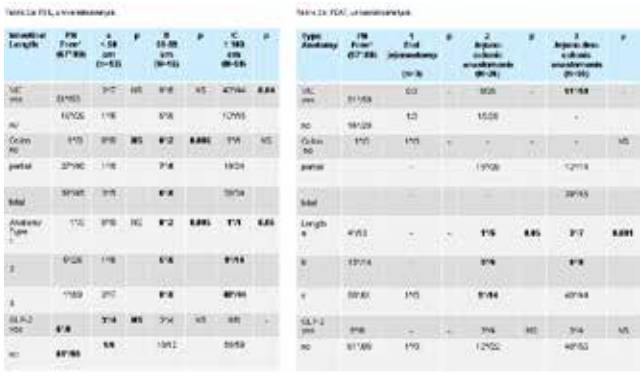


Material and Methods: Retrospective analysis of a prospective database of III-IF adult pts, that underwent Autologous Gastrointestinal Reconstruction Surgery (AGIRS) from 3/2006 to 08/2018. Age, gender, primary diagnosis, pre-surgical anatomy, post-surgical intestinal length (PSIL): grouped as a , b and c (table 1); post-surgical anatomy; (PSAT) type: 1, 2 or 3; presence of ICV, PN reduction >2/7 days. Statistical analysis was done on SPSS v2.

Results: From 259 adults pts with IF, 185 (71%) had III-IF. AGIRS was performed in 88 pts; mean age: 49.5 ± 14.6 years; 51 female. Primary diagnosis: post op IF 48, ischemia 20, post bariatric surgery 5, others 15. The anatomy at first visit was: type 1 in 78 , type 2 in 3, and type 3 in 7 pts. Mean time on PN before AGIRS was 313.14 ± 483.8 days. PSAT was type 1 in 3, type 2 in 26 and type 3 in 59 pts. The mean PSIL was 159 ± 103.4 cm; according to the PSIL, 13 pts were type a; 16 type b and 59 type c.:. Mean Time on PN after AGIRS was: 817.6 ± 661.3 days. Table 1 shows outcomes based on PSIL and PSAT. Eight pts were started on teduglutide (TED); the mean time on therapy is 764±616.8 days; at the end of follow up, 6/8 discontinued PN support and 2 significantly reduced PN volume. Freedom from PN survival is 83% for the whole group; 91 and 93% for PSIL type b and c respectively, and 33% for a. Figure 1a. represents the Cox Regression for overall PN independency. The logistic regression analysis let us to build a novel formula:

Y(PN Free)= 1/(1+Exp-(5.178+3.866x[Length A=1 o Length B o C=0]+1.886x[ICV Yes=0 o No=1]+2.737x[GLP-2 Yes=0 o No=1])

The ROC curve of the formula results for this cohort was 0.82 (Figure 1b)



Conclusions: AGIRS surgery allows converting anatomy to a favourable type for intestinal rehabilitation, as well as recovering intestinal length. TED treatment allowed later PN discontinuation in patients with unfavourable predictors. The multivariate analysis showed that PSIL, presence of ICV and the TED use, could predict freedom from PN in this cohort of adult pts

220.5 - Diagnosis and management of congenital enteropathies: analysis of a large multi-center cohort and the role of Next Generation Sequencing.

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Introduction: A small percentage of children with intestinal failure suffer from congenital enteropathies responsible for chronic diarrhea associated with severe growth failure and dehydration. These disorders usually present early in infancy and result from monogenic mutations in genes affecting intestinal epithelial function. Recently, next-generation sequencing (NGS) technology has revolutionized the approach to molecular diagnosis, although there still remains little information about the associated natural history, and complete clinical phenotype. To better understand the natural history and the impact of NGS, we studied a historical cohort of children with congenital enteropathies.

Methods: A retrospective analysis of children followed in the intestinal failure / congenital enteropathy programs at Necker-Enfants Malades and Boston Children's Hospitals was done. Diagnosis was obtained either from pathology, targeted sequencing, and from 2012 (Boston) / 2014 (Paris) by NGS (whole exome, or targeted gene panels). Genetic findings were validated clinically and / or functionally.

Results: 85 patients were included (53% female, age 2 months to 25 years). Three out 85 patients died. In 82% (70 / 85) of cases, a diagnosis could be established. 25 (29%) patients were diagnosed with microvillus inclusion disease (MYO5B mutation), 19 (22%) patients were diagnosed with tufting enteropathy (EPCAM mutations). Other diagnoses included DGAT1 mutations (8,5%), TTC37 / SKIV2L, and SLC26A3 [UMO1] mutations. Since 2012, 37 out of 46 patients (80%) obtained a molecular diagnosis, including the discovery of novel genes (DGAT1, UNC45A, WNT2B). 9 out of 42 patients at Necker-Enfants Malades underwent intestinal transplantation. In a number of patients, diagnosis facilitated by NGS led to significant changes in clinical management such as removal of high-risk immunosuppressive medications.

Conclusion: We carried out an analysis of a large cohort of children with congenital enteropathy, across two major pediatric centers. Mutations in MYO5B and EPCAM were responsible for 51% of our cohort, with considerable genetic heterogeneity in the rest of the cohort. Since 2012, most patients underwent NGS, with a molecular diagnosis achieved in 80% of cases[UMO2] . NGS was critical in achieving a diagnosis particularly in atypical or hypomorphic presentations and enabled clinically significant changes in management as well as the discovery of novel disease-causing genes.

220.6 - Effective radiation dose and bone marrow radiation exposure as a result of radiological investigation in a cohort of multivisceral transplant patients

Debbie Saunders [1], David Biddle [2], Claire Walker [2], Cara Morrison [2], Natalie Mortimer [2], Sara Upponi [2], Frank Phillips [3], Lisa Sharkey [3], Dunecan Massey [3], Jeremy Woodward [3]

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Introduction: A patient who experienced a rare form of leukaemia following multivisceral transplantation prompted an investigation of cumulative radiation exposure due to radiological investigations in a cohort of multivisceral transplant patients from our centre. In addition, bone marrow dosimetry was calculated in view of the high incidence of bone marrow suppression in this group of patients.

Methods: Dose data for CT examinations was retrospectively collected using PACS. Effective doses for each phase of each scan were estimated using 2016 updated conversion coefficients. The total number of scans and total effective dose were calculated for each patient and the stochastic risks for general cancer risk of 4.1% / Sv and leukaemia risk of 0.63% / Sv stated by the International Commission on Radiological Protection (ICRP) were estimated. Bone marrow dose per Dose-Length-Product (DLP) conversion factors were created for each anatomical region using the ImPACT Calculator, which allowed total bone marrow doses to be estimated for each patient. Bone marrow dose rates were compared against the acute radiation dose rate threshold for reduced haematopoiesis of 0.25-0.5 Gy / year suggested by the ICRP.

Results: Radiation doses were calculated for 80 patients undergoing multivisceral transplant procedures (+/- liver) at Addenbrooke's Hospital, Cambridge UK between 1998 and 2018. The average age was 49 years (range 16 – 61). The majority of the radiation dose was incurred by CT scans – 1700 in total over an average of 4.4 years per patient (SD 2.6yrs). Mean number of scan phases per patient was 33.7 (SD 17.8). Maximum number of scan phases for one patient was 83. Mean effective dose was 291 mSv (SD 224 mSv), Maximum effective dose was 1057 mSv (4.3% general cancer risk, 1.1% Leukaemia risk). 5 patients received cumulative doses in excess of 800mSv and 2 exceeded 1Sv. The highest bone marrow dose was 0.66Gy, 0.4Gy / month. 74 patients exceeded the ICRP recommended limit of 0.02 Gy / month and 11 exceeded 0.25 Gy / year and 11 patients exceeded the monthly threshold for >120 days.

Conclusions: Significant radiation exposure is experienced by this cohort of patients and the threshold dose rate for reduced haematopoiesis is often exceeded with significant potential implications for the development of cancer and bone marrow suppression.

220.7 - Human intestinal tissue-resident memory CD8 T cells comprise two transcriptionally distinct populations

Michael FitzPatrick [1], Nicholas Provine [1], Lucy Garner [1], Tim Ambrose [1], Srikanth Reddy [4], Georgios Vrakas [4], Peter Friend [4], Paul Klenerman [1, 2, 3], Philip Allan [1, 2, 4]

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Introduction: Tissue-resident memory (T_{RM}) T cells, long-lived effector T cells in tissue that do not recirculate, are critical in inflammatory, infectious, and neoplastic conditions[1]. However, the study of human T_{RM} cells has been hampered by an inability to prove long-term tissue residency. We hypothesised that intestinal transplantation could present an opportunity to study long-lived donor-derived T_{RM} cell populations.

Methods: Adult intestinal transplantation recipients were identified via longitudinal cohort studies at Oxford University Hospitals NHS Foundation Trust. Thirteen samples of intestinal graft biopsies were obtained from eight patients (Table 1). Donor- and recipient-derived T cells in intestinal transplant mucosa were identified using flow cytometry and antibodies to discordant HLA Class I proteins (Fig 1A)[2]. Proposed residency markers CD69 and αE integrin (CD103) were included in the panel. Fluorescence-activated cell sorting was used to sort donor- and recipient- derived intestinal T cells for 5' single-cell RNA sequencing using the 10X Genomics platform.

Table 1: Demographics of study subject cohort.

Characteristic		
Number of subjects		8
Number of samples		13 (1-4 per study subject)
Age (years)		41 (23-65)
Transplant type	SBTx	7
	MMVTx	1
Time from transplant at time of sample	0-3 months	4
	3-12 months	3
	12 months +	4

SBTx – Isolated small bowel transplant; MMVTx – Modified multivisceral transplant.

Results: The proportion of donor-derived T cells was negatively correlated with time post-transplant, and was highly variable between subjects, with some subjects maintaining significant donor-derived populations up to 5 years post-transplant (Fig 1B). Donor-derived T cells uniformly expressed CD69 (>99%), and CD103 was highly expressed (84%), with increased expression at late times (Fig 1C). Single-cell RNA sequencing was performed on cells sorted from a single healthy subject 1 year post-transplantation. Data from 974 cells were of sufficient quality for analysis. Analysis of gene expression revealed conventional CD4 T cells, CD4 T_{REGS}, and 2 distinguishable CD8 T cell populations within the graft-resident donor-derived cells (Fig1D). The CD8 clusters differed in expression of key residency (CD103) and functional markers (GzmB and HLA class II) (Fig 1E).

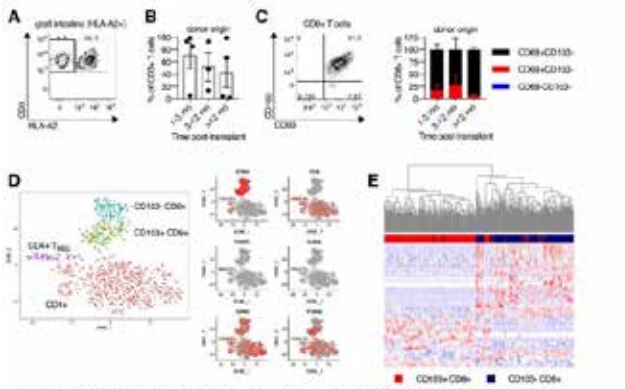

Figure 1. Single-cell RNA-sequencing of human intestinal tissue-resident CD8+ T cells reveals two populations.
(A) HLA-serotype-specific antibodies can distinguish between recipient-derived gut-infiltrating and donor-derived gut-resident T cells within the transplanted intestine. **(B)** Frequency of donor origin tissue-resident T cells within the transplanted intestine over time. **(C)** Representative flow cytometry staining (left) and group summary (right) for expression of the tissue residency markers CD103 and CD69 on donor origin CD8+ T cells. **(D)** Single-cell RNA-sequencing of donor origin T cells reveals two transcriptionally distinct populations of CD8+ T cells, which differ in expression of CD103. **(E)** Heatmap of differentially expressed genes between the two populations of donor origin CD8+ T cells.

Conclusion: Donor-derived T_{RM} cells can persist in the graft for at least 5 years post-transplant, with highly variable dynamics between patients. Single-cell transcriptomic profiling and flow cytometry indicates two transcriptionally and phenotypically distinct CD8 T_{RM} populations within the human intestine. Further study of the regulation, differentiation, and biology of these populations is warranted, as well as their role in intestinal transplantation.

1. Mueller & Mackay (2015) Nat Rev Immunol

2. Zuber J. et al. (2016) Sci Immunol

230.5 - Washington D.C. single-center experience in adult and pediatric intestinal transplantation

Cal Matsumoto, Jason Hawksworth, Alex Kroemer, Juan Guerra, Pejman Radkani, Suki Subramanian, Raffaele Girlanda, Stuart Kaufman, Nada Yazigi, Khalid Khan, Hannah Sagedy, Ashley Voyles, Shannon Huntley, Annelise Nolan, Thomas Fishbein

Georgetown University Hospital

The results of intestinal transplantation (ITx) have improved over the last decade. Adult and pediatric ITx was first initiated at our center in November 2003. We retrospectively reviewed our experience with ITx. Primary immunosuppression consisted of IL-2 receptor blockade induction with maintenance steroids, Tacrolimus, and Sirolimus. Sensitized recipients or recipients with a positive cytotoxic crossmatch received Thymoglobulin induction.

272 ITx have been performed in 263 patients from November 2003 to November 2016. 17 were retransplants, 8 were retransplants with the primary transplant at another center. Overall average age is 23.0 ± 21.3 years. 134 (49.3%) pediatric (<18 yrs), average age 3.42 ± 3.87 yrs (range 3 months – 17 yrs) and 138(50.7%) adult, average age 42.04 ± 12.0 yrs (range 18 – 66 yrs).

Grafts comprised of 155 isolated intestines (iITx), 69 liver-intestine (LI), 41 multivisceral (MVTx), and 7 modified multivisceral (mMVTx) transplants. 156 recipients received an en-bloc colon graft and 8 received a concomitant kidney graft. Most common indication in pediatric recipients were Gastroschisis (26), NEC (25), pseudoobstruction / motility (15), and volvulus (15). Adult indications were Pseudoobstruction / Motility (24), Mesenteric ischemia (19), and Inflammatory Bowel Disease (13).

Overall 1 and 3 year patient survival are 85.2 % and 70.4 % respectively. 1 year isolated ITx, Liver-Intestine, modified MVTx and MVTx patient survival were 88.7%, 91.1%, 85.7% and 61.4%. Overall pediatric 1 year patient survival was 88.5% and adult 1 year patient survival was 81.9% (p=0.133). 1 year retransplant (n=17) patient survival was not significantly lower: 76.5% vs. 85.8% (p=0.32).

Overall 1 year freedom from rejection (FFR) was 76.0%. FFR in adult and pediatric recipients was 67.2% and 85.5% respectively (p = 0.0005). Liver inclusive grafts had a higher 1 year FFR at 85.2 % vs 70.1 % (p =0.007). Dividing up our center experience volume in exactly half, the 1 year survival in the first half (n= 136 cases) was 81.5% and the second half 89.2% (p= 0.09).

This data reflects a cumulative experience of ITx at a large single institution with an extensive pediatric and adult ITx experience. 1 year patient survival has shown a tendency for improved results in the latter half of our experience.

230.6 - Multivisceral Transplant without an ostomy – 5-year experience

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[2] University of Miami Miller School of Medicine, Department of Pediatrics, Division of Gastroenterology
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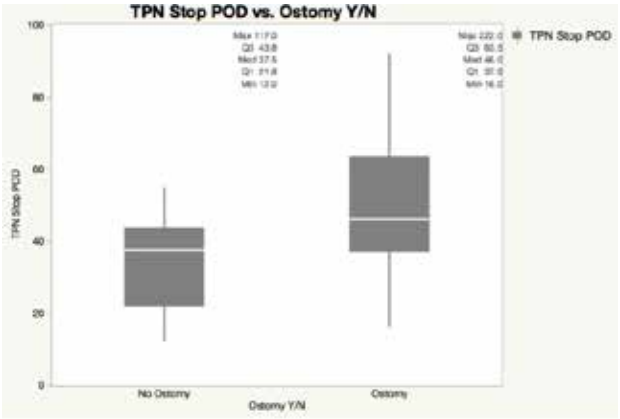
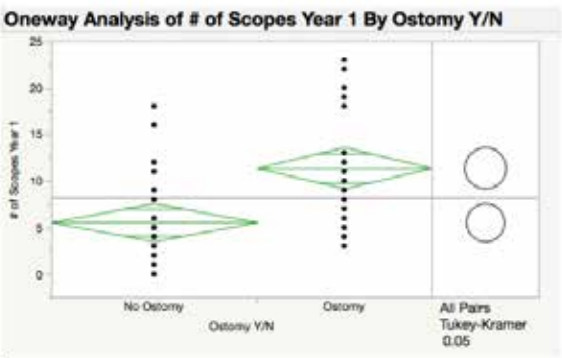
Introduction: Strides continue to be made in the care of patients following Intestinal Transplantation (ITx) yet, rejection continues to be a threat to its' success. A temporary ostomy to assess the mucosa and easily perform a biopsy remains the diagnostic gold standard. However, patients with an ostomy may have high output and decreased renal function. A change in intestinal flora, as stool and mucosa are exposed to air, may trigger rejection.

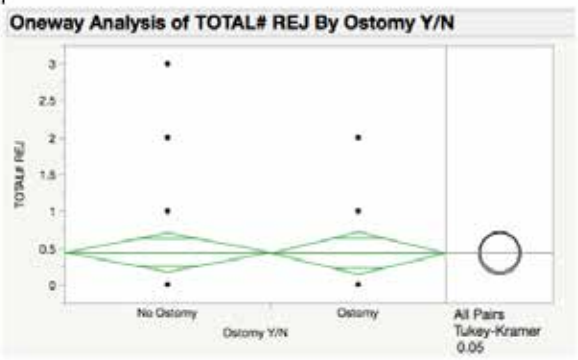
Methods: We retrospectively reviewed 101 primary ITx performed from Jan 2013 to Dec 2018. 27 Isolated Intestine-Colon transplants and 7 Modified MVT were excluded. 67 patients underwent a MVT. 4 died in OR from bleeding and 1 within 72 hours thus excluded as abdominal closure was not performed. Standard immunosuppression was induction with antithymoglobulin/rituximab and maintenance with tacrolimus/mTOR inhibitor.

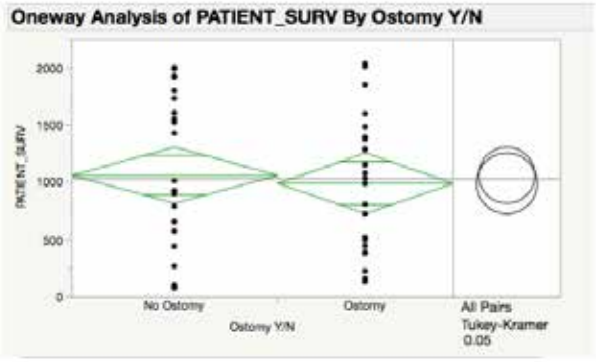
Results: Of 62 patients, 50 had 1-year follow up. 26 were pediatric (1-15yr) and 24 adult (19-68 yr). In 54% (27/50), no ostomy was performed. In 46%, an ostomy was performed- ileostomy in 12% (6/23), colostomy in 32% (16/23), hybrid colon ostomy in 2% (1/23). There was no difference between groups (Ostomy/No Ostomy) in length of stay (LOS) or admissions within the first year. LOS was 79 days with Ostomy(13-232) and 80 days (14-360) in No Ostomy. There was a trend for earlier discontinuation of parenteral nutrition in No Ostomy(32 days) vs. Ostomy(53 days).



Initial endoscopy occurred earlier in Ostomy at 10 vs. 27 days in No Ostomy[F (1,48) = 15.99, p=0.0002]. Number of scopes performed in the 1st year were significantly less in patients with No Ostomy(mean = 6) vs. Ostomy(mean = 11) [F (1,48) = 15.17, p=0.0003] (Fig 2). Despite this, there was no significant difference in rejection. There was a trend toward increased rejection in patients with Ostomy(35%, 8/23) vs. No Ostomy(19%, 5/27). There was no difference in creatinine pre-transplant (non-renal) nor at 1-year post. However, the majority of patients with an ostomy (colostomy + hybrid colon) had colon in continuity making dehydration less likely. Patient 1-year survival did not differ at 82% (4/23) for those with Ostomy and 78% (6/27) with No Ostomy.







Conclusion: MVT without an ostomy continues to be feasible and safe without an increased risk of rejection nor death. Postop care seems to be easier and preservation of kidney function may impact long term ITx outcomes. Lack of ostomy greatly adds to patient satisfaction and quality of life.

230.7 - Disease Recurrence After Intestinal and Multivisceral Transplantation

Monu Goel, Amanda Pruchnicki, Elizabeth Lennon, Jennifer Robinson, Hirak Pahari, Yasser Fouda, Mohammad Osman, Raffaele Girlanda, Masato Fujiki, Guilherme Costa, Kareem Abu-Elmagd

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Introduction: Similar to other organ and cell transplantation, visceral allograft recipients are at risk for disease recurrence. This single center experience addresses the risk of disease recurrence in both the allograft and extra-gastrointestinal systems in patients who underwent transplant due to a potentially recurrent disorder.

Methods: The database of a total of 78 patients with potentially recurring disease including thrombophilia (n= 29), global gut dysmotility (n=24), Crohn's disease (n=18), and gastrointestinal neoplastic disorders (n=7) were reviewed and analyzed. Of these, 53 were transplanted at Cleveland Clinic and 25 were transplanted elsewhere. All patients were adults with 63% female. The visceral allografts were isolated intestine (n=52), liver / intestine (n=6), modified multi-visceral (n=11), and full multi-visceral (n=9). All patients were disease free at the time of transplant, with the exception of the thrombophilic patients who were fully anticoagulated. The diagnosis of disease recurrence was established based on clinical, hematologic, radiologic, and histopathologic studies.

Results: With a mean follow-up of 80 ± 75 months from the transplant date, 7 patients developed disease recurrence with an overall incidence of 9% in this cross-sectional study. The risk of disease recurrence was higher with global dysmotility (17%) compared to thrombophilia (10%) and Crohn's (6%). The 4 transplant recipients (3 isolated and 1 modified multivisceral) with gut dysmotility recurrence had no evidence of mechanical obstruction, or allograft rejection. None of the gastrointestinal neoplastic disorder recipients developed *de novo* disease or recurrence. The hypercoagulable patients developed recurrent vascular thrombosis in the extra allograft vascular system, with the exception of one patient who developed a nonocclusive Carrel patch clot. Recurrent Crohn's was a histologic diagnosis based on identification of granulomas in surveillance biopsies. None of the recipients with disease recurrence lost the allograft or required retransplantation except two of the gut dysmotility recipients who underwent successful retransplantation.

Conclusions: Disease recurrence is a potential risk after intestinal and multivisceral transplantation with no significant impact on outcome. Longitudinal follow-up is required to determine the long-term impact on allograft function and quality of life.

250.5 - Early Predictors of Enteral Autonomy in Pediatric Intestinal Failure: Development of a Disease Severity Score

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Introduction: Patients with short bowel syndrome (SBS) are dependent on parenteral nutrition (PN) while their bowel attempts to compensate for loss of function. Our objective was to create a SBS disease severity score that would predict the probability of achieving enteral autonomy (EA) using clinical variables available in the early postoperative period.

Methods: A retrospective cohort study of SBS children managed by our Intestinal Rehabilitation Program (IRP) was completed. Data abstracted included demographic, anatomic and outcome variables including serum conjugated bilirubin, proportion of enteral nutrition (EN) and episodes of sepsis specifically at 6 months post gut loss. A univariate analysis and Cox proportional hazards (CPH) model was performed. A score predicting EA was created based on weighting of Cox model coefficients. For all analyses, an alpha-value of <0.05 was considered significant.

Results: 139 patients were analyzed (61% males). Ninety-five (68%) achieved EA. Those who achieved EA had a longer residual small bowel (75% vs 24%; p<0.0001) and colon (100% vs 75%; p<0.0001) and were less likely to have the ileocecal valve removed (26% vs 57%; p=0.0005). At 6 months, children who achieved EA had higher enteral tolerance (100% vs 30%; p<0.0001), a lower conjugated bilirubin (0 vs 71.5umol / L; p<0.0001) and less septic episodes (1.0 vs 2.0; p=0.0112). Cox proportional hazards modeling found >50% residual small bowel (HR 2.68 [95%CI 1.60-4.49], p<0.001), ICV intact (HR 0.61 [95%CI 0.37-1.02], p<0.06) and >50% enteral tolerance at 6 months (HR 5.70 [95% CI 2.77-11.74] p<0.001) were positively associated with EA. Conjugated bilirubin >34umol / L at 6 months was negatively associated with EA (HR 0.42 [95%CI 0.27-0.66], p<0.001). A severity score was created by weighting CPH parameter estimates [small bowel length >50%, ICV intact, CB<34umol / L and EN>50% for a maximum score of 8. Disease severity strata were developed (severe [0-2; 25.7% EA], moderate [3-5; 52.9% EA] and mild [6-8; 97.1% EA]. Disease severity strata were developed (severe [0-2; 9 / 35 (25.7%) EA], moderate [3-5; 18 / 34 (52.9%) EA and mild [6-8; 68 / 70 (97.1%) EA].

Conclusion: We propose a paediatric intestinal failure disease severity score that predicts probability of EA, stratified into mild, moderate and severe. The score allows prognostication of individual patients, and could assist research by adjusting outcome reporting or stratifying recruitment.

250.6 - Results of a Multicentric Retrolective Study of Teduglutide Treatment in Benign Short Bowel Syndrome in Germany

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Introduction: Teduglutide (TED) is a medical treatment for intestinal functional rehabilitation of short bowel syndrome (SBS) patients with chronic intestinal failure (cIF). Its application and effectivity is routinely monitored in a structured home care service program by a multicentric approach in Germany. From these prospectively documented data, a retrolective data base was generated in order to study treatment characteristics and outcome parameters in a clinical routine setting of TED-treated cIF-patients.

Methods: For the present interim analysis, prospectively collected clinical data until December 2018 were retrolectively analyzed. Statistical analyses were performed with SPSS using repeated measures ANOVA and Friedman-Test with subsequent Bonferroni-adjusted post-hoc analyses for TED treatment characteristics up to one year.

Results: So far, 29 patients (f:17 / m:12, median age 52 years) were included in this interim analysis. Causes of SBS included vascular (n=12) and inflammatory diseases (n=6), ileus (n=4), injury (n=4) and others (n=3). Median time on parenteral support (PS) before TED was 30 months. At TED start, 72% of patients (21/29) received individually compounded parenteral nutrition (PN); the remaining 28% received standardized PN. PS was administered by patients themselves (n=15), by relatives (n=3), by nurses (n=8) or others (n=3). TED treatment resulted in a significant reduction in PN calories and volume requirements as well as reduced infusion days per week and shortened infusion times (see Table 1).

	i.v. Volume per Week [L] (±SD)	i.v Energy per Week [kcal] (±SD)	Infusion Time [h] (±SD)	PN days per week (±SD)
Baseline	13.2 (±7.9)	7.450 (±4.232)	11.0 (±3.0)	5.3 (±2.2)
Week 12 ± 1	11.3 (±7.7) *	6.301 (±4.241)	10.8 (±3.0)	4.5 (±2.2)**
Week 23 ± 2	10.3 (±7.3) **	5.176 (±4.123) *	9.8 (±4.2)	3.8 (±2.4)***
Week 49 ± 5	8.4 (±6.7) **	4.611 (±4.311) ***	7.4 (±5.6) *	3.2 (±2.6)***

Table 1: Changes in parenteral support characteristics on teduglutide treatment. n=24; * p < 0.05, ** p < 0.01, *** p < 0.001 vs. baseline; PN= parenteral nutrition

The reduction of infusion time was positively correlated with the reduction of PN volume (p<0.001; r=0.75) and calories (p=0.003; r=0.59) after one year of TED treatment. After one year, 22 of 29 (76%) patients were considered responders to TED treatment (with a minimum of 20% i.v.-volume reduction).

Conclusion: In this multicentric real-world analysis of severely PS-dependent SBS/cIF-patients, TED displays effectivity with regards to improvement of intestinal absorptive function as indicated by significantly reduced weekly i.v.-volume and calorie requirements. In addition, the findings demonstrate a reduction of effective infusion days and times, which both importantly affect patients' wellbeing. These data indicate the effectivity of TED treatment in a national routine treatment setting in concordance with clinical trial data and guideline recommendations.

250.7 - Impact of donor selection on early graft loss in Intestinal Transplantation.

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Introduction: The decision to accept or not an intestinal graft can be difficult and it is based on the donor data and the clinical experience of the procuring surgeon. Our aim was to analyze potential donor-related risk factors impacting survival.

Patient / Methods: Donor data from the last 50 intestinal transplants (IT) performed in 44 pediatric patients were retrospectively reviewed (2010-2018; median age at transplant 3.4 yo; 2 LSBT, 42 MVT, 2 modified MVT, and 4 ISBT; 40% retransplants). Analyzed variables were donor / recipient age and weight ratio, cause of death, chronic or infectious disease, cardiorespiratory arrest (CRA) or hypotension, days in the Intensive Care Unit (ICU), and macroscopic appearance of the graft at the procurement and at reperfusion. Results were measured as early graft loss (<6 months) and / or incidence of immunological events.

Results: Unstable donors and those with prolonged cardiac arrest were directly rejected at the offer. Median donor age and weight was 16 months (1 day-18yo) and 10 kg (range 3-68Kg), respectively. The main cause of death was traumatic brain injury (n=17), followed by cerebral hypoxia (n=14), cerebral hemorrhage or infarction (n=13), and meningitis (n=6). Ten donors had chronic disease before death, 14 had suffered a CRA (median duration of 20 minutes; range 1-45), and 18 hypotension. The mean length of stay in the ICU was 2.9 days (range 0.5-9). Graft reperfusion was poor in 2 cases.

In total, 19 / 50 grafts were lost in 17 patients, after an average time of 10 months (range 1-50), 68% early after transplant, and most of them due to immune complications (61%). In 2 patients the graft never functioned until death. Four patients were retransplanted (100% of the ISBT grafts). Patient and graft 1- and 5- year survival was 83% / 73% and 70% / 69%, respectively.

The data analysis showed a higher incidence of early graft loss in chronically ill donors and in longer CRA times ($p<0.05$), and when macroscopic appearance after reperfusion was suboptimal. Donor age or weight, donor / recipient age and weight ratio, cause of death, CNS infection, length of stay in ICU, did not significantly impact on graft survival.

Conclusions: Immune complications are the main reason for the early graft loss in IT. However, ischemia reperfusion injuries observed in marginal donors, as chronically ill patients or longer CRA times, can accelerate the appearance of these complications, leading to irreversible consequences.

260.5 - An algorithm for progress from parenteral nutrition to oral nutrition for adult intestinal transplant recipients

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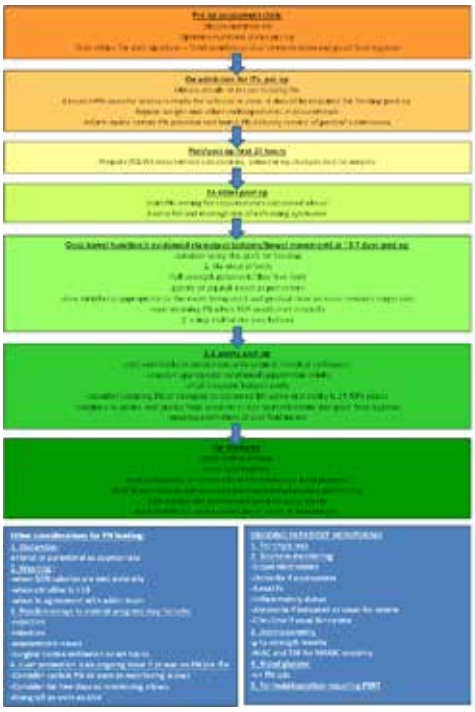
Introduction: Nutritional care is an integral part in the management of patients pre-, peri- and post- intestinal transplant (ITx). However, the published literature is limited on the topic, and there are no clinical trials. The available published literature is based on individual expert opinions and does not include nutrition protocols in ITx. This work aims to combine the available suggestions for nutritional care for adults pre-, peri-, and post-ITx into a step wise, easy-to-follow algorithm of care.

Methods: The current available literature (Pubmed) was reviewed based on following keywords; bowel transplant; intestinal transplant; adult; human; nutrition; and / or their combinations. Since both authors are experienced registered dietitians who have been working with ITx recipients over a decade, expert clinical opinion was also considered.

Results: We created multicenter collaboration of nutrition care for patients undergoing ITx. Based on our literature review and expert opinion, a detailed, easy-to-use nutrition algorithm was developed (Figure 1). This algorithm will act as a prompt for nutritional considerations in the management of adult ITx recipients per-, peri- and post operatively and hopes to generate discussion and information amnesty, harness feedback from the expert community and, in time, develop further iterations as more information is generated and shared.

Conclusion: The current algorithm is a suggested best fit for the aim stated, bearing in mind the lack of published data available. Further development is needed to have an easy-to-use nutritional care algorithm for future clinical practice.



260.6 - Pediatric Home Parenteral Nutrition (Hpn) In France: A National Survey On The Behalf Of The French Pediatric Hpn Network

OLivier GOULET, et al.

The French Pediatric Home-PN network

Chronic intestinal failure (CIF) requires long-term parenteral nutrition (PN). In France, 7 centers are certified as Pediatric Home-PN (PHPN) and supported by the French Social Security. The aim was to review the activity of the 7 PHPN.

Population and methods: Survey: Jan 1, 2014- Dec 31, 2017: Patients characteristics, HPN indications & duration, turn- over, PN weaning, complications: catheter-related blood stream infections (CRBSIs), cholestatic liver disease (CLD) (total bili > 30 micromol / l).

Results: 624 patients < 18 years of age (56.9 % boys) attended one of the 7 PHPN program during the period. Turn-over: 18.7% entering and 13.2% leaving. Increasing population from 265 in 2014 to 352 in 2017 (+33%). Mean & median age at inclusion were 33 & 9 months. Primary digestive disease (PDD) involved 95% of the children. Indications for HPN were short bowel syndrome (SBS): 40.8 ± 7.3 % - congenital enteropathies: 21.9 ±8.5 % - chronic intestinal pseudo-obstruction:15.7 ± 8.9 % – Total aganglionosis: 8.3 ±6.8%; IBD : 4.3 ± 4.2%. Broviac type central venous catheter used in 98%. All patients received tailored PN bags made by hospital pharmacy (16%) or by Baxter-Faconnable® (84%). Intravenous lipid emulsions (ILE) were SMOFlipid® (84%), Clinoleic® (8%), MCT / LCT (6%) or Intralipid® (2%). Mean and median duration of HPN were 82 and 54 months. Causes of resuming HPN were: weaning off PN (79%), transition to adult (15%), death (5%) (90 % of death are cancer or immune deficiency) and intestinal Tx (1%). The main complication was CRBSIs caused by Staphylococcus coagulase negative (70 ± 18%) and Staphylococcus aureus (12.0 ± 11.5 %) (5 fungal infection). Taurolidine lock therapy (TLT) made CRBSIs incidence decreasing from 1.02 per 1000 PN days in 2014 to 0.61 in 2017. Fifteen patients (2.6%) had total bilirubin >30 micromol / l, including 5 cirrhosis, listed for Tx.

Conclusions: HPN is a safe and efficient therapy. SBS is the main HPN indication, with the highest rate of PN weaning. CRBSIs and CLD are potentially life-threatening complications, but their rates were low and deaths (4%) were mostly due to the underlying disease. CRBSIs incidence per 1000 days PN decreased dramatically (- 40%) with TLT. Need for intestinal Tx is very limited according to the low rate of life-threatening complications. Patients must be referred early to expert centers for optimal management and follow-up.

Data will be updated for the Congress including results of the year 2018

260.7 - Effective transitioning of adolescents into adult intestinal transplant services – survey of NITE members

Philip Allan [1, 2], Lindsay Hogg [3], Monica Smith [3], Heather Howe [2], Lisa Vokes [4], Alison Smith [2], Jane Hartley [3], Georgios Vrakas [2], Srikanth Reddy [2], Peter Friend [2], Girish Gupte [3]

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Introduction: Transition of paediatric intestinal transplant recipients is important in allowing patients and their families a continuum of care from current paediatric team to an adult team. In some cases this may be within the same hospital / organisation, and at other times may be to other centres nationally. The long-term outcome and well-being of adolescent patients is clearly much better in terms of compliance and longevity if trust is built up between the patient and the adult centre with the familiarity of their paediatric teams. Over the past 3 years we have transitioned 8 paediatric patients over the age of 18. We have learnt from having a dedicated discussion with transition nurse and psychologist empowers the patient and families towards a smooth transition journey from paediatric to adult centres.

Method: We undertook a survey of members of the NITE network to understand how transition occurs and what typical problems are encountered. A 10 question survey was sent using Surveymonkey

Results: From the survey 19 / 60 (32%) individuals invited responded from 16 centres across Europe. 8 / 19 (42%) were from a paediatric centre, 8 / 19 (42%) were from a combined centre and 3 / 19 (16%) were from adult only. The majority (84%) had a policy for transitioning patients, over 60% thought about commencing transition when patients were aged 14-18, but majority (57%) started transitioning at 16-18, and the first combined clinic was only 31% 16-18 but 48% >18yrs. The majority of responses did not have access to a dedicated transition nurse (63%) or psychologist (63%). Lastly, majority of endoscopic procedures were carried out using propofol or GA (63%).

Conclusion: From our experience, transition needs careful planning, a dedicated team to facilitate and early conversations to ensure adolescents are ready to transition effectively. This will require centres to develop extended roles for multi-disciplinary team to support transition, eg dedicated nurse and psychologist, but also start transitioning patients to the same endoscopic strategy that adults undertake and consider appropriate immunosuppression when adolescents may be considering starting a family.

300.5 - Milk fat globule epidermal growth factor-8 (MFG-E8) has site specific effects on intestinal lengthening in neonatal short bowel syndrome, studied in piglets

Petro George [1], Jennifer Chalmers [2], Marihan Lansing [1], George Slim [1], Pamela Wizzard [1], Patrick Nation [1], Donald McCarthy [3], Patricia Brubaker [2], Paul Wales [2], Justine Turner [1]

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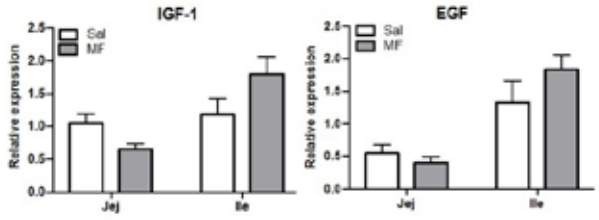
Introduction: Whether acquired or congenital, short bowel syndrome (SBS) remains the leading cause of intestinal failure in neonates. Structural adaptation is essential for survival including, uniquely for neonates, the potential for intestinal growth in length. Milk fat globule epidermal growth factor-8 (MFG-E8) is present in human milk and known to increase intestinal fat absorption. It has homology with epidermal growth factor (EGF), which is known to enhance structural adaptation, and so the potential role of MFG-E8 treatment in neonatal SBS was explored.

Method: Using neonatal piglets aged 2-5 days, two surgical models for SBS were studied, both with 75% total intestinal resection, but either distal resection with jejunal-colonic (JC) anastomosis, or mid resection with jejunal-ileal (JI) anastomosis. Piglets were maintained on parenteral nutrition and trophic feeds to enhance adaptation, with 5mg/kg-d of MF-EG8 or saline (control) given daily by gastric feeding tube. On day 7, bowel length was measured and tissue collected for histology and quantitative real-time polymerase chain reaction analysis of mucosal transcripts including trophic peptides, fat transporters and markers of proliferation. Comparisons utilized student t tests / ANOVA.

Results: All piglets gained equivalent weight during the trial (p=0.65). JI piglets demonstrated significant intestinal lengthening (p<0.001), that was more than 2-fold greater in ileum than jejunum (p<0.001). Lengthening was further enhanced by 22% in ileum following MFG-E8 treatment (p=0.03). In contrast, JC piglets did not increase intestinal length and did not benefit from treatment. In JI piglets, insulin like growth factor-1 (IGF-1; p=0.004) and EGF (p<0.001) expression were increased in ileum and, expression for both was enhanced by treatment in ileum as compared to jejunum (see Figure). In addition, EGF-Receptor (p=0.020) and claudin-2 expression (p=0.026) were also increased in ileum. No other differences in transcripts were noted.

Figure



Sal=Saline control; MF=MFG-E8 treated; Jej=jejunum; Ile=ileum
Relative expression IGF-1 increased in ileum versus jejunum (p=0.005)
Relative expression IGF-1 increased with treatment in ileum (p=0.023)
Relative expression EGF-1 increased in ileum versus jejunum (p<0.001)

Conclusion: MF-EG8 demonstrated site specific trophic effects, only noted in a JI model with remnant ileum. This may limit the utility of this treatment for SBS, where loss of ileum is common. However, the mechanisms of these site specific effects and the roles of IGF-1 and EGF in gut growth warrant further exploration in neonates, particularly given that developmentally relevant conditions, like necrotizing enterocolitis, predominantly target the ileum.

300.6 - The REVE study, preliminary results. A Monocentric Single-arm study to characterize the long-term safety, efficacy, and pharmacodynamic of GLP-2 analog (Revestive®) in the management of short bowel syndrome pediatric patients on home-parenteral nutrition (HPN).

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Introduction: GLP2-analog treatment has been demonstrated to be efficient in adult and children patients with SBS. This study was designed to evaluate the efficacy and the safety of Teduglutide during one year in children with long-term intestinal failure due to SBS.

Methods: Children with SBS followed in our center with > 2 years on HPN, SB length < 80cm, stable on long-term PN (no decrease of PN in the past 6 months) were consecutively included in the study. At baseline they underwent a 4 days hospitalization to perform a stool balance analysis with the duplicate meal technique, blood tests, abdominal ultra-sound, densitometry, coloscopy if age >12 years old, and to initiate the treatment. Teduglutide was administered sub-cutaneously at the dose of 0.05mg/kg/day. Visits were every 2 weeks for 8 weeks, then every 4 weeks, then every 12 weeks from week 12 until week 48. At week 48, a second hospitalisation will take place to repeat the stool balance analysis. This study was registered on clinical trials NCT03562130.

Results: Six months after the first inclusion, 12 children had been enrolled. Mean age was 10 years old (range 5-16). Two children had SBS type 1, six had type 2, and 4 type 3. The results of their stool balance analysis (baseline) are shown in table 1.
At week 12, nine children (100% children who reached the week 12 endpoint) experienced a decrease >20% of PN requirements (mean 30%). For the three children who reached week 24, further decrease of PN intake was achieved (mean 44%, from baseline).
All the children experienced a reduction in stool frequency, an improvement of the stool consistency and a reduction of the ostomy flow.
Citrulline plasma levels increased from 14 µmol/l to 26 µmol/l (mean) in the nine children who reached week 12.
Five children suffered from mild abdominal pain in the first month of treatment. Only one severe adverse event was reported with an increase ostoma output and abdominal pain which led to a hospital admission for 3 days at week 17; no direct link was made with the treatment which was maintained.

Conclusion: All the children included in the study had severe malabsorption as shown by the stool balance analysis. The first results are encouraging on the safety and the efficacy of the treatment. PN reduction still occurred after week 12 and week 24. The results of the second stool analysis at week 48 should confirm the intestinal absorption improvement that is observed clinically.

Food Intake, oral +/- tube feeding *	1709 kcal/day
Stools	1400g/day
Lipid absorption	40%
Nitrogen absorption	49%
Carbohydrates absorption	67%
Total Energy Absorption	55%

Results expressed in mean

* Two patients received tube feeding on top of oral feeding

300.7 - Isolated intestinal transplantation: Are we shifting the paradigm?

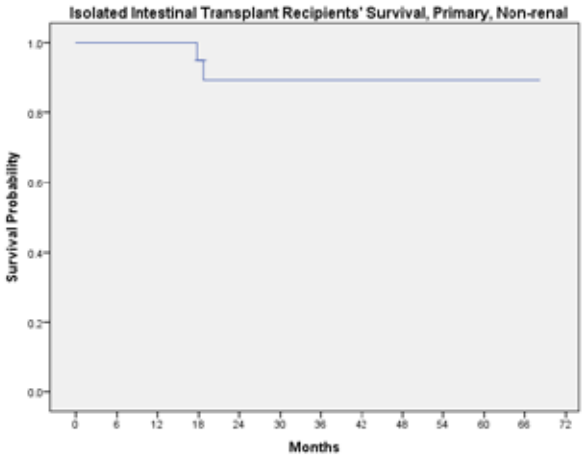
Thiago Beduschi, Jennifer Garcia, Gennaro Selvaggi, Akin Tekin, Ahmed Farag, Yehuda Raveh, Ramona Nicolau-Raducu, Philip Ruiz, Rodrigo Vianna

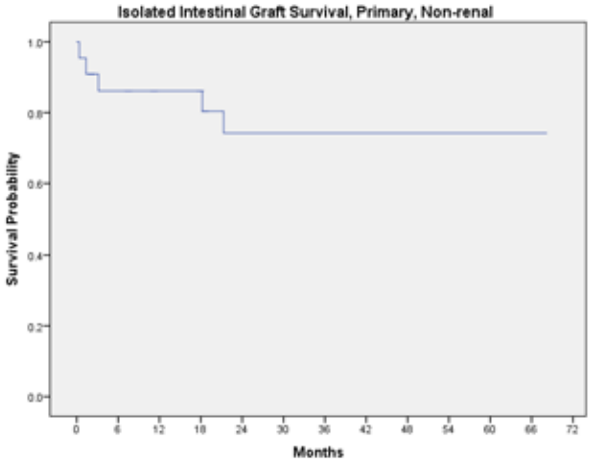
Division of Liver/GI Transplantation, Miami Transplant Institute, University of Miami/Jackson Memorial Hospital

Introduction: Isolated intestinal transplant (IIT) is the definitive therapy for intestinal failure. Outcomes have improved tremendously in the last decade. Our center has performed almost 500 intestinal inclusive transplants. Intestine-Colon may be the best nomenclature for better defining the current procedure.

Method: We describe all the patients who received IIT from 2013 to 2018 in our center. It represents our most recent Era with the evolution of surgical technique, immunosuppression regimen, graft monitoring and patient management. Immunosuppression consisted of induction with thymoglobulin and rituximab, maintenance with tacrolimus and mTOR inhibitor and use of basiliximab or vedolizumab for the first 3 months.

Results: 31 IIT were performed in 30 patients at our center. 13 were male. 11 of the recipients were pediatric. Recipient age went from 1 year old to 65 years old. Main indication for transplant was short gut. Positive crossmatch was found in 14% of the transplants. Moderate or severe rejection has happened in 32% of the patients. Only 1 patient underwent to enterectomy within 90 days due to rejection. One patient lost the graft due to volvulus. One patient had the graft removed during emergent surgery due to rupture of mycotic aneurism. Two patients developed PTLD. GVHD was not seen in this cohort. Chronic rejection or chronic graft dysfunction was not observed. Kaplan Meyer 5 year patient and graft survival for primary, non-renal transplants, was 92% and 77% respectively. 5 year patient survival including re-transplants and intestine-kidneys transplants is 87%. Patient survival 1 year remains 100% for all the patients.





Discussion: Survival of intestine-colon transplant has greatly improved over time. Historically, rejection was the main reason for graft and patient loss. In this cohort, only half of the graft losses were due to rejection. Mortality or graft loss due to causes unrelated directly to transplant was the majority in our experience. New immunosuppressive strategies have shown excellent results preventing rejection. Chronic rejection is a well-known long term complication for IIT, although no cases were seen up to date. 100% patient survival for the first year and 92% patient survival for 5 years surpasses all the data available not only for intestines but for all other organs. We believe we are entering a new era in intestinal transplant, with extremely high patient survival even when compared with other modalities of treatment for intestinal failure.

310.5 - Early Intestinal Barrier Dysfunction Early Post Intestinal Transplantation Is Driven by the Absence of Protective Type 3 Innate Lymphoid Cells and the Persistence of Proinflammatory Type 1 Innate Lymphoid Cells

Jiman Kang, Leonid Belyayev, Katrina Loh, Stuart Kaufman, Khalid Khan, Jason Hawksworth, Cal Matsumoto, Michael Zasloff, Thomas Fishbein, Alexander Kroemer

MedStar Georgetown Transplant Institute

Introduction: Innate lymphoid cells (ILCs), the most recently described family of lymphoid cells, play fundamental roles in mucosal barrier immunity, tissue homeostasis, and immune regulation through the activation of host-derived cytokine expression; however, their roles in intestinal transplantation (ITx) has yet to be defined.

Methods: Lamina propria cells were isolated and the following phenotypic definition was used for ILCs: lineage negative, viable lymphocytes expressing CD45 were identified as type 1 and 3 ILCs by expression of CD56, NKp44, CD117, and CD127. Four distinct subsets were further defined as NKp44-ILC1, NKp44-ILC3, NKp44+ILC1 and NKp44+ILC3.

Results: We compared ILC phenotypes via flow cytometry in stable ITx recipients with healthy functioning allografts >6 months after ITx to fresh ITx recipients at day 0 after reperfusion. Surprisingly, we found that protective NKp44+ILC3s (p=0.02) were significantly diminished in fresh allografts compared to NKp44+ILC3s in stable recipients 6 months out. In addition, we found comparable numbers of potentially proinflammatory ILC1s (NKp44-ILC1, NKp44+ILC1) and NKp44-ILC3 in both fresh and stable ITx recipients, indicating a dysbalance between protective and proinflammatory ILC subsets in fresh but not stable recipients. Intracellular cytokine staining confirmed that NKp44+ILC3 produced protective IL-22, while ILC1s and NKp44-ILC3 produced pro-inflammatory IFN-g, TNF-α, and IL-17. Importantly, serial prospective immunomonitoring of fresh ITx recipients revealed that protective NKp44+ILC3 repopulates by 1 month postoperatively, suggesting that protective and proinflammatory ILCs re-equilibrate in ITx patients over time. Critically, the frequencies of repopulating protective NKp44+ILC3 correlated positively with IL-22 dependent antimicrobial peptide (AMP) expression including β-defensins and RegIII$_\gamma$, which are important for intestinal barrier protection. In line with this, we further noted that there was a significant increase in the frequency of protective NKp44+ ILC3 in healthy ITx tissue compared to inflamed tissue 1 month after ITx.

Conclusion: Our study indicates that reconstitution of protective ILC3, which is absent immediately post transplant, positively correlates with improved epithelial barrier function through increase of IL-22 dependent AMP expression. In contrast, abundance of proinflammatory ILC1 and ILC3 may be contributing to epithelial barrier breakdown and early clinical complications.

310.6 - Risks Factors For The Development Of Graft-Versus-Host Disease (Gvhd) After Intestinal And Multivisceral Transplantation

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Medstar Georgetown Transplant Institute

Introduction: Graft versus host disease (GVHD) after intestinal and multivisceral transplantation occurs more frequently when compared to other solid organ transplants. This study reports the incidence, location and outcomes for GVHD patients after intestinal transplantation. Analysis was performed in order to establish risks factors in a high volume center

Methods: Medical records were reviewed from the entire intestinal transplant database from 2003 to 2018. The diagnoses of GVHD were based on clinical features, chimerism assays and pathologic specimens. For analysis, a $p< 0.05$ was considered to have statistical significance

Results: During this period, a total of 272 intestinal transplants were performed, with 23 patients (8.5%) being diagnosed with GVHD. The median time to onset was 79 days, with a 100% of cases diagnosed within the first year after transplant. Chimerism data was available for 18 patients and it was positive in 17 with a range of 2 – 98%. The skin was the most frequent affected organ. Immunosuppression was augmented in all cases. After univariate and multivariate analysis the main risks factors for the development of GVHD were retransplantation (p=0.005), multivisceral transplant (p=0.003) and colon-inclusive grafts (p=0.02). Donor thymoglobulin administration was not associated with GVHD risk reduction. Patient survival was severely affected by GVHD, with a one-year mortality of 39%, mainly due to infectious complications.

Conclusion: This study suggests a strong association between Multivisceral transplants as well as retransplants and, interestingly, colon inclusive-grafts with the development of GVHD. This might be in the context of an increased amount of donor-derived lymphoid tissue at the time of transplant. This information regarding immunological derived complications and GVHD - risks factors should be considered at the time of graft selection.

310.7 - Spleen preservation attenuates GVHD in multivisceral transplant recipients.

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Purpose: The immunological benefits of the spleen are well acknowledged, but splenectomy is often performed in recipients of multivisceral transplantation. Technical reason and the lack of room in the abdominal cavity are the key arguments to justify removal of the native spleen. We aimed to analyze the beneficial role of the spleen in MVTx recipients in a series of pediatric intestinal transplantation.

Patients and methods: A total of 103 IT (55MV, 25SB, 22CLSB, 3MMV) were performed in 84 patients (male-60%-, mean age 5.3yrs) between 1999 and 2018. Mean time on the waiting list was 272days waiting list mortality was 25%. Main indications for the transplant on the first instance were short bowel syndrome (69%), motility disorders(12%) and epithelial diseases(9.5%). For the present study we included only pediatric (<18 years) cases that underwent multivisceral transplantation. Patients were divided patients in three groups, native spleen preservation, native spleen removal and spleen graft inclusion. We analyzed survival, GVHD, hemolytic disorders.

Results: From the whole series, only 55 patients were included, all of them received a multivisceral graft. The spleen was included in the graft in 18.1% of patients, splenectomy was performed in 40%, in several of them after failed attempt of preservation; and native spleen was preserved in 41.8% Rejection in different forms was more frequent in patients who preserved the spleen, 4% presented humoral rejection, and acute cellular rejection was two times and chronic rejection four times more frequent compared with patients who underwent splenectomy. None of the patients with the spleen included in the graft presented humoral or chronic rejection, PTLD was also (1.8 times) more frequent in this group. The proportion of GVHD was significantly lower in the group of spleen preservation compared to splenectomy and graft spleen (RR 2.75, OR 3.33) ($p<0.05$). We also found a trend towards less hemolytic disorders in patients with spleen preservation.

Conclusion: Native spleen preservation demonstrated to attenuate the occurrence and severity of GVHD in pediatric MVTx recipients. This technique should be considered in all patients, although technical difficulties, prolonged ischemia of the graft and other factors can preclude the success of the procedure.

320.1 - Changes in gut microbiota and its metabolic activity in pediatric intestinal failure patients receiving long-term parenteral nutrition

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Introduction

Our aim was to characterize the gut microbiota and its metabolic activity in children with IF compared with healthy controls and to explore associations with clinical parameters.

Methods

Sixty-six serial fecal samples (median of 3 per patient) were collected from 15 IF patients (median age 4.3y) dependent on parenteral nutrition (PN) for a median of 3.6y. Single samples from 25 healthy controls were collected. Gut microbiota was characterized using 16S rRNA sequencing. Short-chain fatty acids (SCFA) were quantified with gas chromatography and D and L lactate using a modified enzymatic commercial essay.

Results

At the first sample, IF patients had lower concentration of total SCFA ($p=0.008$), propionic and butyric acid ($p<0.001$), and higher D and L lactate than controls ($p<0.001$). Total bacterial load (16S rRNA gene copies / g) was lower in patients ($p=0.003$). Their microbial community was characterized by a lower α-diversity (Shannon index, $p<0.001$), taxon richness (number of distinct species, Chao richness, $p=0.006$) and evenness (a metric of species distribution, $p<0.001$) than controls (Figure 1). The microbial community structure of IF patients was distinct from that of controls ($p=0.002$) and presented a higher degree of dispersion (inter-individual variation). Surgical IF patients had lower α-diversity ($p<0.001$) than functional IF patients. Duration of PN was negatively associated with Chao richness ($\beta=-0.29$, $p=0.04$) and the percentage of calories provided by PN (%PN) was negatively associated with Shannon index ($\beta=-0.33$, $p=0.02$) and Chao richness ($\beta=-0.34$, $p=0.02$). Enteral fibre intake (g / kg) was positively associated with Shannon diversity ($\beta=0.42$, $p<0.01$). Duration of PN and %PN explained 5.5% and 6.3% of the variation in microbial community structure ($p<0.01$). The relative abundance of 110 / 200 most abundant genera was significantly different between patients and controls. Patients had higher abundance of Enterobacteriaceae, Lactobacillaceae and Staphylococcaceae, and lower abundance of Bacteroidaceae and Bifidobacteriaceae.

Conclusion

The microbiota of pediatric IF patients is distinct to that of healthy controls with altered SCFA, lower bacterial diversity, loss of dominant microbial taxa and increased abundance of sub-dominant and potentially harmful species. Associations between microbial and PN associated characteristics offer the potential to use the gut microbiota as a biomarker to guide clinical practice during intestinal adaptation.

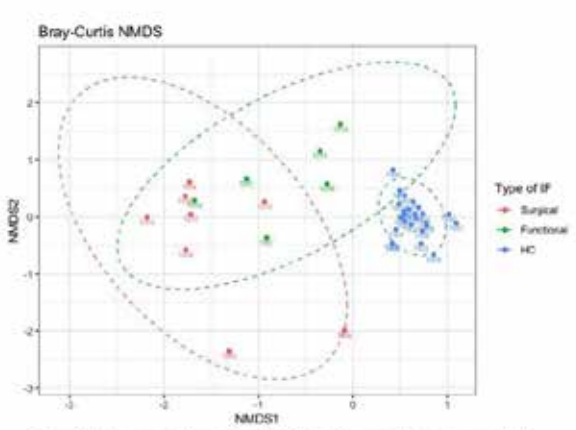

Figure 1. Non-metric multidimensional scaling (NMDS) of operational taxonomic unit (OTU) community structures for the first sample for surgical and functional intestinal failure (IF) patients and healthy controls (HC). Samples that are clustered closely together are considered to be more similar in terms of microbial species composition than samples that are more separated.

320.2 - Extending the indications of Intestinal transplantation. Cytoreduction and modified multivisceral transplantation for patients with end-stage pseudomyxoma peritoneii.

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Background: Pseudomyxoma peritoneii (PMP) arising from a low grade appendix tumour can be cured by cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. However, 40% of patients devolop residual or recurrent disease. The inevitable disease progression eventually results in nutritional failure from small bowel obstruction and often abdominal wall failure with fistulation. This leads to poor quality of life and is eventually fatal. Median life expectancy is 10 months in patients requiring parenteral nutrition. Radical cytoreduction and modified multi-visceral transplantation could benefit selected patients.

Methods: Between 2013-2018, 13 pmp patients underwent transplantation. Patients had previous surgery for PMP and further cytoreduction was not feasible due to extensive bowel involvement. Patients had complete or intermittent bowel obstruction with intestinal failure ± fistulation. 11 of the 13 patients were on parenteral nutrition and 2 patients had impending gut failure. 4 patients underwent radical debulking and 7 complete cytoreduction. 6 Patients had isolated intestinal transplant and 7 received modified multi-visceral grafts. Median operating time was 13hours.

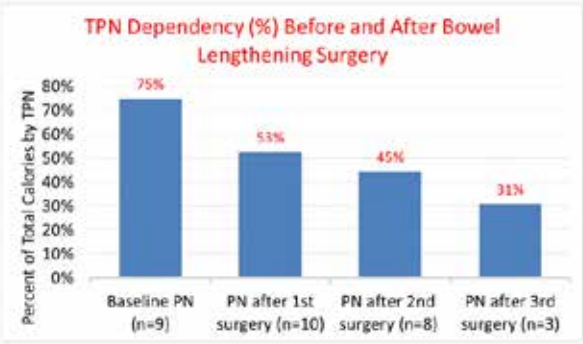
Results: Post-op stay on ITU average 4 days (range 1-45). Nine patients surviving at time of review (Follow up 1 month to 42 months following transplantation); 2 died (Day 26 and day 64) due to post operative complications, 1 due to GVHD at 5 months following transplantation and 1 due to recurrent pseudomyxoma at 40 months. Two patients had acute rejection and 1 patient had borderline rejection of intestinal graft treated with methylprednisolone. QOL data using EQ5D and SF36 showed significant improvements following transplantation with marked reduction in pain.

Conclusion: Cytoreductive surgery followed by modified multi-visceral transplantation is technically feasible for end stage PMP. It could potentially extend life giving independence from TPN with an excellent QOL. Our recommendation is to undertake the procedure in patients with low grade disease where complete cytoreduction is likely to be feasible and with impending or established intestinal failure.

320.3 - Ultra-Short Bowel Syndrome (USBS) – Does the lengthening procedures improve the outcomes? Intestinal Rehabilitation Program (IRP) Children's National Medical Center (CNMC) Washington DC - USA

Clarivet Torres, Vahe Badalyan, Parvathi Mohan, Anthony Sandler

Children's National Medical Center-USA



To evaluate the outcomes of the USBS with < 10 cm or < 10% of the expected bowel length for gestational age enrolled in the IRP at CNMC. 24 USBS patients, who had at least 2 years follow-up over the past 10 years, were included. Outcomes involved death, transplant, time to normalized conjugated bilirubin (CB) and parenteral nutrition (PN) requirement. Platelets, albumin, CB, weight and height Z score were obtained at entrance and end of the study. At entrance, median age was 3 months, mean bowel length 15 cm; 6 had IC valve, 9 had < ½ of colon. Median PN need was 100%. 21 of 24 had liver disease, 19 had a mean CB of 7.5 mg/dl, (liver biopsy in 13/21 showed fibrosis, stage 3-4 in 8). 18/19 (95%) patients with cholestasis normalized their CB with treatment over a median time of 11 weeks. Fourteen patients had 23 lengthening procedures (LP) at CNMC with no complications. 12 had the 1st LP at CNMC; 7 Bianchi; 4 STEP and 1 Bianchi & Step. Median age at 1st LP was 21 months. 8 had a 2nd STEP and 3 had a 3rd STEP (1 had 2 prior STEP in other institution). 2/14 patients with LP were transplanted and 3 weaned off PN (one each after the 1st, 2nd and 3rd LP). The mean PN needs decreased in the non-transplant patients from 75% prior to 1st LP to 50% and to 44% after the 2nd STEP. In 3 patients who had 3rd STEP the PN decreased from 68% to 31%. Of the 24 patients, one is lost to follow up, 7 were considered candidates for a liver- small bowel transplant; 2 declined to be listed (one is now off PN and the 2nd have decreased the PN needs by 35%). Five were listed, 3 were transplanted, one weaned off PN without transplant and one was unlisted, his PN decreased from 100% to 33%. Three patients died (single ventricle, genetic syndrome and post-transplant). Of the remaining 18; 8 (44.4%) weaned off their PN and 10 have decreased their PN needs from a median of 100% to 26%. Laboratory parameters and growth significantly improved. Overall survivability is 87.5% and among those who were not transplanted is 90.5%.

Children with USBS can improve their liver functions and nutritional parameters with the ability to decrease or wean off their PN with careful medical/surgical approach. Intestinal lengthening procedures help them to improve their enteral nutrition. The IRP has enabled these patients to approach school age and have normal growth. Although 87.5% of the cohort has IFALD, 96 % of them resolved their cholestasis. Survivability rate is excellent.

320.4 - Use of Arterial Embolisation to Facilitate Exenteration during Multi-visceral and Intestinal Transplantation

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Introduction: Exenteration during multi-visceral and intestinal transplantation is associated with significant blood loss that increases patient instability intra-operatively and may affect the subsequent post-operative course. This is particularly the case for multi-visceral transplantation (MVT) for porto-mesenteric thrombosis (PMVT).

Methods: Embolisation was undertaken in theatre following anaesthesia and placement of lines. Amplatzer arterial plugs (St Jude), either type I (8mm in length) or type II (16–24 mm) were utilised. In the case of full MVT, the plugs occluded both coeliac axis (CA) and superior mesenteric arteries (SMA). In circumstances where the stomach was retained the SMA, hepatic and splenic arteries were occluded and the left gastric artery preserved.

Results: Pre-operative embolisation was performed in 13 patients who have had either MVT, liver/small bowel transplant (LSB), or small bowel/ pancreas/colon transplant (SBP). Nine of the 13 cases were embolised for severe portal hypertension (PHT). We have compared blood loss and use of blood products in this group to a historical cohort of intestine containing transplants in patients with severe PHT (table 1).

Blood loss and products

	Embolised = 9 Median (range)	Non-embolised= 22 Median (range)	P value
Blood loss (ml)	8000 (1395 – 27400)	15400 (4700 – 66000)	p = 0.04
RBCs (units)	6 (0 - 32)	18 (4 - 82)	p = 0.02
FFP (units)	4 (0 – 26)	11 (4 – 26)	p = 0.03
Platelets (units)	0 (0 – 6)	4 (0 – 11)	p = 0.04
Cryopercipitate (units)	0 (0 – 10)	4 (0 – 20)	p = 0.16
Reperfusion lactate (mmol/L)	4.3 (1.9 – 11.0)	7.1 (2.6 – 10.7)	p = 0.11

By performing embolisation in the operating theatre there was minimal delay in the explant procedure and no increase in the cold ischaemic time. There was a reduction in intra-operative blood loss, blood products and metabolic instability. One patient undergoing a full MVT for PMVT required no blood products intra-operatively. There were no complications associated with the embolisation procedure.

Conclusion: We believe that arterial embolisation is a very useful technique to minimize the blood loss associated with severe PHT during intestine containing transplantation. It reduces blood loss, blood products and metabolic instability. The use of arterial plugs substantially reduces the time required for embolisation and the selective occlusion of visceral arterial branches allows for the preservation of the stomach.

320.5 - The colon as an energy salvage organ for children with short bowel syndrome

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[1] *Hopital Necker-Enfants Malades*
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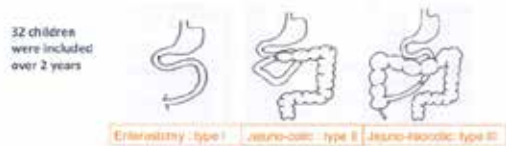
Introduction: Short bowel syndrome is the main cause of intestinal failure.The role of the colon as an energy salvage organ has been demonstrated in adult patients but not in children. The aim of this study was to measure the absorption rate in children with SBS using stool balance analysis and to correlate the anatomical SBS type to absorption rate, citrulline plasma level and small bowel length.

Methods: This was a retrospective study over a two years period. All the children older than 1 year with neonatal SBS and PN dependency who underwent a stool balance analysis in our center were included. Children were divided into three groups according to the anatomical type of SBS (ESPEN classification). The level of PN dependency was estimated using the PN / REE index (PN energy intake on resting energy expenditure calculated using Schofield equation). Citrulline plasma levels were measured. Intestinal absorption rate was assessed using the stool balance analysis. Anatomical types of SBS were compared with bowel length, citrulline levels and intestinal absorption rate by analysis of variance. A predicted average percentage of absorption per SBS type, adjusted for relative bowel length was calculated.

Results:



	6 Hirschsprung's disease 2 gastroschisis 1 NEC	5 gastroschisis 4 volvulus 3 NEC 1 atresia	7 volvulus 2 NEC 1 Atresia	p
Bowel length, cm (IQR)	60 (41)	28 (17)	15 (34)	0.004
Absorption rate, % (IQR)	68 (23)	60 (37)	67 (33)	0.449
Citrulline plasma levels, mcmol/l (IQR)	15 (18)	14 (15)	9 (9)	0.141

Patients with an intact colon (type 3) had a significantly shorter remnant bowel (p=0.04). Citrulline plasma levels were lower in SBS type 3 patients but not significantly different (p=0.141). Total energy absorption rate did not differ significantly between the three groups. PN dependency index (PN intake / REE) was104% + / - 26%. For the same SB length, absorption rate was 40% in SBS type 1, 70% in SBS type 2, 80% in type 3.

Conclusion: Children with SBS and a remnant colon showed similar absorption rate than children with type 1 SBS although they had significantly lower small bowel length. Citrulline levels did not show a significant correlation with total absorption rate which strengthened the hypothesis that a part of the absorption rate is due to the colon. The citrulline is a strong marker of enterocyte mass but not of colonic mass. This study confirms the role of the colon in energy salvage in children with SBS. Plasma citrulline levels should be interpreted according to the type of SBS – the remnant colon. Efforts should focus on conservative surgery and early restoration of a colon in continuity.

320.6 - Potential biomarkers to guide immunosuppression management in intestinal transplant recipients

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Background: Balancing immunosuppression to control rejection and prevent infection is critical to optimize patient and graft survivals after intestinal transplantation (ITx). We previously demonstrated that ≥4% peak donor T-cell chimerism in blood (macrochimerism) is associated with reduced graft rejection, DSA development and slower recipient T cell repopulation in the graft. We hypothesize that the absence of blood macrochimerism and faster recipient T-cell replacement in the graft may be used as biomarkers to predict impending rejection.

Methods: Serial surveillance intestinal biopsies were performed at regular intervals following transplant. T-cell chimerism was assessed from peripheral blood and ileal graft tissue with multicolor flow cytometry using donor- and recipient-specific HLA antibodies.

Result: 11 multivisceral transplant (MVTx), 1 liver-intestine transplant (LITx) and 9 isolated ITX (iITx) recipients were included. Patients and grafts were ABO compatible and randomly paired for HLA without crossmatch. Patients received immunosuppression induction with antithymocyte globulin and steroids, followed by lifelong tacrolimus-based maintenance therapy. One and three-year patient survival was 90.5% and 74%, respectively. T-cell macrochimerism developed in 14 recipients, peaked within 48 days and persisted for as long as 378 days (median 150 days). Patients with macrochimerism had a significantly greater moderate to severe rejection-free survival (p=0.001) and overall graft survival (p=0.016). Macrochimerism was detected more commonly in MVTx recipients (10 / 11 MVTx, 0 / 1 LITx and 4 / 9 iITx), and was associated with reduced de novo Class I (p=0.0003) and II (p=0.0038) DSA development (Fig. 1). Early postoperative recipient T-cell replacement ≥5% in the lamina propria of the ileal graft was associated with subsequent rejection (p=0.00047) in patients without macrochimerism (Fig. 2) and remained elevated following resolution of rejection. When macrochimerism is present and the donor is greater than 1 year of age, early recipient replacement of lamina propria T cells ≥5% may indicate imminent rejection. In donors less than 1 year of age however, rapid recipient replacement of the graft mucosa cell population is frequently seen without rejection.

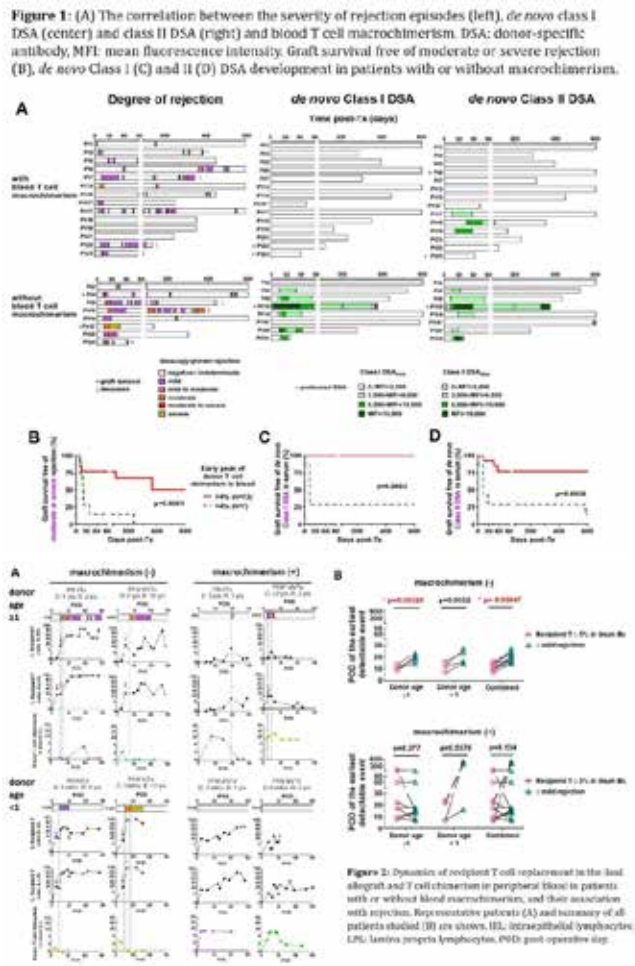

Figure 1: (A) The correlation between the severity of rejection episodes (left), *de novo* class I DSA (center) and class II DSA (right) and blood T cell macrochimerism. DSA: donor-specific antibody, MFI: mean fluorescence intensity. Graft survival free of moderate or severe rejection (B), *de novo* Class I (C) and II (D) DSA development in patients with or without macrochimerism.

Figure 2: Dynamics of recipient T cell replacement in the ileal allograft and T cell chimerism in peripheral blood in patients with or without blood macrochimerism, and their association with rejection. Representative patients (A) and summary of all patients studied (B) are shown. IEL: intraepithelial lymphocytes; LPL: lamina propria lymphocytes; POD: post-operative day.

Conclusions: Peripheral T-cell macrochimerism and early recipient T-cell replacement in the graft could serve as potential biomarkers for guiding personalized immunosuppression in intestinal transplant patients.

320.7 - Is there a life after surgery for acute mesenteric ischemia? A retrospective study of 184 survivors

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Introduction: Although intestinal failure (IF) patients cared in expert centers have good long-term outcomes, acute mesenteric ischemia (AMI) is known as an independent risk factor of an impaired prognosis and is still considered a hopeless condition by many physicians. The aim of this study was to investigate the long-term outcomes of survivors from bowel resection for AMI.

Methods: Retrospective cohort study of consecutive patients referred to a tertiary care IF unit from 2006 and 2015 after bowel resection for AMI. Patients with ongoing or non-surgical AMI were not included. Cox regression analyses assessed predictors of parenteral support (PS) independence and AMI recurrence. Results are shown as Hazard Ratios (HR) and 95% Confidence Interval (CI).

Results: We included 184 patients (median age 51) referred to our unit median 3 months after surgery for AMI. Upon diagnosis, AMI was the first ever reported cardiovascular event in 53% of patients and lactate plasma levels were within normal range in 49%. Early-stage AMI was misdiagnosed (median diagnosis delay: 2 days) and under-treated (revascularization rates: 15%) resulting in bowel resection and IF in all patients. After multidisciplinary (i.e.nutritional, vascular and digestive) rehabilitation, 3-year survival probability was 86%, with no AMI recurrence in 94%, no stoma in 70% and no PS dependence in 47% of patients. In multivariate analysis, initial revascularization [HR=2.4; 95%CI=1.1-5.2; p=0.02], remnant bowel length > 50cm [51-150cm: HR=3.8; 95%CI=1.8-8.0; >150cm: HR=9.7; 95%CI=3.9-23.8; p<0.001] and restoration of bowel continuity [HR=4.7; 95%CI=2.0-11.4; p=0.001] were predictors of long-term PS independence (Figure 1). We observed 11 cases (6%) of AMI recurrences median 11.4 months after the primary AMI episode. The probability of AMI recurrence was 3% in patients without persistent mesenteric ischemia (MI) and rose to 7% in patients with persistent MI treated by revascularization (unadjusted p=0.15) and 48% in patients with persistent MI left untreated by revascularization [adjusted p<0.001, HR=14.1 95%CI=3.9-51.7)] (Figure 2).

Conclusion: Surgical AMI patients initially presented at an early, potentially reversible but misdiagnosed and under-treated stage. Expert multidisciplinary rehabilitation, however, allowed high PS-free long-term survival. The utmost attention should be given to timely recognition, revascularization and expert care at both the acute and rehabilitation stages of AMI.

Figure 1. Parenteral support dependence probability (Kaplan-Meier curves) according to restoration of bowel continuity.

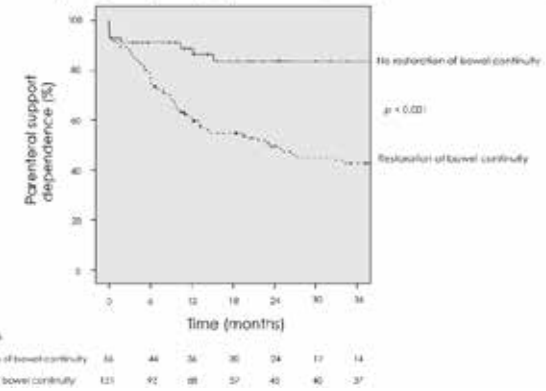
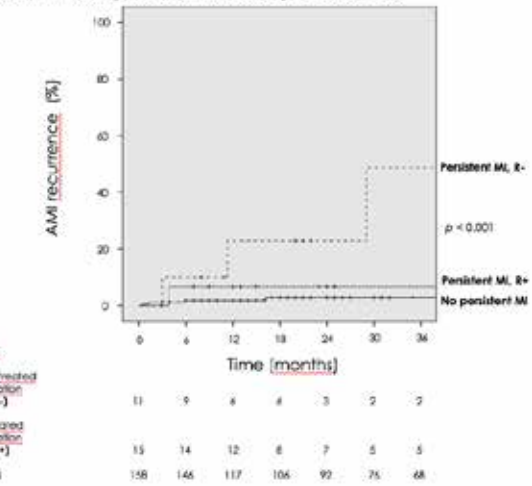


Figure 2. Probability of acute mesenteric ischemia recurrence according to the persistence of mesenteric ischemia and subsequent revascularization (Kaplan-Meier curves).



320.8 - Identification of biomarkers for risk, diagnosis, and prognosis of GVHD after bowel transplantation and central role of graft resident memory T cells in pathogenesis

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Introduction: Graft-versus-host disease (GVHD) is a relatively common and highly morbid complication after intestinal transplantation. Its pathophysiology remains poorly understood. Resident memory T cells (TRM) are a newly described T cell subset with memory phenotype localizing to peripheral tissue. We hypothesized that the pathophysiology of GVHD might be related to increased donor TRM in the graft that subsequently migrate into host blood and tissue.

Methods: Intestinal transplantation from deceased donors was performed using our standard method. Graft and blood lymphocytes from 10 patients with GVHD and 34 without were longitudinally analyzed using flow cytometry.

Results: Levels of CD4 and CD8 TRM were approximately 20% higher in the grafts of GVHD vs. stable patients prior to implantation and significantly higher at the time of GVHD (p = 0.02 and 0.04). There was also a mean 60.3% higher level of CD8 TRM in the native bowels of GVHD patients compared to controls and 20-30% higher levels of IFN-γ and TNF-α expression in both the grafts and native bowels of GVHD patients. The percentage of CD4 and CD8 TRM in the blood of GVHD vs. stable patients significantly increased during GVHD (p = 0.005), and expression of HLA-DR, CD57, and PD-1 was significantly higher. There were also significant increases in CD8 effector memory cells (p = 0.0056) and decreases in naïve cells (p = 0.0034). Notably, CD8 / PD-1 was also significantly elevated prior to transplantation in patients who later had GVHD (p = 0.025), and a pre-transplant CD8 / PD1 level >45% was an absolute predictor of later GVHD. Moreover, we found significantly higher percentages of HLA-DR, CD57, and PD-1 in patients with GVHD who died vs. those who survived, and values that always correlated with mortality were CD8 / CD57 > 35%, CD4 / HLA-DR > 15%, CD8 / HLA-DR > 45%, and CD4 / PD1 > 35%.

Conclusion: In the largest longitudinal analysis to date, we demonstrate that increased TRM percentage and inflammatory cytokine expression in graft bowel correspond with increased TRM in blood and native bowel as well as increased cytokine expression in native bowel at time of GVHD. Thus GVHD pathogenesis may depend on donor TRM in graft bowel migrating to the blood and native tissue of recipients. Recipients with higher PD-1 expression, indicating T cell exhaustion, might be more vulnerable, providing a possible biomarker for GVHD risk, while increased expression of maturity and activation markers correlate with prognosis.

320.9 - The Double-Barrel Enteroplasty: A Novel Intestinal Lengthening Procedure for Short Bowel Syndrome

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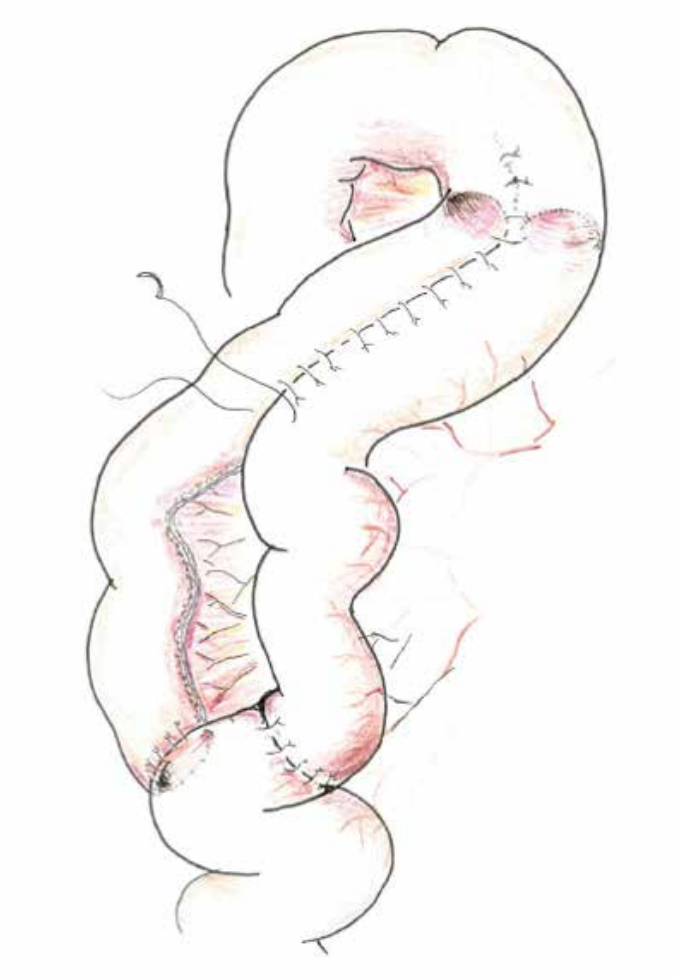
Advances in the management of Short bowel syndrome (SBS) has resulted in children with shorter lengths of small bowel coming off TPN and achieving enteral autonomy. Although existing bowel lengthening procedures such as the Bianchi Longitudinal Intestinal Lengthening and Tailoring (LILT) procedure and Serial Transverse Enteroplasty (STEP) have enjoyed moderated degrees of success, they have not been without complications and better alternatives are still being sought after. We present our experience with a novel bowel-lengthening procedure for SBS termed the double-barrel enteroplasty (DBE) that is simpler to perform, is less disruptive to anatomy and has the potential to achieve similar to superior results to existing bowel lengthening procedures.

Methods: Ten patients have undergone the DBE at the Children's Hospital at Westmead between January 2011 and November 2018. Baseline characteristics, complications, time to TPN weaning and growth parameters were recorded prospectively.

Results: The mean age at operation was 21 months (range 4-41 months). Mean pre-operative small bowel length was 74.6cm (36-167cm) with a mean length of 35.6cm (17-60cm) undergoing enteroplasty. Mortality and progression to transplantation remains zero. Six patients have achieved complete enteral autonomy within 2.8 months (0.5-5 months). The most recent patients are still weaning TPN. All patients have normalising growth parameters. One patient required an extension of the DBE for on-going proximal dilatation.

Discussion: The DBE is a safe, effective and potentially superior alternative to existing bowel lengthening procedures for SBS. Advantages include its simplicity to perform, less disruption of bowel and mesentery, less anastomoses, decreased possibility of stenosed segments and maintenance of neuromuscular integrity.



320.10 - "Stoma or no stoma that is the question": a single-center experience of intestinal transplantation without stoma

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Introduction: Our recent data suggests that protocol-driven, routine surveillance endoscopy and biopsy in the absence of clinical features of allograft dysfunction, does not appear to confer any survival advantage to patients and grafts. This observation called into question the necessity of stoma creation in all intestinal transplant (ITX) recipients. At our center, our practice evolved to ITX without stoma (ITX-NS) since 2015 initially in carefully selected patients. We report our preliminary clinical outcomes of ITX-NS.

Methods: Data analysis was limited to adult ITX without liver allograft between 2015 and 2018. There were 34 ITX which were divided into "Control group (with conventional stoma for surveillance)", n=18 grafts in 16 patients and "Study group (ITX-NS)", n=16 grafts in 15 patients. We compared clinical outcomes such as graft / patient survival, episode of acute rejection (ACR), frequency of endoscopic evaluation, initiation of enteral nutrition and duration of parenteral nutrition after ITX, body weight change, usage of anti-diarrheal medicines and renal function between the 2 groups.

Results: Clinical outcome was similar between the 2 groups as table 1. Dose of anti-diarrheal medicines at 30 days after ITX was significantly (p=0.034) lower in the study group. Fifty-six percent of patients in the control group needed maximal dose to control amount and consistency of stoma output. Whereas, 19% of study group needed maximal dose and 38% did not need any anti-diarrheal medicine.

Table 1. Comparison of clinical outcome between the 2 groups

	Control group (n=18 grafts)	Study group (n=16 grafts)	p
Patient survival (%)			0.380
• 1 year	100	86	
• 3 year	88	86	
Graft survival (%)			0.336
• 1 year	88	68	
• 3 year	79	68	
Episode of ACR	6 (33%)	4 (25%)	0.595
Frequency of endoscopic evaluation (median)	2.5 times	1.5 times	0.686
Start day of enteral feeding after ITX (mean)	8	11	0.159
Last day of parenteral nutrition after ITX (mean)	24	25	0.796
Body weight (kg, mean)			
• At ITX	58	66	
• 6 months after ITX	66	67	
• 1 year after ITX	72	78	
Serum creatinine (mg/dL, mean)			
• At ITX	1.0	0.8	
• 30 days after ITX	1.3	0.8	
• 6 months after ITX	1.6	1.1	
• 1 year after ITX	1.9	1.1	

Conclusion: ITX-NS appears to be a safe practice model without obvious adverse impact on outcome compared to standard intestinal transplantation with stoma for the purpose of surveillance endoscopy and biopsy. There is theoretical benefit such as better fluid and electrolyte balance, sparing renal function, better abdominal wound care and patient satisfaction. As of now our center's policy is not to create stoma after ITX except in patients deemed to be at high risk to develop ACR (loop ileostomy) or in patients who do not have distal colon for anastomosis (creating end colostomy). Longer-term follow up with more cases will help confirm safety and benefit of such an approach.

350.5 - Acute Rejection Following Intestinal Transplantation in a Cohort of 442 Transplants Performed Over Nearly 25 Years: The University of Miami Experience

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Background: Intestinal transplantation has emerged as a viable therapy for irreversible intestinal failure. Rejection continues to challenge the long-term patient and graft survival. Recently, the incidence of acute rejection has been reduced to 30-40% due to the use of potent immunosuppressive protocols. Herein, we demonstrate the experience of our center in regards to the incidence of acute cellular rejection after intestinal transplantation over almost 25-years.

Methods: Retrospective analysis of 442 intestinal transplants from 1994-2018 with diving the recipients into 5groups depending on the induction immunosuppression used;group1(44 / 442):high dose steroid(34 / 44),OKT3(7 / 44),orcyclophosphamide(3 / 44);group2:anti-CD25(159 / 442);group3:alemtuzumab(113 / 442);group4:rabbit antithymocyte globulin(rATG)(34 / 442);group5:rATG / rituximab. Types of intestinal transplant included: isolated intestine(I)(n=124), liver-intestine(LI)(n=38), modified multivisceral(MMV)(n=39), and full multivisceral(MV)(n=241) allografts.

Results: The incidence rate of acute rejection of any grade over the first 60 post-transplant months was 59%(262 / 442). Actuarial estimates of acute rejection free survival at 1,3,6,12,24,60months were 33%,21%,21%,17%,11% and 11% in group1; 53%,42%,37%,35%,29% and 25% in group2; 76%,51%,44%,38%,30% and 23% in group3; 53%,50%,50%,50%,44% and 33% in group4; 85%,69%,68%,61%,58% and 58% in group5, respectively. Factors associated with a decreased risk of acute rejection were recipients in group5(rATG + rituximab) followed by recipients who received MV or MMV allografts then recipients who received alemtuzumab induction(P<0.000001). In group5,rATG / rituximab seemed to be associated with a low risk of developing acute rejection whether during or beyond the first post-transplant month(P<0.000001). Overall incidence of acute severe rejection was 20.6%(91 / 442). Within each induction immunosuppressive group, the incidence rate of acute severe rejection among recipients who developed acute rejection was 7.6% in group5, 29.4% in group4, 16.8% in group3, 19.5% in group2 and 27% in group1. Overall incidence rates of graft loss during the 1st60 post-transplant months were 13% and 12.2% in recipients who developed acute rejection, respectively. Overall incidence rate of chronic rejection was 1.6%(7 / 442).

Conclusion: rATG / rituximab induction immunosuppression protocol demonstrated a low hazard rate of developing acute rejection even after the 1st month.

350.6 - The impact of circulating DSA in visceral transplant recipients without histological evidence of rejection: How should we treat or not treat?

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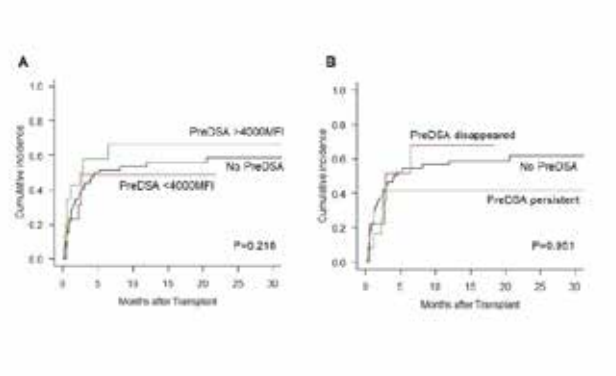
Backgrounds: There has been accumulating evidence that donor-specific antibody (DSA) has a negative impact on the outcome of visceral allografts. Prospective DSA monitoring allows detection of circulating DSA without histological evidence of acute rejection. However, its association with acute rejection and natural course without treatment are yet to be determined.

Methods: Between 2012 and 2019, 94 visceral transplantation with 25 liver-contained grafts were performed at a single institution. Induction therapy for preformed DSA included rituximab or bortezomib. DSA were monitored at 1 and 2weeks, followed by 1, 3, and 6 months, and yearly after transplant. De-novo DSA was not treated without histologically proved rejection. The characteristics and impact of DSA in terms of predictability of rejection, and its correlation of severity of acute rejection were analyzed.

Results: One-year cumulative rejection rate in the entire cohort was 67%. With the protocol of anti-B cell therapy, preformed DSA did not increase the risk of rejection, regardless of the status of liver-free allografts, high titer (>4000 MFI) or persistence of DSA.



Moreover, there was no difference in severity of rejection with the presence of preformed DSA (n=12) compared to that without DSA (n=36). However, 3-years graft survival was inferior in patients with preformed DSA to those without (52% vs. 64%, p=0.069), due to increased infectious complications.

De-novo DSA was detected in 32 patients (35%) with an HLA-ABDR mismatch as the only predictor (Odds ratio 1.7, p=0.036). De-novo DSAs were more likely to be class II with high inclusion of anti-DQ DSA (69%). Prospective monitoring detected de-novo DSA in 25 occasions without ongoing rejection. Accordingly, it turned negative without rejection episode in 19 (76%) (Silent DSA), while subsequent rejection occurred in 6 occasions (24%) (DSA before rejection). In 10 occasions, de-novo DSA turned positive during the rejection episodes (DSA during rejection). The rejection episodes that induced DSA circulation was with a more severe grade.

		De-novo DSA turned positive		
		without rejection	before rejection	during rejection
		n= 19	n= 6	n= 10
DSA				
Duration of detection, months		1 [1 -48]	3 [1 -18]	1 [1 -6]
Number of DSA in a patient		1 [1 -4]	2 [1 -4]	1 [1 -5]
Class (%)	I	4 (21.1)	0 (0.0)	2 (20.0)
	II	13 (68.4)	5 (83.3)	7 (70.0)
	Both I / II	2 (10.5)	1 (16.7)	1 (10.0)
Anti-DQ (%)		11 (57.9)	5 (83.3)	8 (80.0)
ACR				
Duration, days		NA	4.7 ± 5.7	10.4 ± 11.3
Grade (%)	mild	NA	5 (83.3)	3 (30.0)
	moderate	NA	0 (0.0)	2 (20.0)
	severe	NA	1 (16.7)	5 (50.0)
Led to graft loss (%)		NA	0 (0.0)	1 (10.0)

DSA, donor specific antibodies, ACR, acute cellular rejection
() indicates percentage, [] indicates range.

Conclusions: Increased immunosuppressant induction to treat preformed DSA may compensate the rejection risk, but can negatively impact the overall graft survival. With prospective monitoring and no preemptive treatment, high proportion of de-novo DSA was self-limiting, and rarely precipitated rejection episodes particularly with a severe grade.

350.7 - Post-Transplant Proliferative Disorder Following Intestine Transplantation: Contemporary Single Center Experience

Jason Hawksworth, Asha Zimmerman, Alexander Kroemer, Pejman Radkani, Juan Guerra, Khalid Khan, Nada Yazigi, Stuart Kaufman, Sukanya Subramanian, Hannah Sagedy, Thomas Fishbein, Cal Matsumoto

MedStar Georgetown Transplant Institute

Objectives: The purpose of this study was to examine the characteristics and risk factors for post-transplant PTLD in the intestinal transplant population.

Methods: Retrospective review of intestinal transplant recipients between 11/2003 and 11/2017 at a single-center academic institution. Demographic, immunologic characteristics, treatment, graft survival and patient survival were compared between those who developed PTLD and those who did not.

Results: Of the 234 patients who underwent intestinal transplant, 21 (9%) experienced an episode of PTLD. There was no significant difference between the two groups with regards to age, sex, initial disease type, EBV High risk status, donor characteristics, or prior episodes of acute rejection. Those with PTLD were more likely to have received Thymoglobulin induction compared with controls (54% vs 26%, p = 0.005) and a multivisceral transplant including a liver (20% vs 3 %, p = 0.024). The most common presenting signs and symptoms were EBV viremia (89%), lymphadenopathy (57%), and fever (38%). Fifty-seven percent of patients had graft involvement. PTLD was fatal in 29% (6/21) of cases and required explant in 14% (3/21). When comparing those who died from PTLD and those who survived, there was no difference in age, Ki-67, CD20 positivity, type of PTLD, rates of CNS or BM involvement, or treatment type. Patient and graft survival at 5 years was lower in those with PTLD compared to those without (50% vs 70%, p = 0.044 and 45% vs 67%, p = 0.019, respectively).

Conclusions: While the incidence of PTLD has improved in the contemporary period, our experience shows that induction immunosuppression with thymoglobulin is associated with PTLD. Additionally, patients with PTLD had worse graft and overall survival than those who did not.

360.5 - Successul implementation of remote consultation for patients recceiving home parenteral nutrition

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Introduction: Our national Intestinal Failure Unit provides care for patients from across the UK and beyond. Type 3 IF patients are routinely reviewed at 3-6 month intervals. Between Mar 2007-2017 there was a 90% increase in type 3 patients attending our outpatient. Coping with the increasing demand whilst maintaining outpatient capacity and standards is a key component of IF care. Telemedicine provides a strategy for achieving this.

Methods: QI methodology was used to implement and evaluate remote video consultations. Implementation began Dec 2015 via patient consultation and small tests of change. Clinical data were obtained from a prospectively maintained database forming part of ESPEN audit standards. A face to face discussion via the internet using the video call service Skype. An anonymous qualitative satisfaction questionnaire was subsequently completed.

Results: During the study period, patients receiving HPN rose by 13.7% to 285. Twenty-one patients used telemedicine service, totaling 55 contacts. Mean potential distance traveled by telemedicine cohort was 118.6 miles (10-441.8), mean cumulative miles saved was 8600 miles. Twelve patients used the service on multiple occasions. Seventy percent of patients rated their satisfaction with the system at ≥90%, with the mean satisfaction of 83%. The mean duration between outpatient appointment offered reduced from 103.7 days to 100.4 days in 2017. One patient had a CRBSI following commencement of telemedicine. 9.5% of the telemedicine cohort were admitted with an HPN complication, compared to an admission rate of 23.5% for the whole HPN cohort.

Conclusions: Telemedicine can release some HPN clinic capacity and help reduce the increasing pressure for patient access to HPN services. Whilst maintaining compliance with NICE and ESPEN guidance, patient satisfaction and patient safety

360.6 - Long term results of a series of pediatric patients with short bowel syndrome treated at an Intestinal Failure, Rehabilitation and Transplant Program

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Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina

Introduction: Patients (pts) with short bowel syndrome (SBS) have high morbidity and mortality mainly related to their residual intestinal anatomy / function and clinical status. Better outcomes are achieved when this condition is managed at a comprehensive multidisciplinary unit.

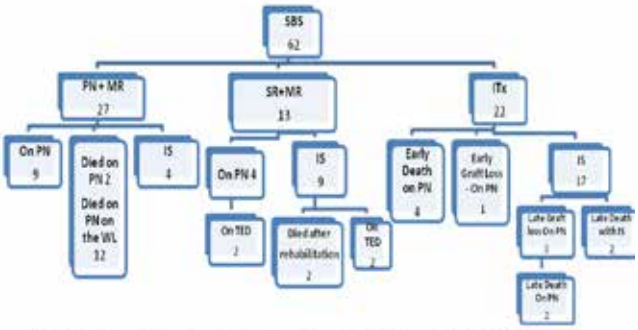
Aim: To analyze long-term results and chances of achieving Intestinal Sufficiency (IS) of all children with SBS referred to a comprehensive Intestinal Failure, Rehabilitation and Transplant Unit from 3 / 2006 to 12 / 2018

Material and methods: This is a retrospective review of a prospectively filled database, including pediatric pts with SBS .Demographic data, diagnosis, nutritional status, parenteral nutrition (PN) support, as % of the basal metabolic rate (no protein Kcal), intestinal anatomy type (1 -terminal jejunostomy-; 2 -jejuno colonic anastomosis; 3 -jejuno-ileo colonic anastomosis; subtypes by length: A< 40 cm and B > 40 cm; treatment implemented [Groups: PN+MR (PN + Medical Rehabilitation); SR+MR (Surgical + Medical Rehabilitation) and ITx (Intestinal Transplantation)]. were analyzed on SPSS.

Results: 62 pts with SBS out of 102 pts with chronic intestinal failure admitted in our program, were analyzed. 41 were male, 25 premature, 48 with neonatal SBS. Etiology of SBS included: gastroschisis (15), intestinal atresia (11), Hirschprung (10), NEC (10), post natal volvulus (7) and perinatal volvulus (4).

Pts´ anatomy type, PN at referral, initial and last follow-up visit nutritional status, are shown in Table 1. Median (IQR) time on PN before referral 0.62 (0.25-2.2) years. Figure 1 shows treatment implemented and outcomes. In the long term 30 (48.4%) pts were able to achieve IS; 25 % of the pts of the PN+MR group, Median IQR 1.2 (1-2.4) years since PN initiation (sPNi); 69% of the SR+MR group Median (IQR) 5.3 (1.4-8.9) years sPNi; and 76% of the ITx group (Median (IQR): 7 (2.5-10.8) sPNi, (PN+MR vs SR+MR and ITx: p= 0.004). From the ITx group, 5 pts failed in the long-term, re-starting PN, 2 died. Other 2 ITx pts died with IS. The overall 1, 5 and 10-year survival sPNi: 97%, 65.4% and 61.2% respectively, independently of the treatment implemented.

Figure 1. Treatment implemented and outcomes



PN= parenteral nutrition, MR= medical rehabilitation, SR = surgical rehabilitation, ITx= Intestinal transplantation, IS intestinal sufficiency, TED= teduglutide

Table 1. Patient's anatomy type, PN at referral, initial and last follow-up visit nutritional status

Age (days)	Anatomy type	PN support*	N° PN infusions/ Week **	BMI/age Z score First Visit**	Height/age Z score First Visit**	BMI/age Z score Last FU**	Height/age Z score Last FU**
389 (190-1522)	1 29% 2a 3% 2b 53% 3b 15%	108% (92-138)	6.7 (0.64)	-1.3 (-2.6;-0.2) # 42% < -2	-2.3 (-4.3;-1.2) ## 60% < - 2	-0.53 (-1.28;0.28) # 12% < -2	-1.68 (-2,59; -0.75) ## 36% < -2

* Mean (SD) ** Median (IQR), FU: follow-up
# p 0.009, ## p 0.119 Mann Whitney

Conclusions: Although IS could be achieved under each line of therapy group, SR+MR allowed higher rate of IS with long term maintenance; ITx had higher chances of achieving IS, but there is drop out in the long term. Long-term survival of pts with SBS can be achieved when they are managed under a comprehensive program.

360.7 - Ex vivo tumor resection and intestinal autotransplantation – a single center 10-year experience

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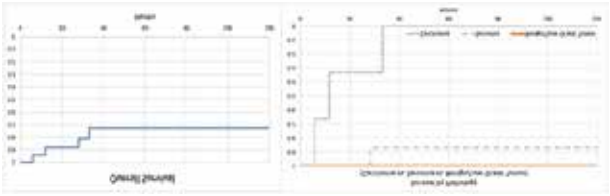
Columbia University Irving Medical Center, New York, United States

Introduction: Ex vivo surgery – explant organs en bloc, resect and reconstruct outside of the body in the cold preservation, and reimplant unaffected parts of organs - may improve a chance at complete (R0) resection for conventionally unresectable tumors. For the tumors involving superior mesenteric vasculature, patients typically present with persistent abdominal pain and sometimes intestinal / biliary obstruction, intestine-tumor fistula, or chylous ascites. Attempting to resect such tumors in vivo may not only result in incomplete tumor resection, but also loss of bowel integrity by vascular compromise and subsequent organ ischemia. Here we describe our experience of ex vivo approach for effective tumor resection with intention of maximum bowel preservation.

Methods: We retrospectively reviewed 17 consecutive patients who underwent ex vivo surgery and intestinal autotransplantation at our institution 2009-2018.

Results: Ex vivo surgery was performed for patients with a tumor involving mesenteric vasculature from pancreatic origin (n=5) or retroperitoneal soft tissue tumor (n=12). The procedure was chosen based on tumor location and degree of vascular involvement, which resulted tumor resection with intestinal autotransplantation with / without Whipple procedure (n=10) or multiviceral exenteration and autotransplantation (n=7). Of these seventeen patients, two patients had inadequate perfusion of intestine autograft which was explanted at planned second look laparotomy, requiring TPN and intestine transplantation. For fifteen patients with successful intestinal autotransplantation, average remaining bowel length was 320cm with minimum length being 190cm with IC valve. For GI complications, two patients had prolonged ileus of which one patient required temporary TPN support. Two patients had prolonged high output ileostomy and one patient had chronic diarrhea. Tumor types were carcinoma (n=3), sarcoma (n=10), or benign / low grade tumors (n=4). The overall survival was 88% / 73%, at 1-year / 5-year, respectively. Perioperative (90-day) mortality was 0%. 88% (15 / 17) patients had R0 resection, and 65% (11 / 17) had no recurrence to date with median follow-up of 2 years.



Conclusions: With experience, in selected patients with conventionally unresectable tumors involving superior mesenteric vasculature, ex vivo tumor resection and intestinal autotransplantation can offer effective tumor removal with a reasonable bowel preservation.

370.5 - Post-transplant ulcerative ileitis (PTUI): risk factors and outcomes

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MedStar Georgetown Transplant Institute

PTUI is an infrequently described and incompletely characterized complication of intestinal transplantation (ITx). Similarities to Crohn's disease include localization to terminal ileum, risk for stricture, and response to biological and antimicrobial agents. Etiology of PTUI and impact on long-term graft function remain unclear. In order to gain insights into PTUI, we retrospectively studied patients receiving an ITx between 11 / 2003 and 12 / 2012 who survived at least 3-years. PTUI was found in 38 of 103 patients (37%) at a median interval of 1.6 (0.04-9.8) years after ITx. Presenting symptoms included diarrhea (34%), abdominal pain (32%), lower GI bleeding (14%), occult iron deficiency (10%), and fever (17%); half of the cohort had no symptoms. Potential risk factors for PTUI that were considered in the analysis included 1) recipient variables such as age, gender, liver disease, CMV status, NOD mutation status, and underlying disease, 2) donor factors such as type of ITx, D / R weight ratio, style of ileostomy construction and closure time, and operative and recovery times, and 3) immune factors such as results of cross-match, sensitization, HLA mismatching, and immunosuppressive induction. In univariable analysis, significant ($p<0.05$) predictors of PTUI included non-inclusion of graft colon / graft ICV (OR = 8.242, p=0.0001), Santulli ileostomy (OR=3.900, p= 0.005), age < 18 yr (OR=3.071, p=0.012), recipient NOD2 mutation (OR=2.860, p=0.030), shorter warm ischemia time (OR=0.985, p= 0.014), and longer hospital stay (OR=0.979, p=0.037). PTUI might also have been associated with reduced incidence of post-operative abscess (10.5% vs. 26.2%, p=0.057) and acute rejection occurring after 1-yr (26.3% vs. 12.3%, p=0.071) but not chronic rejection. PTUI did not affect 5-year graft survival, being 89% in those with PTUI and 81% in those without (p=0.168). This study suggests that absence of an ICV and the resulting increased contact of distal ileal graft mucosa with colonic succus and microflora are a key precipitant of PTUI and that the presence of NOD2 mutations promotes ileal injury in this setting. The high frequency of morbidities resulting from PTUI suggests that inclusion of graft colon with ICV should be considered in ITx whenever possible.

370.6 - The Role of T helper 17 cells in Severe Intestinal Transplant Rejection Renders it a Third Form of Inflammatory Bowel Disease

Leonid Belyayev [1, 2], Mohammed Sadat [2], Khalid Khan [2], Jason Hawksworth [2], Cal Matsumoto [2], Thomas Fishbein [2], Stuart Kaufman [2], Sukanya Subramanian [2], Jiman Kang [2], Alexander Kroemer [2]

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Introduction: Severe allograft rejection is one of the strongest prognostic factors leading to eventual graft loss and mortality in intestinal transplantation (ITx), specifically if the rejection is refractory to traditional therapeutic maneuvers such as T cell depletion with thymoglobulin(thymo). A characterization of the alloreactive T cell phenotype in severe rejection of both thymo treatment responsive and non-responsive patients has been lacking and is key for unlocking a precision medicine approach.

Methods: A cohort of 57 ITx patients with severe cellular rejection both before, during, and after treatment with thymo, alongside 128 uncomplicated controls, was selected from our IRB-approved Immunomonitoring and Tissue Bank Study. A polychromatic flow cytometry (PFC) panel with and without PMA / Ionomycin re-stimulation and culture was used to analyze peripheral blood and intestinal allograft samples to characterize surface receptor phenotype and cytokine production.

Results: Immunomonitoring of blood via PFC revealed that peripheral CD3 T cells uniformly deplete in both responders and non-responders ($p=.47$), confirming that monitoring CD3 T cells in peripheral blood fails to correlate with treatment responsiveness. However, CD3 IHC analysis of rejecting allografts confirmed that the degree of T cell depletion in the allograft correlates with clinical responsiveness. Graft immunomonitoring via PFC showed CD4+ effector memory, terminally differentiated effector memory, and pro-inflammatory CD4+ Th17 cells persist both before and during treatment with thymo. PFC cytokine profile evaluation using ex vivore-stimulated T cells showed a significant increase in IL-17 production ($p<.05$) from the Th17 cell population in rejection versus controls, which was also corroborated by rtPCR-arrays demonstrating a striking increase in the Th17-related transcriptome signature in rejection vs controls. Moreover, the Th17 cells of these patients co-expressed high levels of TNF-α, reminiscent of immunological features of inflammatory bowel disease (IBD). Indeed, when 10 non-responder patients were treated with the anti-TNF-α IBD medication infliximab, 9 experienced histologic and clinical recovery from rejection.

Conclusions: Severe ITx rejection is characterized by a Th17-mediated alloimmune response. Given the immunological similarities to IBD, we postulate that severe ITx rejection can be considered a third IBD, which has important clinical treatment implications.

370.7 - Effectiveness of Infliximab therapy following intestinal transplantation

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Background: We have used Infliximab (INFLX) following intestinal transplantation (ITx) as a rescue agent for early, severe ACR (S-ACR), refractory ACR (R-ACR), and for treatment of chronic mucosal inflammation (CMI). This study aims to review our experience with INFLX in an effort to examine efficacy.

Methods: An IRB-approved, retrospective review of a prospectively maintained single-center database of all ITx recipients receiving INFLX was performed. INFLX therapy was used on a case-by-case basis based on clinical condition / indication starting in 2005. S-ACR was defined as Grade 4 or exfoliative acute rejection. R-ACR was defined as partially treated, ongoing ACR incompletely responsive to standard therapy. CMI was defined as an IBD-like condition including active enteritis with a lymphocyte predominant infiltrate and / or ulcerations not attributable to rejection. INFLX was typically administered at 5mg / kg / dose. Doses were administered at 6-8 week intervals for patients with CMI.

Results: 22 patients (12 children; 14 with liver-inclusive allografts) were treated with INFLX for 23 different episodes of allograft dysfunction: S-ACR (n= 5), R-ACR (n=8), and CMI (n=10). For S-ACR, the median time for INFLX after ITx was 35 (IQR 30, 44) days. All patients lost their allograft. For R-ACR, the median time for INFLX after ITx was 1.3 (1.0, 3.6) years. In combination with ATG, 3 / 8 recovered allograft function. For CMI, the median time to for INFLX after ITx was 2.7 (1.4, 4.7) years. These patient have received a median of 7 (4,13) infusions. 7 / 10 experienced clinical / pathological improvement while 3 had inadequate response. 1 patient stopped INFLX due to PTLD and 1 due to an infusion reaction.

Conclusion: INFLX has been an effective biologic agent for gastroenterology patients with IBD and has been reported to be effective in the treatment of ACR after ITx. Our experience indicates that IFLX is ineffective as a salvage therapy for S- ACR. It may have a role as an adjunct therapy for R-ACR when combined with ATG. INFLX appears to be quite effective in the management of post ITx CMI. Larger, multicenter studies should be considered to further investigate the efficacy of INFLX after ITx.

POSTERS OF DISTINCTION THURSDAY JULY 4, 2019 SESSION 1

P2A01 - Analysis of the impact of graft reduction techniques on long-term outcome of intestinal transplantation

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Introduction: The scarcity of paediatric donors has led some units to use larger donors and perform graft reduction to overcome the shortage of small size matched full grafts. The aim of this study was to compare the outcome of patients receiving reduced grafts to those with full size grafts.

Method: The records of 94 Itx performed were reviewed. Patients were divided in two groups, reduced grafts (Group 1) and full size grafts (Group 2) and their details were compared.

Results: 94 Itx were performed in 87 patients, 23 with reduced grafts, 19 Liver and Itxx and 4 Isolated Itx. Demographics are shown in Table1

Table 1: Demographic aspects

Characteristics	Group 1	Group 2
Recipient Age in months	15 (7-138)	40.5 (8-194)
Recipient Weight in kg	8.4 (5.58-31)	12.8 (6.53-52)
Recipient Weight z score	-1.95 (-6.14 to -0.24)	-1.336 (-4.24 to -1.6)
Recipient Surgical procedures	2(1-*)	2(0-8)
Recipient Residual length	29	60
Donor age	108 (12-480)	72 (2-492)
Donor weight	30 (12-70)	21 (4.5-70)
D: R weight ratio	2.7 (1.3-6)	1.34

The length of intestinal resection varied from 45cm to 212cm, usually performed in the mid gut. The cold ischaemic time was a median of 422 minutes in Group 1 and 382 minutes in Group 2. With respect to abdominal closure, both groups had the same incidence of primary closure (56, 62%), however the use of an abdominal prosthesis was commoner in Group 2 (17% vs. 9%). Feeds were started in a median time of 6 days in Group 1 and 5 days in Group 2, while PN was stopped 26 days after SBTx in Group 1 and 18 days in Group 2 (median). Main complications are shown in Table 2.

Table 2 : post-transplant complications

	Group1	Group2
Intestinal leak (%)	9.36	17.46
Perforation (%)	27.27	14.75
Post-compartmental syndrome	22.72	4.76
PTLD	22.94	20.96
GVHD (%)	13.63	11.47
Acute rejection (%)	1 (0-6)	2(0-6)
Chronic rejection (%)	18.18	8.06
Survival time (days)	1018 (8-6478)	1405 (1-6842)

Discussion : Children receiving reduced grafts were younger, more likely to be inpatients at the time of transplant, had longer post-operative ICU and hospital stay, and were transplanted with older donors and with higher D/R weight ratio. This decision of reducing a graft could be influenced by the severity of illness in these patients.

Conclusion : Children with reduced grafts can have a successful long-term outcome comparable with full size grafts

P2A02 - Developmental and cognitive profile of children with intestinal failure

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Introduction: Children with intestinal failure (IF) are at risk of neurodevelopmental problems due to underlying disease, multiple operations, inadequate nutrition and prolonged hospitalisation. In this study we searched for prevalence of neurological impairment among children with IF and its ´ association with risk factors.

Methods: We conducted a prospective cross-sectional study at the nationwide tertiary referral IF centre of the Helsinki University Children ´ s Hospital during 2017 and 2018. IF patients aged three to sixteen years (n=40) were invited to participate. Those with genetic syndrome or severe neonatal intracerebral haemorrhage (n=12) were excluded. IF was defined as less than 50% of small intestine remaining or requirement of parenteral nutrition for more than three consecutive months. The cognitive and motor skills were evaluated using validated tests; Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III), Wechsler Intelligence Scale for Children (WISC-IV) and Movement Assessment Battery for Children, 2nd edition. To investigate the associations for severe neurocognitive impairment, children who had IQ <66 or serious neurocognitive impairment (n=8, 27%) were compared to those who had IQ ≥ 66 or were estimated to have normal or mildly abnormal cognitive function (n=22, 73%).

Results: Median age of participants (n=30, males=24) was 7.5 (range 3 to 16) years. The median IQ, VCI and PRI scores were 78 (IQR 65-91), 74 (IQR 60-92) and 79 (67-91) respectively. Ten (35%) patients had an IQ score under 70 (-2 SD), compared to 2.2 % in the normative population. The motor impairment was significant in 10 patients (36%) and milder in 8 (28%) patients. The patient characteristics and comparisons of the patients with severe neurocognitive impairment with others are presented in table 1. The children with severe neurocognitive impairment had less remaining small bowel, greater number of laparotomies and general anaesthesia and longer hospitalisation after birth than others. Children whose PN was started after the age of 12 months had normal median IQ of 96 (86-105), whereas median IQ was 74 (60-85) in children whose PN was started early after birth (P=0.0045).

Table 1. Patient characteristic of all patients with intestinal failure and comparison of patients with normal or mildly impaired cognition to those with severe cognitive impairment

Characteristics	All study patients (n=30)	Patients with normal or mildly impaired cognition* (n=22)	Patients with severe cognitive impairment** (n=8)	P-value***
IF aetiology: SBS/dysmotility/other, n	23 / 5 / 2	15 / 5 / 2	8 / 0 / 0	0.1434
Gestational age at birth, weeks (IQR)	35 (28-38)	36 (27-38)	30 (28-38)	0.5548
Children born ≤ 28 weeks, n (%)	8 (27%)	6 (27%)	2 (25%)	>0.9999
Birth weight, grams (IQR)	2235 (1014-3288)	2480 (1088-3378)	1225 (823-3076)	0.3387
Children with BW ≤1500 g, n (%)	13 (43%)	8 (36%)	5 (63%)	0.2420
Short bowel percentage, % (IQR)	30 (21-72)	43 (25-100)	20 (12-25)	**0.0052**
No. of general anaesthesia, n (IQR)	9 (8-14)	8 (7-11)	14 (12-16)	**0.0100**
No. of laparotomies, n (IQR)	4 (2-5)	3 (2-5)	6 (4-11)	**0.0067**
Duration of hospitalisation after birth (months)	4.8 (1.2-10)	3.8 (0.0-9.3)	9.5 (5.0-13)	**0.0471**

* Defined as IQ < 66 (n=7) or diagnosed to have serious neurocognitive impairment by neurologist (n=1)

** Defined as IQ ≥ 66 (n=19) or estimated to have normal or mildly impaired cognitive function by psychologist (n=3)

*** p-value is calculated for comparisons between patient groups of normal or mildly abnormal neurodevelopment, and severely abnormal neurodevelopment

Conclusion: Clinically significant cognitive and motor impairments are common among paediatric IF patients whose disease manifested during neonatal period. We strongly recommend systematic neurological assessment of all children with IF.

P2A03 - An assessment of psychiatric needs pre- and post-multivisceral transplant

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Introduction: As intestinal transplant becomes a more viable treatment option, there has been increased interest in quality of life and other psychosocial metrics. Systematic review suggests that quality of life improves post-transplant. However, there is limited data regarding psychosocial issues present at initial evaluation and post-transplant. Given that psychiatric issues are associated with increased mortality in solid organ transplant, this study aims to highlight psychosocial patterns that are present at initial evaluation and post-transplant.

Methods: This study was a retrospective chart review of 28 patients who received intestinal transplants between 8/3/10-1/3/17 at an academic hospital in the United States. Psychosocial variables from encounters with health psychology senior staff and trainees were extracted. Descriptive data were evaluated from pre and post-transplant encounters.

Results: Pre-transplant, the most common initial diagnosis was adjustment disorder (68%) with more significant pathology occurring in the remaining patients. 3/28 patients had comorbid substance use issues. 12/28 patients were on psychotropic medications during initial evaluation with 50% of those on multiple medications. Figure 1 describes data from initial psychological assessment. Of those eventually transplanted, 8 required further intervention prior to psychosocial clearance.

Figure 1. *Pre-Transplant Psychological Evaluation for Multivisceral Transplant Patients (N=20).*

Psychological Assessment	Mean	Range	
		Min.	Max
Montreal Cognitive Assessment	24.65	17	30
Rapid Estimate of Adult Literacy in Medicine-Short Form	6.36	0	7
Hospital Anxiety and Depression Scale			
Anxiety	3.95	1	12
Depression	4.55	1	8
Insomnia Severity Index	8.6	0	21

Among the 28 patients, psychology was consulted an average of 2.71 times. Of those that required follow-up, there was an average of 8.25 follow-ups. Most common reasons for consult were; depression, pain, anxiety, eating related issues, mental status concerns, or other. Of the 28 patients, 19 had post-transplant psychiatric diagnoses. Although adjustment disorders were the most prevalent (8/19), more significant pathology was found in remaining patients including opioid abuse (4/19), PTSD (3/19), and pain disorders (3/19).

Conclusion: Present analysis suggests that many pre-transplant patients have significant psychopathology. Post-transplant a number of psychosocial issues persist and can emerge on an inpatient and outpatient basis. Development of behavioral health protocols for the most common consultations will be a valuable clinical service. These interventions may improve psychosocial outcomes, decrease patient noncompliance and reduce disease burden and cost. Future prospective studies, extending period of follow up, and assessing a wider range of predictors and outcomes are needed.

P2A04 – Successful intestinal transplant recipients have comparable return to work rates as other solid organ transplants

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Background: Intestinal transplantation is an established therapy for patients with intestinal failure suffering from complications of total parenteral nutrition. While the immunogenicity of the bowel has imparted unique hurdles as compared to other solid organs, one and five year survival rates have steadily improved[1]. With increased long-term survival, other metrics of success are of interest. Re-entry to the workforce is an important quality of life indicator that has not previously been reported for intestinal transplant recipients. Re-employment after other solid organ transplantation varies from 22-63%, with kidney recipients demonstrating the greatest rate of re-employment (63%) and lung recipients the lowest (22%)[2].

Methods: All patients who received an intestine inclusive transplant between 2003 and 2018, at our institution, with a post-transplant survival greater than one year were retrospectively identified. Employment, (defined as financially compensated work), was assessed through a questionnaire addressing current work status and return to work within 1-5 years and 5-10 years of transplant. Results are reported as percentages.

Results: 60 patients (>18 years of age) transplanted from 2003-2018 were alive at the time of this study. Data from 52 of the 60 patients was available for analysis. 25 (48%) patients were male, 27 (52%) patients were female. Median age at the time of transplant was 41 years (range 20-66) and 40 years (range 13-56), respectively.

20 patients out of 52 reported active employment (38.5%). 22 patients (42.3%) reported employment within 5 years of transplant. Of the 38 patients that were beyond 5 years from transplant, data for 31 was available. 16 of these patients (51.6%) were employed. Among the 32 patients who were unemployed, 3 (9.4%) were retired, 3 (9.4%) participated in volunteer work, and 3 (9.4%) were pursuing higher education.

Conclusion: Despite the complexity of intestinal transplant, rates of employment among intestinal transplant recipients are comparable to that of other solid organ transplants. This suggests that intestinal transplant patients are capable of re-integrating into society and leading productive lives. Future aims include elucidating the variables such as support structure, disability prior to transplant, and educational level that may impact re-employment.

P2A05 - Technique of Deceased Donor Vascularized Abdominal Wall Allograft Procurement

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Purpose: Vascularized abdominal wall allografts (AWA), which cover solid organs in patients with loss of abdominal domain or extensive abdominal wall damage, remain an essential adjunct to recipients of intestinal and multi-visceral allotransplantation. Ensuring adequate vascular flow to the allograft during solid abdominal organ procurement is critical. Our study aims at developing a standardized technique for AWA procurement.

Methods: Four AWA procurements were performed (2 cadaveric, 2 deceased donors) over a 2-year period. Our study aims to: A) minimize cold ischemia time, B) provide meticulous dissection of the IE vessels while avoiding traction injury and C) provide appropriate vessels to be utilized as extension grafts during re-implantation. In brief, our technique involves incising the skin one inch lateral to the rectus muscle, detaching the flap from the costal margin, identifying the inferior epigastric (IE) vessel pedicles bilaterally and excising the pedicles with the femoral vessels.

Results: Cold ischemia times are prolonged if the AWA is removed prior to the other solid organs. The IE vessels were injured during 2 procurements from traction injury as a result of excess dissection. Iliac vessels are not ideal extension grafts, as these are often sent with liver and pancreas grafts.

Conclusions: The abdominal wall flap should be raised at the start of procurement and placed on the thighs with the inferior rectus attachments intact to avoid traction injury to the IE vessels (Fig.1). The peri-vascular fat around the IE vessels should be preserved to minimize traction injury (Fig.2). The IE vessels should be dissected down to the femoral vessels immediately prior to aortic cross clamping to minimize cold ischemia time. A long segment of the femoral artery and vein should be preserved with the IE vessels to provide adequate length for re-implantation. The carotid artery and saphenous vein may be utilized when additional length is required. Adhering to these principles, improvement in successful AWA procurement may be achieved.

Figure 1

Figure 2

P2A06 - Intestinal failure associated liver disease in patients receiving Home Parenteral Nutrition: Experience from a large tertiary referral hospital in United Kingdom

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Objectives and Study: Intestinal Failure Associated Liver Disease (IFALD) remains common in children with intestinal failure (IF). Aim of this study was to determine incidence and risk factors of IFALD and to understand if the current definition of IFALD is sufficient.

Methods: Patients on home PN for > 12 months were recruited from a tertiary IF clinic. IFALD was defined according to the 2015 ESPGHAN paper, data analysed retrospectively. 1.Early IFALD ('red flag'): bilirubin>20 µmol/L 2.Established IFALD: bilirubin>100 µmol/L > 2 to 4 weeks 3.Advanced IFALD: 2 + portal hypertension Underlying IF aetiology, PN duration, incidence of catheter related blood stream infections (CRBSIs), bilirubin, ALT, ALP, GGT, platelets, liver ultrasound and biopsy results were obtained from the case notes.

Results: 52 children were identified;19/52 had short bowel syndrome (SBS), 17/52 motility disorder and 16/52 enteropathy/epithelial disorder. Median length of PN was 4 years (range 1-18 years.)

IFALD was more common in females (11/29 ; 37% versus 4/23;17%; p = 0.22) and in patients with small intestinal bacterial overgrowth (SIBO) (3/8;37% versus 12/44 ;27%; p= 0.67). 2/9 (22%) patients on hepatotoxic medications developed IFALD Vs 13/43 (30%) (P = 0.0045). Highest incidence of IFALD occurred in SBS 9/18 (50%). 29/52 (56%) had persistently normal LFTs and bilirubin. 6/52 (11.5%) were considered 'red flag' of which 5 had biliary stasis confirmed on ultrasound, 4 had SBS; 1 was treated for SIBO during this period. 2/52 children (3.8 %) had established IFALD (bilirubin>100 µmolL for >4 weeks). No biopsy was performed as LFTs improved; 1/52 patient (1.9 %) had a bilirubin>100µmol/L for 2 weeks following 2 episodes of CRBSI.1/52 (1.9%) patient with SBS had advanced IFALD portal hypertension but no CRBSIs during the study period. 2/52 (3.8%) patients had a liver biopsy as red flag but bilirubin < 100µmol/L and abnormal ultrasound which confirmed established IFALD. Both had SBS and no episodes of CRBSI during the study period. 5/52 (9.6%) children had a normal bilirubin and elevated ALP >6 weeks; 2 demonstrated biliary stasis on ultrasound. 6/52 (3.1%) had a rise in ALP < 6 weeks, normal bilirubin and ultrasound.

Conclusion: In our cohort IFALD was rare. Risk factors for developing IFALD were CRBSI and SBS, although not statistically significant likely due to small sample size. A definition based largely on bilirubin may not be sufficient to detect IFALD.

P2A07 - Mucosal T-cell kinetic in the early phases of rat model of allogenic small bowel transplantationMucosal T-cell kinetic in the early phases of rat model of allogenic small bowel transplantation

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Introduction: Intestinal transplantation (IT) faces many challenges, among them, the necessity to early detect and treat rejection processes. Improving our understanding on the dynamics of allogenic response will be useful to bring candidate targets to these aims. The objective of our study was to determine the kinetics of mucosal T-cells population in the early phase of small bowel rejection using a Heterotopic IT rat model. We made emphasis in phenotypical, activation and exhaustion markers for the early detection of the rejection phenomena.

Methods: Allogeneic heterotopic small bowel IT (n=5) was performed following standard procedure. Brown Norway animals were used as donors and Lewis as recipients. Rats did not receive any immune suppressor treatment. Rejection was monitored by clinical scoring and hematoxylin-eosin staining of intestinal grafts (Gf). T-cells from the peripheral blood (PB) and small bowel mucosa were assessed by flow cytometry. CD3, CD4, CD8, CD25, CD45, CD45RC, PD-1, FoxP3 and anti-Lewis MHC I expression was analyzed. Gf samples were taken at day 0, 3 and 7 post-operative (POD).

Results: No clinical signs of rejection or significant histological changes were observed at day 3. At this time, in PB 7.9 % ± 0,7 of T cells were from the donor, meanwhile in the Gf 42,7% ± 4,6 of T-cells were recipient cells. We observed a significant increase of CD3+CD4+CD25+, CD3+CD4+CD45RC+ and CD3+CD8+CD45RC+ % in comparison with basal levels (PB:$p<0,05$;Gf:$p<0,01$). CD3+CD4+CD25+FoxP3+ cells were also increased in the Gf. At day 7 animals present significant weight loss and histological features compatible with mild to moderate cellular rejection. Differently from day 3 POD, in PB we could not detect donor T-cells. In the Gf 70% ± 7 of T-cells were from the recipient. CD3+CD4+CD45RC+ and CD3+CD8+CD45RC+ % were significantly higher than at day 3 POD (PB $p<0,001$;Gf:$p<0,01$). We detected increased levels of CD3+CD4+PD-1+ and CD3+CD8+PD-1+ cells in the Gf in comparison to basal levels($p<0,01$). No differences in CD25 expression was observed between day 3 and 7.

Conclusion: T-cell replacement in the Gf mucosa is a very fast process and CD25 expression in both PB and the Gf is an early event that precede the histological changes and should be analyzed as a potential biomarker. Considering that T-cells expressing CD45RC have been described as key players in the Gf rejection processes, our results also suggest they could be a relevant target to treat / prevent ACR.

P2A08 - Dysregulation of the regulatory T cell / effector T cell axis in intestinal transplant rejection towards a pro-inflammatory phenotype

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Introduction: Regulatory T cells (Tregs) have recently been established as key players in dampening effector T cell (Teff) mediated inflammation, managing self-tolerance, and preventing autoimmunity and transplant rejection. However, the role of Tregs in immune responses in intestinal transplantation (ITx) is unknown, where a full tissue phenotypic and functional characterization of the Treg / Teff axis is lacking. We hypothesized that this axis in ITx rejection is dysbalanced towards unrestricted Teff-mediated inflammation in the allograft.

Methods: We identified a cohort of 17 ITx patients with a history of rejection along with 24 uncomplicated controls from our IRB-approved Immunomonitoring and Tissue Bank Study. A polychromatic flow cytometry (PFC) panel with and without PMA / ionomycin stimulation and culture was used to analyze peripheral blood and intestinal allograft samples to characterize surface receptor phenotype, transcription factor expression, and cytokine production.

Results: PFC of biopsies showed a significant increase in pro-inflammatory IL-17 producing CD4+ Th17 effector cells in rejection patients as compared to controls. To our surprise, there was also an overall increase in the proportion of FoxP3+ Tregs in rejection patients; however, the majority of which were induced (Helios-) with less natural thymic derived Tregs (Helios+), which was not observed in blood. Further Treg subset analysis revealed a significantly higher proportion of pro-inflammatory Th17-like CCR6 expressing and Th1 / Th17-like dual CXCR3 / CCR6 expressing memory Tregs in rejection patients. Therefore, we hypothesized that given Treg plasticity in a pro-inflammatory environment, these Tregs assume an effector like phenotype in ITx rejection. To test this hypothesis, we performed an ex vivorestimulation assay, which demonstrated that both natural and induced Tregs produce more pro-inflammatory IL-17 and IFN-γ rejection than control patients, further corroborating their pro-inflammatory phenotype and dysbalance in the Treg / Teff axis towards a proinflammatory Th17 phenotype.

Conclusion: Our study characterizes ITx rejection as driven by a severely altered Treg / Teff axis with IL-17 producing pro-inflammatory CCR6+ Th17 effector and potentially pro-inflammatory Treg cells, which may have strong implications on future clinical therapies.

P2A09 - Risks of the excluded bowel in patients with chronic intestinal pseudo-obstruction (CIPO)

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Introduction: Management of intestinal failure secondary to severe CIPO is based on parenteral nutrition associated to decompression or diversion enterostomies +/- segmental resections (mainly colectomy). Early prophylactic subtotal enterectomy is not recommended, since small bowel remains partially functional in CIPO. This study evaluates the risk linked to the excluded bowel in such patients.

Methods: Charts of all patients with severe CIPO requiring parenteral nutrition and enterostomies, managed from 1986 to 2017 in our institution, were reviewed. Data about initial management, bowel exclusion, incidence and treatment of enterocolitis and, eventually, transplantation were analyzed.

Results: Forty-two patients were included. Initial management consisted of a complete diverting jejunostomy in 8 patients, ileostomy in 12 and both in 22, leaving an excluded segment of small bowel and colon in 30 and colon in 12 patients.

9 patients used to have daily irrigation and 21 had prophylactic antibiotic therapy.

11 CIPO patients presented at least one episode of enterocolitis (EC). Median age at first EC was 3.6 years [0.9 -12]. EC episodes occurred in the excluded bowel in 4 patients, in the non-excluded intestine in 2, and both excluded and non-excluded intestine were involved in 5 patients.

None of the patient underwent subtotal enterectomy. All patients were treated conservatively, except 3 who underwent 2 ileo-colectomies and 1 diversion, at a median age of 4.6 years [3.6- 9.6].

Finally, 3 patients underwent a liver and intestinal transplantation and 4 underwent an intestinal transplantation.

Overall mortality was 7% (n=3).

Conclusion: CIPO patients have a risk of enterocolitis but mainly mild episodes that are managed conservatively as compared to long segment Hirschsprung disease patients for whom subtotal enterectomy is frequently required. The main goals of CIPO management remain based on nutritional support, fluid/electrolyte restoration, antibiotics for bacterial overgrowth/infections, and control of particularly bothersome symptoms.

P2A10 - Home parenteral nutrition in infants with neonatal short bowel syndrome : a 30 year experience

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Introduction: Short Bowel Syndrome (SBS) can occur at any age, but the majority of paediatric cases result following bowel resection in infants with congenital abnormalities or those developing necrotising enterocolitis (NEC). Parenteral nutrition (PN) is needed during bowel adaptation and if required for an extended period treatment is continued at home (HPN). We describe our experience of HPN patient demographics and outcome in three time periods with different approaches to patient care.

Methods: Inclusion: Infants with neonatal SBS receiving HPN 1987-2015. Exclusion:1) patients acquiring SBS outside the neonatal period 2) patients starting HPN in other units 3) patients born 2016-2018 with outcome still undetermined. Data was collected from dietetic records and HPN database and included cause of SBS, time to discharge and outcome. In patients weaned from PN time to full enteral nutrition (EN) was recorded. Data from three time periods 1987-1996 (Cohort 1), 1997-2006 (Cohort 2) and 2007-2015 (Cohort 3) were compared.

Results:

	1987-1996	1997-2006	2007-2015
Number of patients	5	16	37
NEC	1	6	15
Gastroschisis	3	3	8
Atresia(s)	0	4	5
Mid gut volvulus	1	2	8
Ischaemia	0	1	1
Median bowel length (cm)	35(10-40)	35 (19-60)	40 (5-100)
Median gestation (weeks)	40 (34-40)	35(27-40)	34 (23-40)
Age at discharge (months)	9.8 (5.7-17.2)	11.9 (5.4-33.1)	9.2 (3.2-17.0)
Outcome **Full EN**	1 (20%)	11 (69%)	29 (78%)
Full EN after liver transplant)		2	1
Full EN after liver +bowel transplant			2
Full EN after non-transplant surgery)		1	4
Remains on HPN	0	1 (6%)	3 (8%)
Died	4 (80%)	4 (25%)	5 (14%)
IFALD	4	1	2
Post Liver transplant		2	
Post small bowel and liver transplant		1	2
Sepsis			1
Median Time to Full EN (months) (after non transplant surgery)	219	34 (9.4-142) 59.6	22.5 (8.2-55) 32.25 (31.2-33.0)

142 patients have been managed on HPN since 1987. SBS was the indication in 51% patients. Patient numbers increased, the proportion with NEC rising significantly: Cohort 1 20% patients, Cohort 2 38% and Cohort 3 41%. There was no significant difference in median bowel length. Median age at discharge was lowest in Cohort 3. Survival was 20% Cohort 1, 75% Cohort 2 and 86% Cohort 3. 80% patients in Cohort 1 died of intestinal failure associated liver disease (IFALD) reducing to 6% in Cohort 2 and 3. Median time to full EN was shortest in Cohort 3 and was not improved by non-transplant surgery.

Conclusion: Data shows an increase in the number of infants with SBS requiring HPN, mainly due to a rise in preterm infants with NEC. Cohort 3 shows markedly improved outcomes: 78% patients achieved full EN in median time 22.5 months. Advances in transplantation have contributed to reduction in death from IFALD but 75% deaths in cohort 2 (n=3) and 40% deaths in Cohort 3 (n=2) occurred post-transplant. Long-term PN remains the treatment of choice in children unable to wean from PN. Successful management of infants receiving HPN requires skills of a multidisciplinary nutrition team: aggressive use of enteral nutrition, early discharge, improved management of catheter sepsis, advances in transplantation all impact on survival of infants with SBS requiring HPN.

POSTERS OF DISTINCTION THURSDAY JULY 4, 2019 SESSION 2

P2B11 - Interobserver agreement in histological diagnosis of acute cellular rejection in small bowel allografts: a multicenter study

Thomas Steelandt [1], Emilio Canovai [2], Inca Hundscheid [3], Rachel M. Brown [4], Olivier Corcos [5], Guido Trentadue [6], Jacques Pirenne [2], Kaatje Lenaerts [3], Laurens J. Ceulemans [2], Gert De Hertogh [1], et al.

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Introduction: Outcome after intestinal transplantation (ITx) has improved, however acute cellular rejection (ACR) remains a frequent challenge restricting long-term results. The gold standard for diagnosis of ACR is histological analysis of graft biopsies.

The diagnostic criteria for ACR were defined during the 2003 VIIIth International Small Bowel Transplant Symposium. Although this report provided consensus for international reporting, it has not been validated in a clinical setting. The aim of our study was to evaluate the reproducibility and the interobserver variability of the current histological scoring system in a multicenter study.

Methods: We retrospectively analyzed biopsies on newly stained slides from ITx patients from 3 hospitals. These slides were graded by 2 independent pathologists blinded to clinical information or original diagnosis. One reader was an experienced pathologist from an intestinal transplant center, the second reader was a last year pathology trainee. Biopsies were graded as: no signs of rejection, indeterminate for rejection (IFR) or ACR grade I to III based on current criteria. Only biopsies that were obtained endoscopically with at least 10 identifiable crypts were included in the final analysis.

Diagnoses were subsequently compared between the two readers (weighted Kappa Method) and to the original diagnosis made by several pathologists at other centers (intra-class correlation coefficient).

Results: 401 biopsies were evaluated from 45 patients (27 children, 18 adults) undergoing intestinal transplantation from 2000 to 2014. Median follow-up was 4.3 years (0–12,5). In total, 320 biopsies met inclusion criteria. 38 biopsies in 20 patients were originally described as showing ACR grade 1 to 3. Nine biopsies were IFR.

The overall weighted kappa value for the interobserver agreement was 0.82 (95% CI [0.752;0.882], p<0.001). The intraclass correlation coefficient comparing the pathology panel to the original diagnosis was 0.434 (95% CI [0.365;0.502]).

Conclusion: Despite the difference in clinical experience between the readers, there was a high level of interobserver agreement using the current histological criteria for acute cellular rejection. The lower degree of agreement with the original diagnosis may suggest a learning curve effect, or reflect the focal characteristic of ACR, differentially expressed in the newly cut slides. More importantly, part of the biopsies were evaluated with the old diagnostic criteria.

P2B12 - Ninety-Day Complications in 214 Intestinal Transplant Patients: A Calvien-Dindo Analysis and Long Term Outcomes

Jason Hawksworth, Asha Zimmerman, Alexander Kroemer, Pejman Radkani, Juan Guerra, Khalid Khan, Nada Yazigi, Stuart Kaufman, Sukanya Subramanian, Hannah Sagedy, Thomas Fishbein, Cal Matsumoto

MedStar Georgetown Transplant Institute

Objectives: The purpose of this study was to examine the 90-day complications that occurred after intestinal transplantation and to determine whether they effect 5-year patient or graft survivals.

Methods: Retrospective review of intestinal transplant recipients between 11/2003 and 11/2017 at a single-center academic institution. Complications were classified using the Clavien-Dindo classification system. Five-year graft and patient survival were compared between those with varying degrees of complications.

Results: Of the 214 patients who underwent intestinal transplant, 201 (94%) experienced a Grade II or higher complication, 148 (69%) experienced a Grade III or higher complication, 69 (32%) experienced a Grade IV or higher and 13 (6%) patients died (Grade V) within 90 days of transplant. The average number of complications was 2.6. Medical complications occurred in 156 (75%) patients while 132 (64%) patients had a surgical complication of some kind. Medical complications were categorized as infectious (59%), renal (29%), cardiopulmonary (29%), immunologic (26%), gastrointestinal (12%), hematologic (12%) and neurologic (3%). Surgical complications were categorized as enteric (15%), abscess (15%), chylous (14%), bleeding (14%), wound (13%), thrombosis (7%) and biliary (3%). Patients with Clavien-Dindo Grade IV complications had significantly worse five-year graft and overall survival compared to those with less severe complications (57% vs 72%, p= 0.012 and 58% vs 75%, p = 0.007, respectively).

Conclusions: Complications are common after intestinal transplantation and are predominantly infectious. Patients suffering from severe complications (Clavien-Dindo IV) within the first 90 days after transplantation have worse graft and overall survival at 5 years.

P2B13 - Contribution of Video Capsule Endoscopy to the follow-up of intestinal transplantation

Raphaël Enaud [1,2], Lisa Sharkey [3], Esther Ramos Boluda [4], Joaquín Poza Cordón [5], Olivier Goulet [2], Florence Lacaille [2], Lorenzo Norsa [2,6], Cécile Talbotec [2]

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Introduction: The graft follow-up through conventional endoscopy has technical limitations. The visualization of the entire small bowel by Video Capsule Endoscopy (VCE) may give important information. We collected the experience with VCE after intestinal transplantation, to define its indications and limits.

Methods: Patients with VCE evaluation between January 2014 and December 2018, from one adult and 2 pediatric centers, were included. Clinical and biological data were retrospectively collected.

Results: Thirty-three VCE were performed in 23 patients, including 14 children (22 VCE). Clinical characteristics are summarized in Table. The indications of VCE were control of rejection treatment (24%), protocol control (24%), suspicion of acute rejection (15%) or intestinal inflammation (9%). Adults ingested VCE, whereas in children, endoscopy was required in VCE (68%). The entire small bowel was explored in 23 VCE (70%). Inflammation of the mucosa was seen in 17 VCE (52%), other abnormalities (varices or bleeding) in 3 VCE (9%). VCE was considered in 9 VCE (27%), while VCE was non-contributory in 4 VCE (12%). VCE retention occurred in 3 cases (9%). Interestingly, 5 VCE (15%) demonstrated intestinal inflammation while endoscopy was normal in 3 VCE (9%) or non-contributory in 2 VCE (6%). VCE was useful for diagnosis in 24 cases (73%) and led to a change in management in 6 cases (18%).

	Children	Adults
Number of patients	14	9
Age at the first VCE (years)	12.4 (10.8 - 13)	52.1 (46.3 - 55.1)
Delay between transplantation and VCE (years)	6.9 (5.8 - 9.6)	0.8 (0.1 - 2.4)
Graft type		
Small bowel and colon	7 (50%)	0
Isolated small bowel	5 (36%)	3 (33%)
Liver, small bowel and colon	1 (7%)	3 (33%)
Multivisceral	1 (7%)	3 (33%)

Data are presented as n (%) or median (interquartile ranges)

Table : Summary of patient characteristics.

Conclusion: VCE is a significant improvement for graft exploration after intestinal transplantation.

P2B14 - Predictive Potential of Biomarkers of Intestinal Barrier Function for Therapeutic Management with Teduglutide in Patients with Short Bowel Syndrome

Janine Büttner [1], Sebastian Massberg [2], Bettina Bochow [1], Sabina Naranjo [1], Martina Werich [1], Ulrich-Frank Pape [1,2]

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Introduction:

Teduglutide, an analog of glucagon-like peptide 2, improves intestinal rehabilitation in chronic intestinal failure frequently caused by short bowel syndrome (SBS). However, the mechanisms in the intestinal barrier related to regulation of intestinal permeability (IP) during adaptive response or therapy are not well understood. We analyzed whether measurement of IP or gene expression analysis from mucosal biopsies of selected candidate genes likely associated with IP are useful biomarkers to describe the regulation mechanisms in the intestinal barrier in patients with SBS with or without teduglutide therapy.

Methods:

IP was assessed using a sugar drink test containing lactulose and mannitol and urinary recovery rate was used to determine lactulose / mannitol ratio. Gene expression analyses of mucosal biopsies was performed using qRT-PCR Quantitec Primer Assays for tight junction genes and epithelial markers.

Results:

SBS patients showed increased Lac / Man ratio compared to healthy controls (HC), (n=29 / 34, p=0.0001). Mannitol recovery was decreased in SBS (Mean HC 13.8% vs. SBS 5.4%, p= 0.0001), whereas lactulose recovery was similar to HC (mean HC 0.21% vs. SBS 0.36% p= 0.2). qRT-PCR analyses showed significant differences in gene expression between SBS patients and HC (n=30 / 7) for YBX3 p=0.048, CRB3 p=0.009, CDK4 p=0.048, CASK p=0.03, and SI p=0.02.

For 12 patients, gene expression data were analyzed before and after up to 12 month of teduglutide treatment. Significant differences in gene expression were received for CASK p=0.01 and SI p=0.028. Further, analysis of citrullin levels in this cohort showed increased citrullin levels in patients with teduglutide therapy (p=0.012).

Conclusions:

The analysis of IP gave first insights into changes of intestinal sugar absorption but has not yet been established in SBS patients. Further paired and controlled studies are required to evaluate the specifc influence of both altered bowel anatomy and / or changes in barrier function. Furthermore, altered specific gene expression was shown for both, tight junction formation and genes involved in nutrient transport and should be further analyzed.

P2B15- Preoperative Arterial embolization for Multivisceral Transplantation for Diffuse Portomesenteric Thrombosis: Performance and Outcome Analysis

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Multivisceral transplant (MVT) for ESLD and stage IV portomesenteric vein thrombosis (PVT), is a highly complex procedure fraught with life-threatening thrombo-hemorrhagic complications. Preoperative visceral arterial embolization is a means to facilitate exenteration and minimize bleeding.1 Technical success, however, has to be measured clinically through the attainment of poorly perfused / ischemic viscera, and may be further validated by pathological exam of the eviscerated organs.

We present 3 such patients, (2 were redo), who underwent visceral arterial embolization prior to MVT. A descriptive analysis of recipients is presented in Table 1.

A comparative analysis of the embolization procedure, visceral organs perfusion during exenteration, and gross pathological examination of the visceral specimen is outlined in Table 2.

Patient #1 had an angiographically confirmed initial successful deployment of a proximal celiac trunk plug, but in the laparotomy liver perfusion was preserved. Pathological exam of eviscerated organs confirmed the dislodgement and distal migration of the plug into the GDA. In order to preserve liver flow, patients #2 & 3 underwent selective embolization of the splenic and gastroduodenal branches of the celiac trunk. Successful embolization of the SMA was achieved in all 3 patients, and facilitated resection of ischemic intestine, pancreas and spleen with reduced blood loss (4 / 6 / 6 pRBCs). However, in all 3 cases a severe coagulopathy with significant hemorrhage occurred during hepatectomy (20 / 18 / 12 pRBCs). Patient 1 suffered a full blown DIC, intravascular thrombosis and severe hemodynamic instability that led to intraoperative death. Coagulopathy in patient 2 and 3 subsided post-reperfusion. Circulatory exclusion of the liver in MVT is frequently associated with the development of life-threatening coagulopathy. Heparin prophylaxis is warranted to control consumptive coagulopathy and minimize risk of intravascular thrombosis. Effective heparinization allows a safer management of hyperfibrinolysis with antifibrinolytics when indicated.2

In conclusion, MVT in recipients with “hostile abdomen” is associated with severe hemodynamic, hemorrhagic, and hemostatic perturbations. Hepatic sparing embolization of gastrointestinal viscera facilities exenteration and effectively reduces blood loss. Coagulopathy, however, remains a life-threatening thrombo-hemorrhagic risk, and heparin prophylaxis with diligent hemostatic management are indicated.

P2B16- Secondary Prophylaxis for Catheter Related Thrombosis in Pediatric Intestinal Failure – Comparison of Short vs. Long Term Anticoagulation Prophylaxis Protocols

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Introduction: Catheter related thrombosis (CRT) is a severe and potentially life threatening long-term complication in intestinal failure (IF) but the optimal preventive therapy for CRT is unknown. This study assessed the efficacy and safety of two protocols of secondary anticoagulation (AC) prophylaxis with low molecular weight heparin (LMWH).

Methods: This is a multicenter (N=2), retrospective cohort study of children on home parenteral nutrition (HPN) with a previous episode of CRT. Secondary AC, based on center's protocol, was initiated once a first CRT was identified. In the short-term protocol (N=10) patients received therapeutic dosing until thrombus resolution or up to 4 months and in the long-term protocol (N=26) prophylactic dosing continued until line removal. All patients underwent routine vascular US at 12m after initiation of AC. The primary outcome was CRT recurrence or progression of CRT at 12 months post therapy.

Results: Patient demographics were similar between groups. Median age at first CRT was 7 months (IQR 2.8-16.5) and median time since PN initiation was 4.5 months (IQR 1.9-15.4). CRT frequency was similar between PICC line and tunneled central venous catheter (23% vs 28% respectively, p=0.48) and between insertion sides (27% right vs 21% left, p=0.45). Progression / recurrence of CRT within 12 months of initiation of AC occurred in 7 (70%) patients in the short-term group and 2 (8%) in the long-term group (p=0.0001) in a median of 61 days (IQR 35-173). Total CRT recurrence / progression for the long-term protocol group was 9 / 26 (35%) patients at a median follow up of 19.5 months (IQR 16.2-34.3). Patients with recurrence of CRT had a greater number of catheters / 1000 catheter days (23.5 vs 5.5, p=0.014). The presence of symptoms or complete vessel occlusion at the first CRT episode and frequency of CLABSI between CRT episodes were not associated with an increased risk of recurrence. One patient had a mild allergic reaction, one discontinued treatment following GI bleeding and two at the family and patient's request. Medication adherence was good (>80% of doses) in all patients in the short-term and 89% of patients in the long-term group.

Conclusions: Long-term secondary anticoagulation prophylaxis with LMWH is more effective than short-term therapeutic AC for the prevention of recurrence or progression of CRT at 12 months. Secondary AC prophylaxis should be considered in children with CRT to maintain long-term venous patency while on PN.

P2B17 - A model to study ischemia-reperfusion injury in human intestinal organoids

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Introduction: Ischemia-reperfusion (IR) injury is inevitable during intestinal transplantation. IR damages the intestinal epithelium, which functions as a physical and immunological barrier and is therefore crucial in maintaining intestinal homeostasis. In order to investigate potential therapeutic targets to protect the epithelium during intestinal IR and promote a regenerative response, we aim to validate a model to study IR in human intestinal organoids. Intestinal organoids have been shown to closely resemble self-renewal kinetics, 3D architecture, and cell-type composition of the intestinal epithelium *in vivo*.

Methods: A well-established human experimental model to study IR was used for temporal expression profiling of the *in vivo* intestinal response to IR. The top perturbed pathway was further validated using qPCR. Intestinal epithelial organoids were cultured from crypts isolated from surgical specimens of normal human small intestine. To simulate IR, organoids were subjected to 12 hours of hypoxia (1% O_2) followed by 30 and 120 minutes of reoxygenation. Activation of the UPR response was assessed by qPCR for CHOP, GADD34, BiP and XBP1 splicing, and, in addition, signs of endoplasmic reticulum (ER) stress were evaluated using electron microscopy (EM).

Results: The unfolded protein response (UPR) was the top perturbed pathway during reperfusion of the ischemically injured human small intestine *in vivo*. Subjecting small intestinal organoids to 12 hours of hypoxia followed by 30 minutes of reoxygenation significantly increased expression of UPR-related genes CHOP and GADD34 and splicing of XBP1 mRNA compared to organoids not subjected to hypoxia. In addition, EM showed dilated ER after reoxygenation which is indicative of ER stress.

Conclusion: In line with findings in the *in vivo* human IR model, revealing the response to unfolded protein as a highly regulated process during reperfusion, hypoxia-reoxygenation in intestinal organoids induces significant activation of the UPR. Intestinal organoids can be used to improve insight in the pathophysiology of epithelial IR injury and regeneration, which could lead to new therapeutic targets.

P2B18 - Feeding difficulties in children with Intestinal Failure

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Introduction: Children with intestinal failure (IF) may be at risk for developing feeding difficulties given the negative stimuli associated with feeding, chronic illness and prolonged hospitalization. There is no literature on the prevalence of feeding difficulties in the IF population, its associated factors or intervention strategies. As a first step, we sought to screen for the frequency of the feeding difficulties and eating behaviours in children and herein provide the results of a preliminary sample.

Methods:Children who were greater than 1 year of age with IF and on home PN for > 3 months were included from two centres: Alberta Children's Hospital (ACH), Canada and Hôpital Necker-Enfants Malades , France. The validated *MCH-Feeding Scale* was used to screen for mild, moderate and severe feeding difficulty. The validated parent-rated *Child Eating Behaviour Questionnaire (CEBQ)* was used to screen for eating styles and food avoidant behaviours.

Results: Preliminary data was gathered for n=34 subjects, median age 6 years with diagnoses of short bowel syndrome (n=22), chronic intestinal pseudo-obstruction (n=4), or other (n=8). Analysis of the MCH-Feeding Scale indicated that 24% of the subjects had no feeding difficulty, while 29%, 18%, and 29% reported mild, moderate and severe difficulty respectively. The subset of n=21 completing the CEBQ rated very high on food fussiness, very high on food enjoyment and very low for emotional over-eating relative to the UK reference sample (Fig 1). In particular, the ACH children scored very high on satiety responsiveness.

Conclusions: Preliminary data indicate that approximately half of children with IF have moderate to severe eating difficulties. Interestingly, both food fussiness and enjoyment of food are more commonly featured eating behaviours in this sample. It is unclear whether the feeding difficulties of children with IF are related to the impact of the disease etiology and severity, early feeding history, degree of gastrointestinal symptomatology and / or attempts to assert some control. Future work will examine how IF specific factors including the use of tube feeds are associated with feeding difficulties.

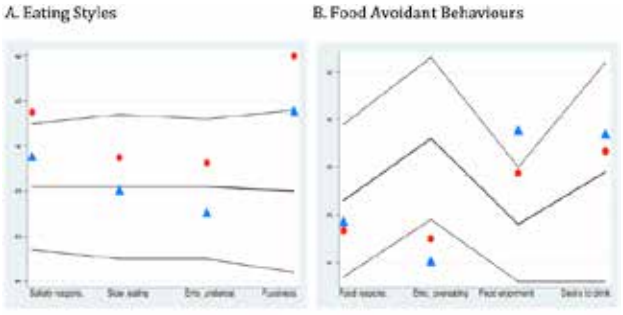

Fig. 1 Comparison of children with IF with Children's Eating Behaviour Questionnaire reference data of UK school children. The black curves represent the mean +/- 2 SD of the children in the UK study, with the Necker (blue triangles) and ACH children (red circles) for each eating behaviour.

P2B19 - Kidney Dysfunction after Intestinal Transplantation: Are We Headed in the Right Direction?

Giselle Guerra MD, Ahmed Farag MD, Jeffrey J Gaynor PhD, Arlene Adderley RN, Felipe Olenscki Gilli, Charisse Henderson RN, Thiago Beduschi MD, Akin Tekin MD, Jennifer Garcia MD, Rodrigo Vianna MD

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Introduction: Acute kidney injury (AKI) is a common complication after Intestinal transplantation (ITx). There are different etiologies for AKI: high Tacrolimus (TAC) levels, dehydration due to ostomy outputs and acute tubular necrosis (ATN) from sepsis, ischemia, and hemodynamic instability. Modifications in immunosuppressive regimen combined with surgical modifications may decrease the reported incidence of AKI.

Methods: Retrospective analysis of 92 intestinal transplants from 2013-2017: 94.6% (87 / 92) received the colon. Induction: Thymoglobulin (2mg / kg x5) and Rituximab (150mg / m2 x1); maintenance: 42=TAC + Everolimus (EVL), 24=TAC + Sirolimus (SRL), 26=TAC alone. Target TAC levels: 10-15ng / ml:0-3 months (mo), 5-10ng / ml:3-6 mo, and 4-6ng / mL:> 6 mo. EVL or SRL started after 30 days with target trough levels of 3-5 ng / mL. AKI was defined by recipients who developed an increase in nadir creatinine and required hospitalizations. Estimated glomerular filtration rate (eGFR) was calculated from routine serum creatinine using the CKD-EPI formula for adults and bedside Schwartz formula for children. Median follow-up: 27 [3-56] mo.

Results: AKI occurred in 26.1% (24 / 92) of Itx; 75% (18 / 24) in the first 6mo. Median eGFR at 2, 3, and 12 mo was 113.5 [85.0-151.4], 99.8 [65.1-131.0], and 97.3 [55.1-125.9], respectively. Operative time wasmarkedly reduced (median time: 288 minutes) as compared to previous eras. Median TAC levels (ng / ml) at 7days and at 1, 2, 3, and 12 mo: 10.6 [7.7-14.1], 10.9 [7.9-14.3], 8.5 [6.8-12.1], 7.5 [5.8-10.5], and 5.7 [7.9-4.0], respectively. Cox regression analysis of the hazard rate (HR) of developing AKI found 2 significant predictors: sepsis (23 / 92, P<.0001) and acute rejection (AR) (7 / 92, P<.0001). Similarly, the HR of developing an eGFR<60ml / min / 1.73m2: older age at transplant (P<.0001), AR (7 / 92, P=.01), and dehydration on > 2 hospitalizations (17 / 92, P=.02). Intestinal graft failure (IGF) occurred in 9 / 92 patients; death with a functioning graft (DWFG) was observed in 12 / 92. Neither the development of an AKI nor an eGFR<60ml / min / 1.73m2 were associated with the HR of developing graft loss (P>.10) or DWFG (P>.5).

Conclusion: Short-term renal dysfunction post Itx still exists. Both surgical modifications and changes in the immunosuppressive regimen have led to diminished AKI and impact on graft failure. Long term follow-up is needed and underway.

P2B20 - Teduglutide Increases Adaptation In A Murine Short Bowel Model By Improving Epithelial Tight Junction Selectivity

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Introduction: Teduglutide is used in chronic intestinal failure in order to reduce the need for and to increase time off parenteral nutrition. A trophic effect is induced through GLP-2 stimulation resulting in an improved uptake of water and sodium. It is unclear if the Claudin-10 and -15 mediated sodium selectivity of the paracellular tight junction in the jejunum is influenced. Thus, the effects of Teduglutide were studied in a murine short bowel model.

Methods: By resecting 40 % of the Ileocecal region (ICR) a severe murine short bowel syndrome was simulated. Subcutaneous Teduglutide (0.1 mg/kg BW) or vehicle administration began 36 h postperatively. Survival, development of body weight, stool consistency, plasma aldosterone levels, tight junction protein expression, FITC-4kDa-Dextran-Flux and dilution potentials using an Ussing chamber were analyzed.

Results: Compared to vehicle, the development of body weight in Teduglutide treated animals was more favourable (weight nadir vehicle: 83,6 ± 1,4 % n=15 vs. Teduglutide 87,8 ± 1,4 % n=12, $p<0.05$). Lower aldosterone levels in Teduglutide treated animals indicated a better volume state in this group (vehicle 988 ± 172 ng/l, n=6 vs. Teduglutide: 512 ± 91.5 ng/l, n=9-11, $p<0.05$). The transmucosal barrier for macromolecules in the jejunum in short bowel conditions increased independently of Teduglutide administration. Occludin and Claudin-15 mRNA expression was increased after ICR, independent of Teduglutide treatment. In the jejunum of vehicle treated animals, cation permselectivity was impaired. At the same time, Claudin-10 mRNA expression in vehicle treated mice was reduced to 55.2 ± 8.5% of baseline, while it was maintained in Teduglutide treated animals at 109 ± 23.7%, n=3-4, $p<0.05$. In line with this, tight junction localization of Claudin-10 faded towards the villus tips in vehicle treated mice while permselectivity and Claudin-10 expression up to the villus tip remained constant in Teduglutide treated animals.

Conclusion: Teduglutide alleviates intestinal insufficiency in this mouse model of short bowel syndrome. Teduglutide not only induces trophic effects but retains epithelial function by maintaining Claudin-10 expression. This translates to improved paracellular cation permeability, facilitating sodium recirculation and thus sodium coupled nutrient transport, leading to improved nutrition status.

POSTERS OF DISTINCTION
FRIDAY JULY 5, 2019
SESSION 1

P3A01 - The first three years of the New Zealand National Intestinal Failure Service: emerging disparities in ethnicity and social deprivation in children with intestinal failure

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Introduction: The New Zealand National Intestinal Failure Service (NZ NIFS) was established in 2015, with the aim of understanding the aetiology and management of intestinal failure (IF) in NZ. One goal of NZ NIFS is to achieve health equity for patients with intestinal failure in NZ.

Method: The NZ NIFS patient registry collected data for patients with intestinal failure in NZ. Intestinal failure was defined by the requirement for intravenous nutrition (IVN) for ≥ 21 days for paediatric patients up to 18 years of age and ≥ 30 days for preterm neonates (< 34 weeks gestation). Data were reported by the primary clinicians of each IF patient in conjunction with the NZ NIFS from October 2015 to October 2018. Demographic data including ethnicity, social deprivation index, cause of IF and clinical outcome were collected.

Results: Data for 208 patients were collected, 116 (56%) were male, 91 (44%) were preterm. Pasifika and Maori children were marginally over represented accounting for 13% and 28% of the patient cohort respectively, compared to 9% and 26% of the NZ paediatric population.

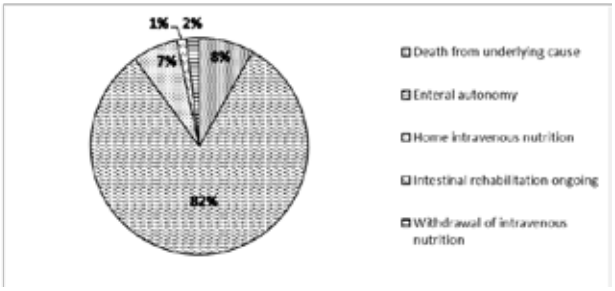
More significantly, IF patients with a high NZ socioeconomic deprivation score were over represented, with 36% in the highest deprivation quintile and 9% in the least deprived quintile, compared to 24% and 19% respectively of the NZ paediatric population.

Most common causes of IF in this group were mechanical obstruction (18%) and short bowel syndrome (18%), although for preterm neonates the prevalence of short bowel syndrome was higher (36%) (Table 1). Ninety seven (47%) children with IF required intravenous nutrition for ≥ 60 days. One hundred and seventy (82%) achieved enteral autonomy, with 14 (7%) discharged on home IVN. No patient required intestinal transplant.

Table 1: Intestinal failure patients in New Zealand by clinical indication

Indication for IVN	Preterm neonates	Paediatric	Total
Abdominal wall defects	10	14	24
Extensive small bowel mucosal disease	0	29	29
Intestinal dysmotility	0	25	25
Mechanical obstruction	10	28	38
Preterm	23	0	23
Short bowel	33	5	38
Other	15	16	31
Total number of IF patients	**91**	**117**	**208**

Figure 1: Clinical outcomes of preterm and paediatric intestinal failure patients in New Zealand



Conclusion: Disease patterns for children with IF are similar to those reported internationally. Future work will focus on further understanding the disparities in ethnicity and social deprivation to achieve equitable outcomes for NZ children with IF.

P3A02 - Racking up the losses: SBS care in Germany - a cost of illness analysis with real life data

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University Hospital of Bonn

Introduction: Short-bowel syndrome (SBS) is considered an orphan disease and no data on the cost of illness (COI) for SBS are available for Germany. This study evaluated the complexity of medical care and economic burden on a center with a specialized intestinal rehabilitation program using real life data.

Methods: 11 consecutive SBS patients of the intestinal rehabilitation program at the University Hospital of Bonn, Germany were included. A total of 979 parameters of treatment-related resources were considered for the year of diagnosis (year0) and a follow-up (FU) of 3 years. This included cost for in- and outpatient care, medication and parenteral nutrition. Subsequently, COI based on these parameters was calculated according to the corresponding service catalogs for Germany.

Results: Median inpatient days were 96 [IQR 59;119] in year0 and decreased to 3 [IQR 0;14] in year3 of FU. In contrast, outpatient visits increased from 1 [IQR 0;11] in year1 of FU to 2 [IQR 0;3] in year3 of FU, with a median of 8 visits [IQR 4;10] per patient in 2017. Median total COI for inpatient treatment amounted to 110889€ in year0. This sum consecutively decreased from 33225€ to 10217€ and 4205€ in year1/2/3 of FU, respectively. While major visceral surgery, open abdomen treatment and reconstructive procedures significantly impacted on COI in year0, catheter-associated complications and related vascular surgery mainly contributed to COI during further follow-up. Contrary to the calculated COI, actual reimbursements for inpatient treatment according to the German Diagnosis Related Groups amounted only to approx. 25%, with a median of 27041€ [IQR 16092;78520]. For outpatient care, calculated median total COI was 3265€ per patient, while reimbursement only amounted to approx. 16.5% (540€) in 2017. Median COI for prescribed medication and parenteral nutrition in 2017 was 6752€ [IQR 4990;15331] and 48485€ [IQR 29740;54442), respectively. Only one patient received GLP-2 analogon treatment, which added 138442€ p.a. to the medication cost for this patient.

Conclusions: The complex medical care required for SBS patients resulted in high COI both for in-and outpatient settings. The identified spectrum of surgical / medical interventions reflected a shift in medical treatment over time. Large discrepancies between COI based on "real life" resource expenditure and actual remuneration were found. This imbalance may endanger adequate care for SBS patients in Germany in the future.

P3A03 - Pre-, peri-, and post-operative predictors of survival after intestinal transplantation: results from a single-center analysis.

Arpit Amin [2], Robert Venick [1], Elizabeth Marcus [1], Joseph DiNorcia III [2], Hasan Yersiz [2], Marjorie-Anne Guerrra [1], Sue McDiarmid [1], Ronald Busuttil [2], Douglas G. Farmer [2]

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Introduction: Intestinal transplantation (ITx) can be a successful procedure for select candidates with intestinal failure (IF). However, there is limited data on variables and characteristics that predict successful outcome. The aim of this study was to analyze a large dataset to determine outcome predictors.

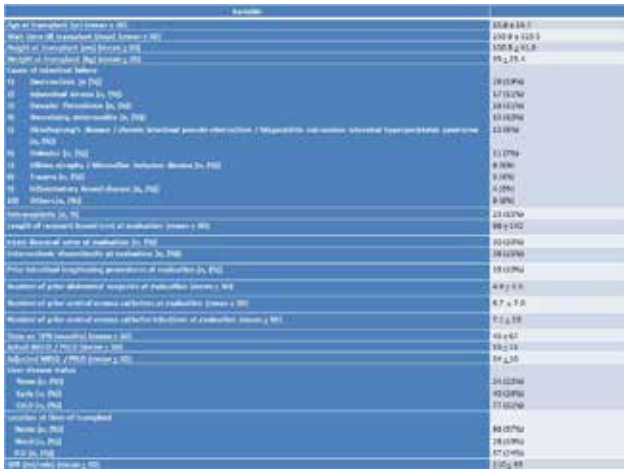
Methods: An IRB approved, prospective database has been maintained since the inception of the program in 1991. Patient inclusion was closed in December 2018. All recipients of intestinal grafts were included. Multiple pre-, peri, and post-transplant variables (n = 35) were collected and included in the analysis. The end point was 1-year patient and graft survival. Standard statistical analysis was undertaken.

Results: 128 patients underwent 151 ITx including 35 isolated intestine (I-ITx), 77 liver-intestine (OLT-SBT), 29 multivisceral (MVT) and 11 modified multivisceral (MMVT).

58% were male, 78% were children, and 77% had surgical IF etiologies. At ITx, the median MELD / PELD at ITx was 34 with 43% hospitalized.

The majority of patients received induction immunotherapy with either interleukin-2 receptor antagonist [IL2RA] (58%) or antibody induction with rabbit antithymocyte globulin [rATG] / OKT3 (34%).

Relevant patient clinical characteristics are summarized in the table below:



Significant predictors for improved graft survival were:

Recipient weight (<20 kg), age group (pediatrics), graft type (liver inclusive intestinal graft), panel reactive antibody < 20%, absence of donor specific antibodies, negative crossmatch, warm ischemia time < 1 hr, use of induction immunosuppression, ventilator time < 7 days, length of stay < 80 days, and transplant era (2001-2018).

Significant predictors for improved patient survival were:

Cold ischemia time < 10 hrs, warm ischemia time < 1 hr, absence of recipient splenectomy, use of induction immunosuppression, length of stay < 80 days, and transplant era (2001-2018).

The patient and graft survival at 1-year was 82% and 69%.

Conclusion: The results of ITx have improved over time. Several perioperative factors were identified that impact early outcome. Especially important for graft survival are variables that can be altered including donor: recipient match, preformed donor specific antibodies, ischemia times, and immunosuppression. Further investigations are required to improve ITx outcomes.

P3A04 - Cost-effectiveness of teduglutide in adult patients with intestinal failure: Markov modeling using traditional cost-effectiveness criteria

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Background: Adults with intestinal failure often undergo rehabilitation with the goal of enteral autonomy. However, at 5 years, intestinal failure has a 25% mortality with nearly half of the survivors remaining on parenteral nutrition (PN)[1]. Teduglutide is a GLP-2 analogue that promotes intestinal adaptation and can decrease PN dependence, resulting in enteral autonomy in some and decreased PN in many more. Unfortunately, teduglutide, an orphan drug, is expensive with an estimated cost of over $400,000 per year. The current study evaluated the cost-effectiveness of using teduglutide in adult patients with intestinal failure.

Methods: A Markov model was used to evaluate the costs (in US dollars) and effectiveness (in quality-adjusted life years or QALYs) of treatment with a presumed starting age of 40 years. Parameters were obtained from published data or estimation. The primary effect modeled was the increased likelihood of reduced PN days / week when using teduglutide, leading to greater quality of life and lower daily PN costs. Future costs and utilities were discounted at 3% per year. Sensitivity analyses were performed on all model parameters.

Results: In the base scenario, teduglutide cost $949,910 / QALY gained. On one-way sensitivity analysis, only reducing teduglutide cost decreased the cost / QALY gained to below the typical threshold of $100,000 / QALY gained. Specifically, teduglutide cost would need to be reduced by over 65% for it to reach the threshold value (Figure 1). Probabilistic sensitivity analysis favored no teduglutide in 80% of iterations at a $100,000 / QALY threshold (Figure 2). However, 13% of iterations actually found teduglutide therapy to be cost-saving.

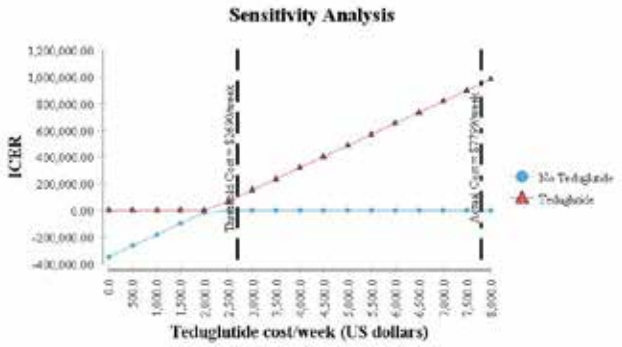

Figure 1. One-way sensitivity analysis of the effect of cost of teduglutide on incremental cost-effectiveness ratio.

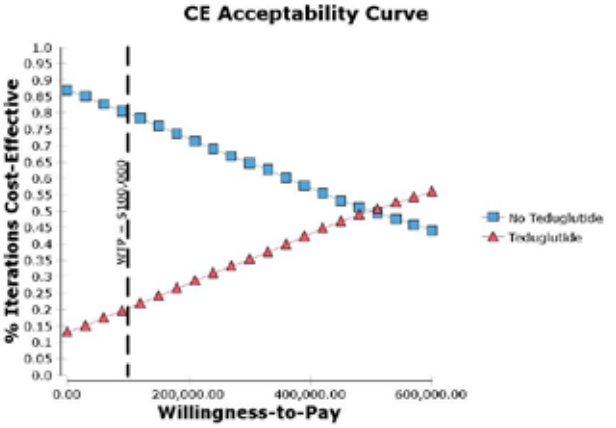

Figure 2. Cost-effectiveness acceptability curve from probabilistic sensitivity analysis.

Conclusions: In summary, teduglutide does not meet a traditional cost-effectiveness threshold as treatment for PN reduction in adult patients with intestinal failure compared to standard intestinal rehabilitation. Subpopulations that demonstrate maximum benefit could be cost-saving. Addressing cost alone would require a significant reduction in teduglutide price to improve cost-utility.

References

1. Messing, B., et al., Long-term survival and parenteral nutrition dependence in adult patients with the short bowel syndrome. Gastroenterology, 1999. 117(5): p. 1043-50.

P3A05 - Young donors (age ≤ 6 months) for Intestinal transplantation (ITX): are they high risk?

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Introduction: ITX is accepted treatment for children with irreversible intestinal failure. Shortage of size matched organs for children especially those with restricted abdominal domain due to various aetiologies resulted in development of various techniques including use of organs from young donors. There is no data on the utilization and outcome of young donors in ITX.

Subject and Methods: Retrospective review of medical records between 1993-2018 of all ITX from donors less than 6 months of age . Donor and recipients demographics, intra and early post-transplant complications, short and long term graft and patient outcome were analysed.

Results: 4 females median age 20 months & weight 9kg underwent ITX from young female DBD donors median age 3.5 months & weight 6kg with median donor to recipient weight ratio 0.5 (Table 1). All donors with brain death, blood group identical / compatible with median cold ischemia time 5.5 hours. No surgical complications noted intra or early post-transplant. Two died early within 3 months of ITx following severe acute rejection. One established early full enteral feeding and required laparotomy for stoma prolapse 3 months post ITX, but eventually died secondary to complications. The second child took longtime to establish feeding due to fluid and electrolyte imbalance , but eventually died following complications associated with stoma closure. One year patient and graft survival was 50%, whilst 3 year patient and graft survival was 0%.

Recipient age months	Recipient age kg	Donor age months	Donor weight Kg.	ITx graft with liver	Complications	Survival months
21.6	9.3	6.6	7	No	GVHD,PTLD	18.27
18.	8.6	2.9	5	Yes	GVHD	26.3
20.9	8.7	1.9	4.5	Yes	Severe rejection	2.6
19.6	13	4.2	6	Yes	Severe rejection	1.4

Conclusion: It is technically feasible to consider young donors for intestinal transplantation. In our experience it is associated with a high mortality. Further investigation to understand the complex interactions between the naive immune system of the young donors with the mature immune system of the older recipients may hold the key to understanding the development of the immunological complications.

P3A06 - Muscle mass after intestinal transplantation in children is greater than in those on home parenteral nutrition

Kushila Rupasinghe [1], Jonathan Hind [1], Girish Gupte [2], Pamela Allen [1], Hina Rizvi [2], Arif Wahid [2], Carly Bambridge [1], Dhamyanthi Thangarajah [1]

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Introduction

Sarcopenia or loss of lean muscle mass is associated with disease states and malnutrition. The effects of both are noted in intestinal failure, intestinal transplant, and adult liver transplantation outcomes. Psoas muscle cross sectional area (PCA) is a validated proxy marker of muscle mass. We look to characterise it in home parenteral nutrition (HPN) and intestinal transplant (IT) patients. Determinants of PCA were explored in IT patients.

Methods

This was a multi-centre, retrospective, case-notes based study. Existing axial imaging was analysed, pre- and / or post-transplant. Control images were from a trauma series of healthy children. The PCA was measured at L4 with the psoas muscle examined for ectopic fat content and perinephric fat presence, a validated marker of visceral adipose tissue. Univariate and linear regression analysis was used to identify factors associated with PCA.

Results

At total of 81 children were included in the study. 51 with intestinal failure or post-transplant (males=26) and 30 controls (males=22).

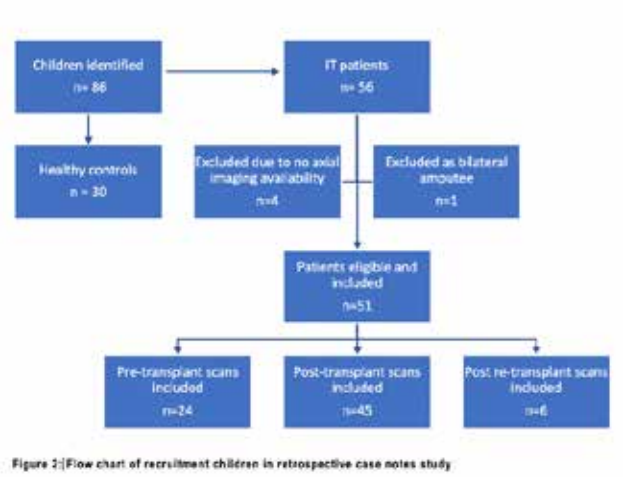

Figure 1:|Flow chart of recruitment children in retrospective case notes study

106 scans were analysed with 24 HPN (males=12) and 43 IT (males=23). See figure 2. In the HPN and IT groups after adjusting for sex, age and pubertal status, PCA was found to be significantly lower than controls; HPN having 1.51cm^2 and IT patients having 1.13cm^2 smaller PCA than controls ($p < 0.05$). In the total intestinal rehabilitation (HPN and IT) group, after adjusting for sex, age and pubertal status, PCA was 1.66cm^2 larger in the IT group than those on HPN ($p < 0.05$). Length of stay in intensive care was a negative predictor of PCA. There was a trend toward lower PCA in patients that had died. IT had significantly more psoas fat than controls ($p < 0.05$) and demonstrated presence of peri-nephric fat on more occasions than controls ($p < 0.05$).

	Control	HPN	p	IT	p
n	30	24		28	
Age	7.99±5.05	4.81±3.67	<0.05**	7.51±4.59	0.69*
Time between scan and transplant	-	404.5 days [174.25 to 654.75]	-	593 days [93.75 to 1119.75]	0.42
Psoas Area (cm^2)	9.6 [7.56 to 19.78]	5.14 [3.77 to 6.16]	<0.05††	8.06 [5.95 to 10.98]	<0.05††
Height (cm)		97.4±4	<0.05**	114.51±24.4	0.12*
Weight (kg)		16.1 [8.4 to 21.72]	<0.05††	19.56 [16.06 to 30.93]	0.16†
BMI		16.8±1.8	0.59*	17.65±2.06	0.52*

Figure 3: Control vs HPN and control vs IT. Measures are mean ± standard deviation or median [interquartile range]. P values calculated from independent t-tests for Gaussian data denoted by *, except where calculated by Mann-Whitney U tests for non-Gaussian data denoted by †. p<0.05 denoted by ** or ††.

Conclusion

IT is associated with greater muscle mass when compared to HPN. This suggests improved nutritional status after transplantation. Adiposity was found to be aberrant in IT patients. PCA is a novel biomarker of nutritional status and may be developed further in intestinal rehabilitation.

P3A07 - Impact of Donor and Recipient CYP3A5 and ABCB1 Genotype on Tacrolimus Trough / Dose Ratios Following Intestinal Transplant

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Introduction: Tacrolimus (TAC) is a mainstay of immunosuppression after intestinal transplantation (ITX), but dosing is complicated by a narrow therapeutic index and broad variability. Studies in kidney and liver transplantation have identified the influence of *CYP3A5* and *ABCB1* genetic variants, both of which are expressed in the intestinal epithelium, on TAC pharmacokinetics; however, no studies have examined the influence of pharmacogenetic (PGX) variation on TAC exposure in ITX.

Methods: This was a single-center, retrospective analysis of adult ITX recipients from 2011-2018. Patients were included if they received a non-liver containing ITX, maintained graft function for 3 months, and had donor and recipient tissue samples stored. DNA was isolated from sample tissue and multiplexed genotyping of *CYP3A5**2,*3,*7 and *ABCB1*c.3435C>T was performed. Donors or recipients with a *1 allele were *CYP3A5* expressers, while patients with a CC genotype were *ABCB1* expressers. A combined analysis was also performed that grouped patients by total donor and recipient *CYP3A5* and *ABCB1* allele score. Weight-normalized TAC trough:dose (T/D) ratios were assessed for each patient during month 1 and at 4, 12, and 52 weeks post-ITX. The primary outcome was difference in mean T/D ratios between the genotypes across time points.

Results: A total of 31 patients were included in the analysis (Table 1). After genotyping, 22.6% of recipients and 32.3% of donors were *CYP3A5* expressers; and 35.5% of recipients and 25.8% of donors were *ABCB1* expressers. Donor or recipient expressers of *CYP3A5* or *ABCB1* had lower T/D ratios at 4, 12, and 52 weeks relative to non-expressers (Figure 1). When both donor and recipient genotype were considered for *CYP3A5* and *ABCB1*, combined non-expressers had the highest T/D ratios, indicating lower dosing requirements. Based on allele score, 5 patients were classified as low score (≤1 active allele), 14 patients were moderate score (2-3 active alleles), and 12 patients were high score (≥4 active alleles). Patients with low allele scores had the highest T/D ratios as well as the highest percentage of therapeutic TAC levels within 1 month of ITX (53.2%vs34.4%vs38.9%;p=0.04).

Conclusion: In the first study evaluating PGX in ITX, our results suggest that both donor and recipient *CYP3A5* and *ABCB1* expression impact TAC dosing. When both genotypes are combined it may be possible to predict patients at high risk for subtherapeutic TAC dosing.

Table 1 – Baseline Characteristics

Baseline Demographics	Study Cohort (n = 31)
Recipient Age, years	46.0 ± 10.2
Donor Age, years	9.5 ± 8.1
Male Recipient Sex	12 (38.7%)
Recipient Ethnicity	
White/European	18 (58.1%)
African-American	6 (19.4%)
Hispanic/Latino	6 (19.4%)
Asian/Pacific Island	1 (3.2%)
Recipient Weight, kg	61.7 ± 12.5
Transplant Type	
Isolated Intestine	23 (74.2%)
Intestine-Kidney	5 (16.1%)
Intestine-Pancreas	3 (9.7%)
Baseline Serum Creatinine, mg/dL	1.2 ± 1.0
Baseline Total Bilirubin, mg/dL	1.1 ± 1.1
CYP3A5 Genotype	
De/Re	1 (3.2%)
De/Rn	9 (29.0%)
Dn/Re	6 (19.4%)
Dn/Rn	15 (48.4%)
ABCB1 Genotype	
De/Re	4 (12.9%)
De/Rn	4 (12.9%)
Dn/Re	7 (22.6%)
Dn/Rn	16 (51.6%)
Combined Analysis	
Low Allele Score (0-1)	5 (16.1%)
Moderate Allele Score (2-3)	14 (45.2%)
High Allele Score (4-5)	12 (38.7%)

Figure 1 – Weight-Normalized Trough:Dose Ratios by Donor and Recipient Genotype

P3A08 - Risks of the excluded bowel in patients with total intestinal Hirschsprung disease

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Introduction: Management of intestinal failure secondary to LSHD is based on parenteral nutrition (PN) associated to proximal jejunostomy. Early prophylactic subtotal enterectomy (SE) is not recommended since the excluded intestine allows growth of the abdominal cavity, which may be needed to host a graft in case of intestinal transplantation. This study evaluates the risk of enterocolitis linked to the excluded bowel in such patients.

Methods: The charts of all patients with LSHD requiring PN and enterostomies, managed from 1986 to 2017 in our institution, were reviewed. Subtotal enterectomy was performed, in our center, only after occurrence of complications due to the excluded bowel. Two patients underwent a subtotal enterectomy during the initial management and before referral to our center. They were excluded from this study.

Results: Twenty seven patients were included.

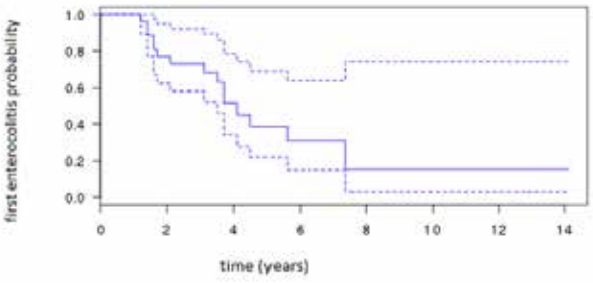
Initial management resulted in totally diverting jejunostomy in 26 patients and a loop jejunostomy in one (median length from duodeno-jejunal flexure to stoma 30 cm [0-90 cm]).

Sixteen patients (59.2%) presented at least one episode of enterocolitis (EC). Median age at first EC was 2.2 years [0.3- 7.1]. Fifteen underwent a subtotal enterectomy (4 as an emergency procedure for). Median age at SE was 3.1 years [1.3- 7.4].

Three patients underwent a longitudinal seromyotomy with transfer of the jejunostomy downstream at initial management for one and at the time of subtotal enterectomy for two (9 months and 4 years).

13 patients underwent transplantation later (7 liver+ intestinal and 6 intestinal).

Conclusion: Patients with LSHD carry a high risk of early complications linked to the excluded bowel. Since there is a paradigm shift regarding the indications of intestinal transplantation in patients with intestinal failure, these data represent a first step to better evaluate the benefice / risk balance of preserving the excluded bowel for growth of the abdomen in view of eventual intestinal transplantation. Furthermore, the risks of repeated sepsis on long term liver function should also be assessed in order to discuss more rationally the better timing of enterectomy in this population having already PN and its associated risk of liver disease.



P3A09 - Physical activity, strength and fatigue in children with intestinal failure on parenteral nutrition

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[2] Department of Rehabilitation Services, The Hospital for Sick Children, Toronto, Canada
[3] Transplant and Regenerative Medicine Centre, The Hospital for Sick Children, Toronto, Canada
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Introduction: With improved survival of children with intestinal failure (IF), it is important to explore the subsequent impact on long-term physical function. This study evaluates functional outcomes of muscle strength, fatigue and physical activity (PA) and identifies clinical factors that may be predictive of impairment.

Methods: Cross-sectional study in children with IF on long term parenteral nutrition (PN) compared to healthy age and gender matched controls (HC's). Assessments included: Bruininks-Oseretsky Test of Motor Proficiency-2 (Strength and Agility subtest) (BOT-2), Grip strength, Paediatric Quality of Life (PedsQL) Physical Function subscale and Multi-Dimensional Fatigue Module, and Benefits / Barriers to PA Questionnaire. PA was measured using an accelerometer. Medical data was collected by chart abstraction.

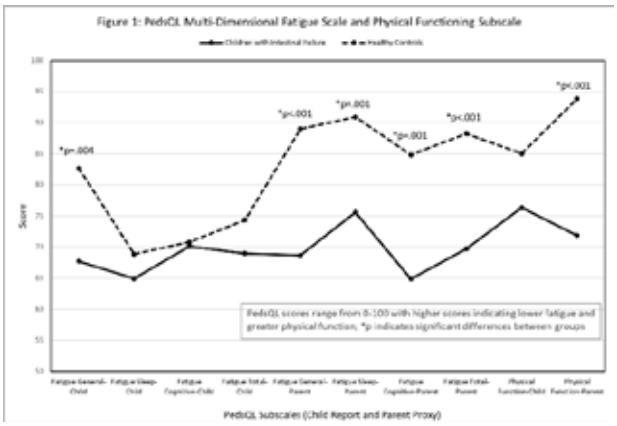
Results: Participants included 21 children with IF (14 male) at a median age of 8.33 (IQR 6.96, 11.04) years and 33 HC's (20 males), 8.25 (6.67, 10.79) years. In those with IF, 13 (62%) were born prematurely (gestational age 35 (33, 38.5) weeks) and the most common diagnosis was gastroschisis (38%). Children received PN for 14 (11, 16) hours / day, with 17 (81%) dependent since infancy. Since birth, there was a median of 4 (1, 9) septic episodes and 15 (7.5, 24.5) in-patient hospitalizations. Mean BOT-2 standard scores [population norm of 50, SD of 10] were 61.27 +/- 6.8 for HC's and 45.67 +/- 9.1 for children with IF, with 6 / 21 (28%) below average (>1SD below mean). 13 / 21 (62%) children fell >1SD below the mean norm for grip strength, compared to only 6 / 33 (18.2%) HC's. Mean steps / day in children with IF was 9842 +/- 4077 compared to HC's with 13104 +/- 5416. There was a significant difference between groups in strength and agility (p<.001), grip strength (p=.001), and total steps / day (p=.047). Medical variables significantly associated with BOT-2 scores are shown in Table 1.

Table 1
Medical Factors Significantly Correlated with BOT-2 Strength and Agility Standard Scores

Medical Factor	R-value*	p-value
Gestational Age	0.458	0.037
Birth Weight	0.546	0.010
Height Z Score	0.506	0.019
# of In-patient Hospitalizations/Year of Life	-0.526	0.014
Length of Hospital Stay (Days)/Year of Life	-0.441	0.045
# of Septic Events in first year of life	-0.462	0.035
# of Septic Events/1000 PN Line Days	-0.575	0.006

*Spearman Correlations

Results of the PedsQL are shown in Figure 1.



Parents report greater fatigue (r=-.538, p=.012) and poorer physical function (r=-.650, p=.001) in children with more hospitalizations. Barriers to PA in children with IF included "I am tired" and "I am worried about my line."

Conclusion: Factors such as prematurity, decreased linear growth, hospitalization and septic events may have a significant impact on physical function outcomes in children with IF on PN. Ongoing development of medical and rehabilitation intervention strategies is vital to optimize outcomes.

P3A10 - Accumulated experience with Sirolimus in Pediatric Intestinal Transplantation

Ane Andres [1], Francisco Hernandez-Oliveros [1], Alba Bueno [1], Alba Sanchez-Galan [1], Javier Serradilla [1], Esther Ramos [2], Alida Alcolea [2], Miriam Nova-Sanchez [2], Manuel Lopez-Santamaria [1]

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[2] *Pediatric Gastroenterology. Hospital La Paz. Madrid. Spain.*

Introduction: The aim was to update our experience with Sirolimus (SRL) in intestinal transplanted (IT) pediatric patients.

Patients and methods: Between 1999 and 2018, 107 TI in 83 patients were performed at a median age of 38 months at transplant (range 6 m- 30 yo); 18 were retransplanted, 6 of them twice. Initial manteinance treatment protocol was Tacrolimus (TAC). Those patients who were partially or completely converted to SRL were retrospectively reviewed.

Results: Since 2008, SRL was used in 31 patients, after a median of 17 months since transplant (range 1 m- 6 years). The main indication was TAC toxicity in 16 (worsening of the renal function +/- hypertension in 13, hypertrophic myocardiopathy in 2, neuropathy in 1) and/or immunological complications in 17 (chronic rejection in 1, hemolytic anemia in 7, GVHD in 5, PTLD in 3, and neutropenia in 1). On the other hand, 10 patients had past medical history of rejection (6 of them moderate/severe), 9 had suffered GVHD, and 8 patients had been retransplanted prior to the conversion. Sirolimus was indicated alone in 20 patients when TAC was contraindicated and combined with TAC in 12 with higher risk of rejection, such as in retransplanted patients.

After a median follow-up of 77 months (1m-11years), the renal function improved in all patients along the follow-up (mean cistatine levels decreased from 3,50±0,52 mg/dl to 1,14±0,31). We did not find more immunological complications after the conversion to SRL compared with those patients on TAC. Six patients died, due to the progression of chronic rejection (1) or GVHD (4), having appeared these complications before the conversion. However, 2 patients developed chronic rejection after the conversion, one of them has recently been retransplanted after 12 years since the first ISBT (10 years with SRL). The second one died 7 years after his third transplant, having taken SRL for the 3 last years. The other 25 are doing well with normal graft function. At the moment of the study, 47 of the global series are alive and 25 of them are on SRL.

Conclusions: Although TAC remains to be the maintenance treatment of choice in IT, half of our alive patients needed conversion to SRL along the follow-up. It seems safe and effective, although it does not totally prevent from immunological complications either. Accumulated experience is encouraging to widen its use in younger children, complex scenarios and after less time elapsed since transplant.

POSTERS OF DISTINCTION
FRIDAY JULY 5, 2019
SESSION 2

P3B11 - Analysis of immune cells draining from the abdominal cavity as a novel tool to study intestinal transplant immunobiology. Prospective multicenter study - INIGMA project.

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We proved that abdominal drainage fluid collected after intestinal transplant (ITx) contains mainly immune cells trafficking from the implanted intestine, and changes of immune cell composition, especially increase of neutrophils, correlated with the appearance of future clinical events (rejection, infection or other events). During the 14th ISBTS meeting, the development of a prospective multicenter study to analyze the role of performing daily analysis of drainage samples that might serve as a reliable tool for predicting clinical events, was proposed. We aim to present the preliminary results of the INIGMA (International Network for Intestinal Graft Monitoring and Analysis) project.

Material and Methods: This is a prospective study started in 2008 by Favaloro University Hospital, Argentina, and evolved as a multicenter study in 2015, including the University of Gothenburg, Sweden; University of Leuven, Belgium and La Paz University Hospital, Spain. The cell composition of the abdominal draining fluid and blood was analyzed during the first post-op days by differential cell counter and correlation with clinical follow-up was evaluated.

Results: 3 of the 4 centers enrolled 28 patients (pts) with complete biochemical and clinical information (Table 1). The cell composition differs from blood and draining fluid; independently of the immunosuppressive protocol used, blood samples obtained the day of the Tx showed an almost complete lymphopenia, while neutrophils were the main population (19/28 pts). In the drains, lymphocytes were the main population counted in non-complicated pts from post-op day 3 to 4 onwards (7/28 pts). When a new shift to a neutrophil dominant content is observed in the drainage, it anticipates the development of a clinical event in the peritoneal cavity (18/28 pts).

Table 2 summarizes the correlation between neutrophils and clinical events; Fischer test: p=0.0002. Sensitivity=90%; Specificity=86%; PPV=94.7%, NPV=75%.

Conclusion: this study supports the concept that multicenter studies are feasible in our field. This analysis validates the findings of the original report, and provides further support to use this innovative approach to monitor the grafts and the transplanted pts. Cell counts from the drainage should be included as part of the daily evaluation of pts receiving an ITx, any shift from lymphocytic to neutrophilic dominance predicts the occurrence of a clinical events, requiring attention, early confirmation and treatment.

Table 1. Patients' characteristics

Center. Pts	Age (years)	Primary pathology	IR (Ind/Main)	Type	Post-Tx clinical event	Group
1.1	9	SBS - volvulus	Simul/TAC, St, MMF	Isolated	No	No event
1.2	4	SBS - volvulus	Simul/TAC, St, MMF	Isolated	No	No event
1.3	7	SBS - volvulus	Simul/TAC, St, MMF	Isolated	No	No event
1.4	23	SBS - trauma	Simul/TAC, St, MMF	Isolated	No	No event
1.5	3	SBS - gastroschisis	Simul/TAC, St, MMF	Isolated	Peroral herpes lesions	No event
1.6	53	SBS - volvulus	Simul/TAC, St, MMF	Isolated	No	No event
3.1	32	SBS	Simul/TAC, St, MMF	Multivisceral	No	No event
3.2	22	SBS	Simul/TAC, St, MMF	Multivisceral	No	No event
1.7	7	Abdominal tumor	ATG/TAC, St, Sir	Multivisceral	Ileal biopsies, mild rejection	Rejection
1.8	1.2	SBS - necrotizing enterocolitis	Simul/TAC, St, MMF	Combined	Ileal biopsies, mild rejection	Rejection
1.9	2	SBS - thrombosis	Simul/TAC, St, MMF	Isolated	Diarrhea, normal ileal biopsies, neg. virological tests, isolated jejunal rejection	Rejection
1.10	5	Re-transplant, CR	Simul/TAC, St, MMF	Multivisceral	Peritonitis, *Enterococcus faecalis*	Infection
1.11	25	SBS - post-surgical complications	Simul/TAC, St, MMF	Isolated	Abdominal collection, *Klebsiella pneumoniae*	Infection
1.12	6	SBS - volvulus	ATG/TAC, St, Sir	Isolated	Peripancreatic abscess, *Klebsiella pneumoniae*	Infection
1.18	28	Nephronophthisis-(Cocoon syndrome)	rATG/TAC, St, MMF	Combined (with Kd)	Peritonitis (dehiscence of colon anastomosis),*Candida albicans Enterococcus avium*	Infection
2.1	30	SBS - volvulus	Alemt/TAC, St	Multivisceral	Wound infection	Infection
2.3	18	SBS - Hirschsprung	Alemt/TAC, St	Multivisceral	Abdominal collection, *Candida albicans*	Infection
2.6	4	Epithelial dysplasia	Simul/TAC, St	Multivisceral	Diarrhea, *Cryptosporidium*	Infection
2.9	16	Intestinal pseudo-obstruction	ATG/ TAC, St, Ritux	Multivisceral	Abdominal collection, *Candida albicans*	Infection
1.13	0.9	SBS - Hirschsprung	ATG/TAC, St, Sir	Isolated	Pancreatitis, Hematoma	Others
1.14	55	SBS - ischemia	ATG/TAC, St, Sir	Isolated	Chylous ascites	Others
1.15	3	SBS - Hirschsprung	Simul/TAC, St, MMF	Isolated	Uncharacterized diarrhea/ fever	Others
1.16	9	SBS - volvulus	ATG/TAC, St, Sir,	Isolated	Eosinophilic gastroenteritis	Others
1.17	47	SBS - trauma	Simul/TAC, St, MMF	Isolated	Hematoma abdominal wall/ mild intra-abdominal fluid	Others
1.19	43	SBS - volvulus	rATG/ TAC, St, Sir	Combined	Uncharacterized fever	Others
1.20	48	SBS	rATG/TAC, St, MMF	Isolated	Chylous ascites	Others
2.2	9	Mesenteric thrombosis	Simul/TAC, St	Multivisceral	Bleeding from the gastric anastomosis	Others
2.8	17	Intestinal pseudo-obstruction	Alemt/TAC, St	Modified multivisceral	Bleeding from the gastric anastomosis	Others

CR, chronic rejection; IR, immunosuppressive regimen; Ind, Induction; Main, maintenance; Simul, Simulect; Alemt, Alemtuzumab; SBS, short bowel syndrome; Tx, transplant; TAC, tacrolimus; Sir, sirolimus; St, steroids; MMF, mycophenolate mofetil; Ritux, rituximab.

Table 2. Correlation of neutrophils appearance and clinical events

Patient	Group	Neutrophils presence (days post-Tx)	Post-Tx day of event	Clinical event
1.7	Rejection	6	7; 10; 14	Mild rejection
1.8	Rejection	9	11; 13; 17; 23	Mild rejection
1.9	Rejection	4	5	Isolated jejunal rejection
1.10	Infection	9	10	Peritonitis, *Enterococcus faecalis*
1.11	Infection	8; 10	8	Abdominal collection, *Klebsiella pneumoniae*
1.12	Infection	5; 9	7	Peripancreatic abscess, *Klebsiella pneumoniae*
1.18	Infection	4; 5; 9; 12; 15; 17; 19	7; 11; 15; 19	Peritonitis, *Candida albicans, Enterococcus avium*; *Re operation* (Dehiscence suture colonic stump); Mild rejection; Severe rejection.
2.1	Infection	1-6; 14	2; 8	Surgical wound infection *E. coli, E. cloacae, E. faecium* infection
2.3	Infection	3; 5	3; 7; 8	Mesogastric abscess *Candida albicans*; Fever; Drainage abscess
2.9	Infection	3; 4	3	Abdominal collection, *Candida albicans*
1.13	Others	4; 12; 13	10	Pancreatitis, Hematoma
1.14	Others	5; 8; 9	11	Chylous ascites
1.15	Others	5	8	Uncharacterized diarrhea/ fever
1.16	Others	7; 9; 12	12	Eosinophilic gastroenteritis
1.17	Others	6, 8; 10	Unclear	Hematoma abdominal wall
1.19	Others	8, 9, 10	8	Uncharacterized fever
1.20	Others	7, 9, 12	14	Chylous ascites
2.2	Others	5	5	Bleeding from the gastric anastomosis

P3B12 - Spiral intestinal lengthening and tailoring (SILT) as a rescue procedure for SBS patients with difficult clinical situations.

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Introduction: Autologous gastrointestinal reconstructive (AGIR) procedures are essential component of intestinal rehabilitation program for patient with short bowel syndrome (SBS). Unfortunately, several patients develop postoperative bowel re-dilatation with loss of bowel adaptation. Spiral intestinal lengthening and tailoring (SILT) technique promises to regain intestinal physiology by tailoring the bowel even if there is no massive bowel dilatation. The aim of this study was to report our experience using SILT in SBS with difficult clinical situation.

Methods: Retrospective review of the single AGIR surgeon was performed from 2012 to date. Patients' demographics, pre- and post-procedure bowel length, surgical complications, and postoperative parenteral nutrition (PN) requirements were analyzed. Data were compared using independent samples, Mann-Whitney's U-test. Data were expressed in mean (IQR)

Results: 9 children with SBS underwent SILT between 2012 and 2017. Rescue SILT was performed in 4 patients with age at procedure of 58.5 months (45-143.3). 3 patients had previous STEP in history of SBS post gastroschisis while one had mild dilatation after AGIR due to long segment Hirschsprung. Preoperative small bowel length measured 66 cm (49.5-75.7) with a diameter of 7 cm (6-8). SILT allowed a median increase in length of 68.5% (p=0.34) and a significant tailoring of the dilated segment providing a reduction in diameter of 63% (p=0.02). No major complications related to SILT were encountered and none of the children required further surgical intervention following a follow-up of 6.5 months (4.5-39.6). Interestingly, a significant reduction of PN requirement at 4 months (p=0.02) associated with improve of liver function was reported.

Conclusion: In this study SILT was reported to have no peri-operative complication and to have good results in complex SBS patients. This procedure offers a safe alternative for SBS children after the failure of conventional AGIR procedures.

P3B13 - Impact of CMV donor-recipient serostatus on long term intestine transplant outcomes

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Background: Donor/Recipient CMV mismatch is a controversial exclusion criteria for graft selection in intestinal transplantation. Case experience was reviewed to determine impact of D/R CMV serostatus on patient and graft survival, CMV disease and resistance.

Aim: To determine the impact of D/R CMV serostatus on patient and graft survival and CMV disease in recent era.

Methods: All children with primary Intestinal transplant between 2001-2016 were analyzed for CMV D/R serostatus and patient outcomes.

Results: 163 Children received primary allografts (74 isolated intestine, 58 liver intestine, 24 multivisceral, 7 modified multivisceral grafts) between 2001-2016. Patient and graft survival were 69% and 53% at 109 months. Outcomes by CMV serostatus are listed in Table 1. CMV prophylaxis consisted of ganciclovir X 14 days in all cases except CMV +/- where the ganciclovir course is followed by 3 months of PO valganciclovir and CMV immunoglobulin at 72 hours, 2,4,6,8, 12, and 16 weeks post operatively.

Conclusions

- CMV serostatus for D/R is an important consideration in intestine transplantation but mismatch is not associated with increased graft or patient morbidity.
- Tissue-invasive CMV disease is significantly more frequent in recipients that receive organs from CMV + donors but can be managed with monitoring and current treatment.

P3B14 - Glucocorticoid treatment improves enteral feeding tolerance in pediatric short bowel syndrome patients with chronic intestinal inflammatory changes

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Introduction: Studies suggest that chronic local and systemic inflammation are related to short bowel syndrome (SBS). We believe that glucocorticoids may reduce inflammation and improve enteral tolerance in pediatric SBS patients. A group of patients from our intestinal rehabilitation program developed chronic intestinal inflammation under biopsy while struggling weaning off parenteral nutrition (PN). We treated them with oral prednisolone taper, maintenance budesonide and sulfasalazine. We will describe the treatment outcome.

Method: Our study included 15 patients whose lab values, pathology results and clinic notes were reviewed, and excluded patients who took steroids for post-transplant immunosuppression or severe food allergy to maintain the homogenous of our patient cohort.

Results: The most common reason for SBS was gastroschisis. The small bowel length range was 20-108 cm. Thirteen patients had more than ½ colon remaining. The median age of starting steroid therapy was 3.3 years. Twelve patients had decreased PN calorie count or normalized follow-up histology. Six patients were able to wean off PN completely with median treatment duration of 5 months, five of which remained on maintenance budesonide for significant period of time (median: 7.5 months), the other one had steroids stopped 5 months before being off PN due to clinical improvement and concern for medication noncompliance. Six out of fifteen children had significant eosinophils in their initial biopsy, five were able to wean off PN while one had significant symptom improvement (GI bleeding stopped). Two patients were not on steroids continuously, as they resumed steroids months later due to histological recurrence of the chronic inflammatory process. Three patients were still not able to be cut down PN calorie. Two patients' intestinal biopsies findings were still consistent with chronic inflammatory process.

Conclusion: For SBS children with histologically confirmed chronic intestinal inflammatory changes, steroid therapy may help to promote enteral feeding tolerance and wean off PN. Patients may respond better if their initial histology has chronic intestinal inflammation with significant eosinophilic infiltrate. Patients may need to remain on maintenance steroids for a period of time even if they were able to wean off PN or significantly reduce PN calories as they may experience regression on enteral tolerance or evidence of GI bleeding as weaning off steroids is attempted.

TABLE 1 Demographic and Basic Treatment Information of Study Subjects

ID	Sex	Race	Primary diagnosis	Intestinal anatomy	Age of starting steroid therapy (years)	Initial intestinal histology before starting steroid therapy	Duration of steroid therapy before study ended (months)	Duration of steroid therapy before off PN (months)	Duration of maintenance therapy (months)	Follow-up intestinal histology	Weaning off PN Y/N
1	M	American Indian or Alaskan Native	Gastroschisis	80 cm small bowel + ½ colon	10	Small bowel bacteria overgrowth and many lymphocytes	12	N/A	N/A	No follow-up studies	N
2	F	White	Gastroschisis and small bowel volvulus	70 cm small bowel + transverse and descending colon	5	Chronic mild non-specific small bowel inflammation	58	N/A	N/A	Normal histology after 33 month therapy	N
3	M	White	Gastroschisis	50 cm small bowel + ½ colon	3	Chronic enteritis	64	N/A	N/A	Normal histology after 59 month therapy	N
4	M	Hispanic or Latino	Necrotizing enterocolitis	20 cm small bowel + whole colon	3	Increased eosinophils in small bowel and colon	54	N/A	N/A	Continued eosinophils in distal small bowel and colonic enterocytes, 3 episodes of acute small bowel inflammation	N
5	F	African American	Midgut volvulus	40 cm small bowel + whole colon	4	Mild intraepithelial lymphocytes	44	36	8	Normal histology after 32 month therapy	Y
6	F	White	Gastroschisis and intestinal atresia	45 cm small bowel + ½ colon	4	Numerous eosinophils in small bowel	20	5	13	No follow-up studies	Y
7	F	White	Intestinal atresia and gastroschisis	65 cm small bowel + transverse and descending colon	3	Villous blunting and inflammation in small bowel and colon, Gastritis with focal eosinophils	39	6	33	No diagnostic abnormality 3 months after off PN	Y
8	M	White	Gastroschisis	32 cm small bowel + transverse and descending colon	1	Chronic enteritis	30	N/A	N/A	Normal histology after 24 month therapy	N
9	F	White	Gastroschisis and intestinal atresia	108 cm small bowel + whole colon	4	Chronic small bowel inflammation	10	3	7	No follow-up studies	Y
10	F	White	Diaphragmatic hernia	75cm small bowel + 2/3 colon	4	Duodenitis, villous blunting, non-specific colitis	4	N/A	N/A	No diagnostic abnormality after 4 month therapy	N
11	M	Not Hispanic or Latino	Gastroschisis	Mid-ileal resection, unknown total length of small bowel + whole colon	0.83	Basocionic prominent eosinophils and inflammation	9	2	7	No follow-up studies	Y
12	M	African American	Necrotizing enterocolitis	24 cm small bowel + 42 cm colon	0.67	Eosinophilic colitis	5	5	0	No follow-up studies	Y
13	F	Hispanic or Latino	Intestinal atresia and gastroschisis	47 cm small bowel + whole colon	0.67	Eosinophilic colitis	18	N/A	N/A	Not on steroids continuously, had recurrent small bowel inflammation, intraepithelial lymphocytes while off steroids.	Y
14	F	Not Hispanic or Latino	Gastroschisis, intestinal atresia and volvulus	25 cm small bowel + ½ colon	3	Small bowel villous blunting, patchy active inflammation in small bowel and colon	1	N/A	N/A	No follow-up studies	N
15	F	Not Hispanic or Latino	Necrotizing enterocolitis	85 cm small bowel + 1/3 cm colon	1.08	Small bowel mural hemorrhage, focal erosion, congestion	7	N/A	N/A	Not on steroids continously, recurrent small bowel inflammation, non specific villous blunting while off steroids.	N

TABLE 2. Change of Calorie Count (kcal/kg/day) over the Course of Treatment

Patient ID	Weaning off PN Y/N	0 Month	3 Months	6 Months	9 Months	1 Year	2 Years	3 Years	4 Years	5 Years
1	N	24	10 (42%)	15 (63%)	10 (42%)	15 (63%)	N/A	N/A	N/A	N/A
2	N	58	40 (69%)	40 (69%)	33 (57%)	30 (52%)	27 (47%)	20 (34%)	20 (34%)	N/A
3	N	40	60 (150%)	52 (130%)	52 (130%)	44 (110%)	55 (138%)	30 (75%)	45 (113%)	44 (110%)
4	N	65	68 (104%)	62 (95%)	50 (77%)	63 (97%)	54 (83%)	57 (88%)	N/A	N/A
5	Y	54	28 (52%)	28 (52%)	25 (46%)	38 (70%)	36 (66%)	0 (0%)	N/A	N/A
6	Y	23	27 (117%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A	N/A
7	Y	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A	N/A
8	N	60	54 (90%)	58 (97%)	75 (125%)	66 (110%)	56 (93%)	N/A	N/A	N/A
9	Y	23	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A	N/A
10	N	60	66 (110%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
11	Y	75	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A	N/A
12	Y	80	57 (71%)	25 (31%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A	N/A
13	Y	55	0 (0%)	0 (0%)	25 (45%)	38 (69%)	32 (58%)	N/A	N/A	N/A
14	N	79	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
15	N	77	63 (82%)	66 (86%)	41 (53%)	29 (38%)	N/A	N/A	N/A	N/A

P3B15 - Results in adult small bowel transplantation after 15 years of experience in University Hospital 12 de Octubre, Madrid

Pilar Del Pozo, Jorge Calvo, Iago Justo, Borja Orive, Óscar Caso, Alberto Marcacuzco, Alejandro Manrique, Álvaro García Sesma, Félix Cambra, Luis Carlos Jimenez, Carmelo Loinaz, et al.

12 de Octubre Hospital

Introduction: A very limited number of groups perform intestinal (IT) and multivisceral (MVT) transplantation worldwide, and even fewer remain active nowadays. IT and MVT results are somewhat worse than those after other types of solid organ transplantation (SOT), thus patient selection remains extremely important.

Methods: From December 2004 to January 2019 we have assessed 105 patients as potential candidates, most of them not eligible; and have performed 31 transplants in 29 patients (21 ITx and 8 MVtx). Almost eighty percent had undergone some previous surgical approach (average 4 ± 2,7). 40% required home parenteral nutrition (HPN) and almost 86% had several complications related to it (thrombosis, sepsis, multiple central line removals...)

Results: Short bowel syndrome (SBS) was found in 60 % (18 / 29) of the patients. Familial Adenomatous Polyposis (FAP) with unresectable desmoid tumors (31%) and ischemia (18%) were the most common indications. Complications were very frequent: rejection (AR; 63.6%) and infection (51%, 37% mesh-related) were the main causes of death in the early postoperative period (0-6 months); and finally renal failure (56%) a frequent cause of morbidity and prolonged hospital stay. Graft was removed in 7 patients (24%; 7 / 29) mainly due to severe AR as well as lymphoproliferative tumors and vascular technical problems. although The overall graft loss rate was of 55% (17 / 31, 10 deaths with functioning grafts). After a mean follow up of 65 ± 61 months for patients and 60 ± 58 months for grafts, our actuarial survival for patients and grafts at 1, 3, 5 and 10 years was 73%, 62.4%, 55%, 51% and 66%, 62%, 55%, 50% respectively. Actuarial patient and graft survival at 3 and 5 years excluding those patients who died during the first year after transplant was 85,4% / 75% and 81% / 71% respectively. 31% of the recipients died during the first year post-transplantation. Those recipients who survive beyond the first year post-transplantation are more likely to be alive.

Conclusions: Small bowel transplantation is an excellent treatment for intestinal failure in selected patients. Our aim is to perform the SBT as early as possible in order to avoid established malnutrition and operate on less deteriorated patients, with not so poor performance status, and fewer potential complications due to HPN.

P3B16 - The Overload Gut Syndrome

Cecile Lambe, Elie Abi Nader, Cecile Talbotec, Olivier Goulet

Hopital Necker-Enfants Malades

Introduction: Short bowel syndrome (SBS) is the main cause for intestinal failure in children. Parenteral nutrition allows survival and growth while physiological intestinal adaptation occurs. Most patients can be weaned off PN after two to three years. In some cases, although adaptation was successful and PN was weaned without difficulty, intestinal symptoms such as abdominal pain, discomfort, abdominal distension and diarrhea occur, along with a decrease in growth rate requiring the resumption of PN - defining the overload gut syndrome (OGS). The aim of this study was to describe the natural history, the clinical and biological characteristics and the management of OGS.

Methods: this retrospective study included all children referred to our center with a history of SBS weaned off PN who needed to return to PN between 2013 and 2018. All children were evaluated in our ward before resuming PN. Clinical history, examination and biological testings, including plasma citrulline levels were collected. A stool balance analysis was performed using the duplicate meal technique and bomb calorimetry.

Results: Nine children were included in the study. Mean age at PN resumption was 10 years and 10 months. PN discontinuation lasted six and a half years (mean). All patients presented with stunting which was more important on height than on weight (loss of 1.5 SD and 1.3 SD respectively). All patients were hyperphagic, five of them received tube feeding on top of oral feeding, with mean ingested calories of 2336 kcalories / day, with a ratio of ingested calories over resting energy expenditure of 205%. Mean number of stools was 4.4 per day, with a mean stool weight of 1400g / day (52g / kg / d). One patient presented with recurrent episodes of D-lactic acidosis. Four patients had bicarbonates concentration under 21mmol / l. Mean total absorption rate was 69%. After PN start, the intestinal symptoms resolved, weight increased by 1.4 SD and height by 0.8 SD at 12 months follow-up. Biological parameters all improved. Mean citrulline plasma levels remained stable (26mmol / l at PN re-start - 24mmol / l at 12 months follow-up).

Conclusion: Overload gut syndrome is a rare complication of SBS in children. It occurs in children with high enteral intake and low absorption rate: the remnant intestine cannot face the calorie load and becomes overwhelmed. Symptoms should be recognized early in order to resume PN in time to avoid consequences on final stature.

P3B17 - Complex relation between timing of acute rejection, severity, and graft loss in isolated intestinal transplantation

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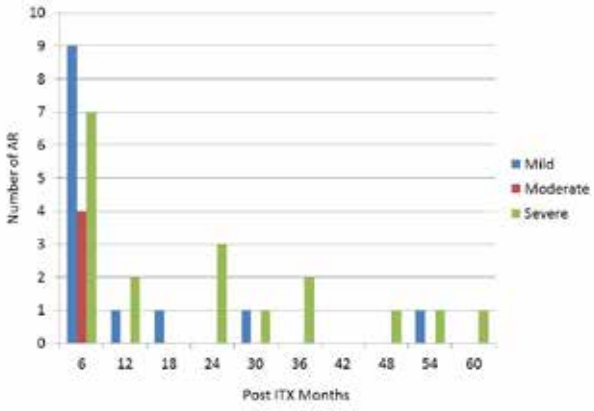
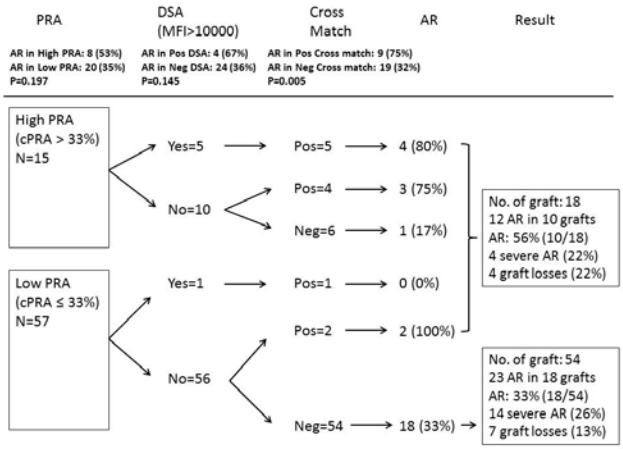
Introduction: Acute rejection (AR) remains a major determinant of morbidity and mortality after ITX. We studied patterns of AR and graft loss to understand potential loci for intervention.

Methods: We reviewed all ITX without concomitant liver graft between 2011 and 2018 at a single-center using a prospectively maintained database. AR, patient and graft survival were outcomes of interest.

Results: We analyzed 72 ITX without liver replacement. Twenty-eight grafts had at least one episode of AR (39%). Majority of AR occurred during first 6 months (57%) post- ITX and remainder occurred sporadically during the entire post-ITX period. Of 35 total episodes of AR among 28 grafts, 13 were mild (37%), 4 moderate, (11%), and 18 (51%) severe AR based on histological grades. Patient survival did not show a difference between ITX with and without AR (p=0.750), though, AR was the most common cause of mortality (n=6, 8%). Censoring death with functioning graft (n=12), AR was the most common cause of graft loss (n=11, 15%). Mild AR tended to develop early (< 12 months) post-ITX. Severe AR was observed evenly during the entire post-ITX period (Figure 1).



There was no graft loss or mortality related to mild or moderate AR. There were 11 graft losses out of 18 episodes of severe AR (graft salvage rate of 39%). Graft enterectomy was performed in 6 patients due to refractory severe AR. Among those, 5 survived and 3 went on to successful re-ITX. Five patients were not candidates for graft enterectomy due to profound sepsis and all died. Early severe AR, occurring < 6 months after ITX, had a poor treatment response (7 severe AR with 6 graft losses). High panel reactive antibody (PRA), positive donor specific anti-HLA antibody (DSA) and cross match appeared related to development of AR. However, there were also 23 episodes of AR in 18 grafts (33%), which occurred despite low PRA, negative DSA and negative cross match; of these 14 were severe AR with 7 graft losses (Figure 2).



Conclusion: Our analysis supports previous reports that severe AR is a major cause for graft loss and mortality in ITX. Presence of PRA, DSA and a positive cross match seem related to risk of developing AR. Of note, patients with no apparent heighted immunological risk factors also develop severe AR with a high frequency of graft loss. Mild to moderate AR has no apparent impact on outcome.

P3B18 - INT 767 – a novel dual Farnesoid-X Receptor (FXR) and Takeda G-protein-coupled Receptor-5 (TGR5) agonist attenuates intestinal ischemia reperfusion injury

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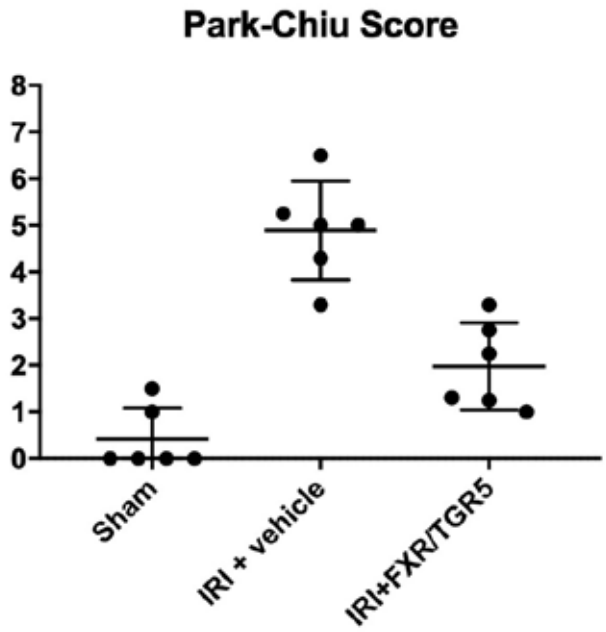
Introduction: Ischemia reperfusion injury (IRI) occurs inevitably during intestinal transplantation and after intestinal infarction. The intestine is especially susceptible to IRI which leads to loss of villi, resulting in systemic translocation contributing to poorer outcomes. The Farnesoid-X receptor (FXR), is a member of the nuclear receptor family. TGR5 is a G-protein-coupled bile activated receptor. Both are abundantly expressed in the gastro-intestinal tract. In pre-clinical models, they have shown to reduce inflammation and improve epithelial permeability when administered before ischemia. The aim of our study was to test the effect of a dual FXR/TGR5-agonist as treatment of intestinal IRI, administered intravenously after onset of ischemia.

Material and Methods: In a validated rat model (Sprague-Dawley, male, 300g) of intestinal IRI (laparotomy and clamping of superior mesenteric artery), 3 groups (n=6/group) were investigated: i/ Sham (only laparotomy); ii/ Ischemia 60min + reperfusion 60min (IRI) + intravenous vehicle; iii/ Ischemia 60min + reperfusion 60min + intravenous FXR/TGR5-agonist (IRI+FXR/TGR5). For each group, 10 additional animals were included for a 7-day survival analysis. FXR/TGR5-agonist INT-767 (Intercept Pharma, USA) or vehicle only was administered intravenously in a single dose at 10 mg/kg, 15 minutes after start of ischemia. Analyzed endpoints: 1/ Histology: Park/Chiu score and villus length; 2/ intestinal barrier function (transepithelial electrical resistance (TEER) and FD20 permeability measurements in Ussing chambers); 3/ Inflammatory cytokines: IL-6 (ELISA), IL-1-β and TNFα (qPCR); and 4/ Anti-inflammatory cytokines: IL-10, IL-13 (qPCR).

Results: IRI led to pronounced damage resulting in high Park/Chiu scores, increased intestinal permeability and systemic inflammation. Dual FXR/TGR5 treatment dramatically improved intestinal histology (Figure) and all other parameters. Survival was substantially improved after treatment ($P < 0.05$). Results are summarized in the table.

Conclusion: We demonstrated that intravenous treatment with a dual FXR/TGR5 agonist (INT-767) after onset of ischemia significantly decreased intestinal damage caused by IRI. These results show that FXR and TGR5 receptors are promising targets for intestinal graft protection. The ability to administer this substance intravenously greatly enhances the potential applicability for the frequent pathology of intestinal infarction as well as for transplantation.



Analysis of different endpoints after Farnesoid-X receptor and Takeda G-protein-coupled receptor 5 agonist treatment in a model of intestinal ischemia reperfusion injury

Endpoints *Median (range)*	SHAM	IRI	IRI + FXR/TGR5	P-value (IRI+FXR/TGR5 *vs* IRI)
Park/Chiu *(0-8)*	0 (0-1.0)	5.0 (3.3-6.5) ***	1.8 (1.0-3.3) ***	P < 0.0005
Villus length *(µm)*	273 (205-296)	104 (66-116) ***	201 (168-280) ***	P < 0.0001
TEER *(Ohm*cm²)* *(Villus length corrected)*	49 (39-63)	14 (9-21) ***	32 (24-37) ***	P < 0.0001
FD 20 Permeability *(pmol/cm²)*	16.5(5.3-40.8)	204.7 (147.9-247.9) ***	106.5 (61.1-119.8) ***	P = 0.0007
IL-6 *(fold change)*		207.4 (148.3-403.1)	155.5 (8.7-181.7) *	P = 0.0492
IL-1-β *(fold change)*		7.8 (5.0-13.8)	3.5(1.9-11.1) *	P = 0.0140
TNF-α *(fold change)*		6.9 (2.4-9.9)	3.8 (2.7-4.4) **	P = 0.0019
IL-10 *(fold change)*		10.7 (5.4-14.4)	16.6 (11.2-21.0) *	P = 0.0257
IL-13 *(fold change)*		11.4(4.2-15.8)	17.3 (11.6-20.4) *	P =0.0139
7-day survival *(%)*	100%	0%	50% *	

Legend: FD 20 = fluorescein isothiocyanate-labelled 20 kiloDalton dextran; TEER= Trans Epithelial Electrical Resistance; IRI = FXR/TGR5: 60 min of ischemia and 60 min of reperfusion without FXR/TGR 5-agonist treatment; IR + FXR/TGR5: 60 min of ischemia and 60 min of reperfusion with FXR/TGR5-agonist treatment;
* IRI vs IR: FXR/TGR5: *P< 0.05, ** < 0.01, ***, P< 0.001.
# IRI vs SHAM # P< 0.05, ## P < 0.01, ### P< 0.001.

P3B19 - The sensory profile of children with Intestinal Failure

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Introduction: Sensory responses are shaped by a person's experiences. A child's sensory processing patterns may support and/or interfere with skill development and functional performance. Children with intestinal failure (IF) endure physical and psychological hardship from a young age that may impact sensory processing. We studied the sensory profile of children with IF.

Methods: *The Sensory Profile 2*, a validated questionnaire-based tool, was used to evaluate processing patterns in the context of everyday life in children with IF (on home PN>3 months). An occupational therapist met with parents to apply the tool to a sample of children from two centres (Alberta Children's Hospital, Canada, and Hopital Necker-Enfants Malades, France). The assessed sensory domains included: seeking, avoiding, sensitivity, registration, auditory, visual, touch, movement, body position, oral, conduct, emotional expression, and attentional responses. Individual scores were compared with normative data to determine z-scores.

Results: Preliminary data for n=30 subjects, median age 5.0 (range 1.3, 14.6) years, included IF diagnoses of short bowel syndrome (n=18), chronic intestinal pseudo-obstruction (n=3) and other (n=9). A developmental diagnosis was noted in 7% of subjects. The sensory domains for which >20% of subjects had z-scores > +2.0 are listed in table 1. Compared to the normal reference data, 20% of the group avoided sensory input at higher rates, while 20% were "sensors" reacting more quickly and intensely to sensory input. Sensitivity to oral touch and taste were higher than average in almost half the children. Among 15-35 month olds, 27% rated with z-scores > +2.0 for general sensory. Among >3 year olds, 26% expressed strong emotional responses with sensory processing.

Conclusions: Preliminary data suggests that a proportion of children with IF have sensory processing issues including oral sensory processing problems. Determining protective factors among those who do not develop oral sensitivity merits further study. Children with IF should undergo assessment of their sensory responses, and prevention strategies for sensory dysregulation in this population need to be developed.

	Z-scores				
SENSORY RESPONSES	< -2.0	-2 to -1	-1 - +1	+1 - +2	> +2
All children					
Avoiding/Avoider	0 %	0 %	67 %	13 %	20 %
Sensitivity/Sensor	3 %	0 %	43 %	33 %	20 %
Oral Sensitivity	3 %	3 %	47 %	17 %	30 %
Children 15 – 35 months					
General Sensory score	9 %	0 %	64 %	0 %	27 %
Children 3:0 to 14:11 years					
Social/Emotional	0 %	0 %	58 %	16 %	26 %

Table 1: Summary of sensory responses for domains in which at least 20% of subjects had a z score of > 2 S.D

P3B20 - Gene expression of intestinal mucosa reveals increased inflammation and disturbed barrier function in PN-dependent children with short bowel syndrome

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INTRODUCTION: To study mucosal homeostasis in children with short bowel syndrome (SBS) during parenteral nutrition (PN).

METHODS: Fourteen SBS children currently receiving supplemental PN and enteral feeding at median age 1.5 years (IQR 1.0-6.5) and six age-matched [2.4 years (1.4-3.5), P=0.869] controls with healthy intestine were included. Duodenal mucosal biopsies were analyzed for morphology, proliferation, apoptosis and inflammation using HE-staining, MIB-1 immunohistochemistry, and for RNA expression of various genes regulating inflammation, permeability, proliferation and apoptosis. RNA expression was quantified using qRT-PCR after normalization to housekeeping genes. Unpaired two-sided comparisons were performed between the groups.

RESULTS: The remaining small bowel length was 20% (9-22%) of expected and duration of PN 1.4 (0.7-6.5) years. Villus length, crypt depth, enterocyte MIB-1 proliferation grade and apoptotic index were comparable between patients and controls (Table 1). Intraepithelial leukocyte count [0.03 (0.02- 0.04) vs 0.04 (0.03- 0.16), P=0.039)] was decreased, while mucosal RNA expression of pro-inflammatory cytokines were increased in patients when compared to controls (Table 2). RNA expression of tight junction proteins zonulin-2 and occluding were lower and claudin-1 higher in relation to controls. Patients also showed increased RNA expression of mucin 2, secreted by goblet cells. RNA expression of various cell cycle regulators and proliferative growth factors was similar in patients and controls (data not shown).

Table 1. Comparison of mucosal morphology, proliferation and apoptosis between SBS patients and controls

Mucosal property	Variable	Patients (n=14) Median (IQR)	Controls (n=6) Median (IQR)	P-value
Morphology	Villus length (mm)	0.50 (0.42-0.67)	0.67 (0.60-0.85)	0.059
	Crypt depth (mm)	0.26 (0.23-0.28)	0.31 (0.25-0.38)	0.248
Proliferation	MIB-1 grade (%)	1.3 (1.0-2.0)	1.5 (1.0-1.8)	0.964
Apoptosis	Apoptotic bodies/10 crypts	0.0 (0.0-0.2)	0.0 (0.0-0.6)	1.0

Table2. Comparison of mucosal RNA expression between SBS patients and controls

Mucosal function	Gene (fold change)	Patients (n=11) Mean (IQR)	Controls (n=6) Mean (IQR)	P-value
Inflammation	TGF-β2	1.60 (1.29-2.15)	1.08 (0.70-1.40)	0.035
	IL-1β	2.51 (0.89-3.59)	1.12 (0.53-1.89)	0.046
	Caveolin-1	1.21 (1.10-1.33)	0.94 (0.86-1.01)	0.016
Barrier function	Zonulin-2	0.73 (0.56-0.84)	1.10 (0.99-1.22)	0.012
	Occludin	0.78 (0.75-0.94)	1.03 (0.75-1.30)	0.082
	Claudin-1	1.19 (0.95-1.36)	0.79 (0.52-1.03)	0.044
	Mucin 2	1.56 (1.33-1.84)	1.07 (0.79-1.30)	0.044

CONCLUSION: Duodenal mucosa of PN-dependent SBS children showed no structural or molecular signs of adaptive hyperplasia, but was characterized by molecular signature of increased inflammation and disturbed barrier function. These findings have important implications regarding SBS pathophysiology in humans.

POSTERS PRESENTED ON WEDNESDAY JULY 3, 2019

P1.01 - Post-transplant vascular complications in isolated intestine and multivisceral transplant patients

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Indiana University School of Medicine

Introduction

Vascular complications such as aortic pseudoaneurysm, AV fistula formation, vascular graft leak, vascular graft thrombosis, and venous outflow obstruction can result in significant morbidity and mortality in abdominal organ transplant patients. In this study, we review our experience with such complications in isolated intestine and multivisceral transplant patients.

Methods

All records for isolated intestine, multivisceral, and modified multivisceral transplants over a 15-year period at a single center were reviewed. All cases of aortic pseudoaneurysm, AV fistula formation, vascular graft leak, vascular graft thrombosis, and venous outflow obstruction were included.

Results

Of 263 transplants, 16 major post-transplant vascular complications were identified (6%). There were five cases of venous outflow obstruction, three of which required revision of the venous anastomosis. One case resulted in colonic necrosis necessitating colectomy, and another required venotomy and thrombectomy. Four patients developed vascular graft thrombosis, one of which was found to have splenic artery thrombosis for which a distal pancreatectomy was eventually required. The second patient developed distal arterial thrombi of the intestinal graft resulting in small bowel necrosis that required resection of the distal ileum. The third patient developed hepatic artery thrombosis which was successfully treated with intra-arterial tPA infusion and anastomotic revision; this patient also had poor portal flow that was successfully re-established with anastomotic revision. The fourth patient was found to have minimal flow in the aortic jump graft with diffuse necrosis of the transplanted organs and died shortly thereafter from complications of severe acidosis. Four cases of vascular graft leak were identified, all of which involved the aortic graft and resulted in exsanguination and death. There were two instances of aortic pseudoaneurysm, both of which were successfully treated with stent graft placement. One case of AV fistula formation was identified that involved the hepatic artery and portal vein and was successfully treated with coil embolization of the hepatic artery.

Conclusion

Vascular complications can result in significant morbidity and mortality in intestine and multivisceral transplant patients. The incidence of vascular complications in this cohort was 6%.

P1.02 - Tacrolimus induced optic neuropathy after multivisceral transplantation

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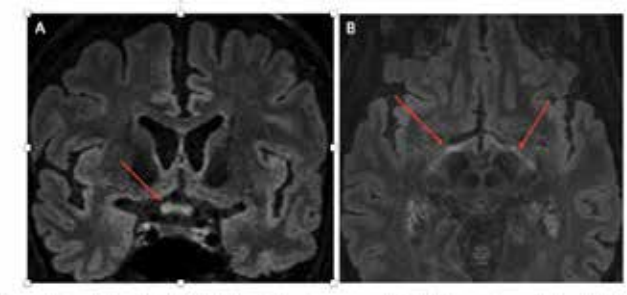
Introduction: Tacrolimus induced optic neuropathy (TION) is a rare condition seen in transplant patients leading to severe vision loss caused by damage to the optic pathway. The underlying pathophysiology is thought to be a combination of ischemic damage due to vasoconstriction of the cerebral microvasculature and direct neurotoxicity.

Method: We describe a case of a 51-year old male, combined multivisceral and renal transplant recipient who developed severe, bilateral TION 3 years after transplantation. Furthermore, a literature research was performed for all published cases describing TION after organ transplantation.

Results: Optic tract inflammation was clearly detected on MRI (Figure). Treatment with intravenous corticosteroids and immunoglobulins was started. Tacrolimus was reduced but not withdrawn completely to avoid rejection, especially of the intestinal component of the graft. Everolimus was associated to maintain sufficient immunosuppression. After three months, vision had recovered completely. The patient experienced no signs of rejection in any transplanted organ during this period and organ function remained stable. Seven other reports in various organs were found in literature (Table). In most, tacrolimus was discontinued completely and outcomes were poor.

Conclusion: Our report demonstrates the importance of swift treatment to reverse optic tract inflammation and highlights the possibility to add everolimus to the immunosuppressive regimen to allow safe reduction of tacrolimus exposure in intestinal transplant patients. By contrast, results from literature show sporadic use of anti-inflammatory medication and poor long-term vision outcomes, often related to delayed diagnosis and treatment (Table).



Legend: Coronal (a) and Axial (b) Fluid-attenuated inversion recovery (FLAIR) MR images show a thickened optic chiasm with high signal (a, arrow) and high signal along the optic tracts on both sides (b, arrows)

Table 1: Published cases of tacrolimus induced optic neuropathy cases after organ transplantation

Patient no.	Publication	Year	Organ(s)	Patient age (years)	Gender	Onset after transplant	Tacrolimus level at time of symptoms (ng/L)	Ophthalmological examination	MRI	Tacrolimus Therapy	Other Treatment	Outcome
1	Brocks	2000	Liver	58	Male	3 months	Unknown	Optic disk swelling, lower light reactivity left	Some subcortical ischemic changes	Discontinued	None	No recovery
2	Lahir	2003	Pancreas	38	Male	3 years	Unknown	Sluggish response to light, bilateral optic pallor, no haemorrhage	Normal	Discontinued	None	Unknown
3	Akashi	2006	Islet	51	Female	5 months	3.4	Normal	Normal	Discontinued	None	Full recovery
4	Minematsu	2010	Heart & kidney	63	Male	5 years	8.8	Optic disk atrophy, sluggish response to light	Left optic nerve inflammation	Discontinued	IV CS & IVIG	No recovery
5	Han	2010	Liver	54	Male	6 months	4.2	No fluorescence filling in the optic disc bilaterally	Not available	Discontinued	None	Partial recovery
6	Ascaso	2012	Liver	56	Female	6 months	2.6	Optic disc pallor	Normal	Continued	IV CS	No recovery
7	Shao	2012	Intestine	30	Male	3 months	13.9	Optic disc pallor + haemorrhage, bilateral delayed fitting	Normal	Reduced	None	Partial recovery
8	Carneval	2010	MVTx & kidney	51	Male	3.5 years	4.4	Normal	Bilateral inflammation of the optic tract	Reduced	IV CS & IVIG	Full recovery

Legend: IV CS = Intravenous corticosteroids, **IVIG** = Intravenous immunoglobulins, **MRI** = magnetic resonance imaging, **MVTx** = multivisceral transplant

P1.03 - Intravenous glucose nocturnal infusion reduces growth hormone secretion in children on total parenteral nutrition

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Introduction: Most children with intestinal failure (IF) benefit from home parenteral nutrition (HPN). It allows a familial life with normal children activities such as going to school, sports, and being at home. In order to do so, PN is provided with cyclic infusion at night. Children with IF on HPN should have normal growth. However, some children grow under their genetic target height and present with decreased height velocity.

Methods: We report the case of two children on HPN who presented with decreased height velocity while their weight gain was normal. After ruling out usual etiology (insufficient protein intake, acidosis, sodium deficiency, IFALD…), growth hormone (GH) deficiency was considered. Extensive testings were performed such as IgF1 levels, GH secretion stimulation test and nocturnal GH secretion. PN dependency was assessed using the PN/REE index (parenteral nutrition non-protein energy intake divided by resting energy expenditure calculated using Schofield equation, expressed in percentage).

Results: These two children needed extremely high PN caloric intake to achieve a normal weight gain with a PN dependency index of 163% and 150%.

Table 1 shows their clinical characteristics.

	Age	diagnosis	Weight SD	Height SD	Genetic Target height SD	Stunting (height) SD	Glucose infusion rate (g/kg/h)	Length of perfusion	PN/REE
Patient 1	13	Ultra-short bowel syndrome (duodeno-rectal anastomosis)	-0.5	-3.8	0.3	-3.8	1.1	13h	163%
Patient 2	11	Ultra-short bowel syndrome (Apple Peel syndrome)	-1	-2	+1.5	-3	1.2	12h	150%

Table 2 shows the results of the biological testings.

	Citrulline	IgF1 µg/l (N)	ASAT/ ALAT UI/L	GGT UI/L	Bili T µmol/l	T4 pmol/l TSH mUI/l	nocturnal Glycemia (Mean)	Maximal nocturnal glycemia	GH Stimulation Peak (N>15)	Nocturnal GH secretion Mean (N > 4)
Patient 1	1µmol/l	145 (166-435)	54/54	29	10	7.6 (N) 1.56(N)	1.25g/l	1.89 g/l	20.7 mUI/l	3.5 mU/l
Patient 2	2µmol/l	62 (111-260)	44/27	14	9	10.4(N) 3.03(N)	1.12g/l	1.45g/l	16.9 mUI/l	3.6mU/l

These two children showed a normal GH peak under stimulation, but a low nocturnal GH secretion meaning they were able to produce GH under stimulation, but their nocturnal physiological secretion was inhibited. Their mean glycemia during PN perfusion was high compared to fasting glycemia which should normally be observed at night in children. Hyperglycemia is a well known inhibitor of GH secretion.

Conclusion: Children with very high PN dependency are at risk of developing reduced height. In some children, GH secretion seems to be inhibited by nocturnal high glucose infusion. A longer PN infusion time can be proposed and/or a decrease in glucose intake with an increase in lipid intake. Also, growth hormone supplementation might be discussed and should be evaluated in this setting.

P1.04 - Anastomotic Ulcers in Children with Short Bowel Syndrome: A Single Intestinal Rehabilitation Center Experience

David Freestone, David Mercer, Brandy Gerhardt, Sarah Iwanski, Ruben Quiros

University of Nebraska Medical Center

Anastomotic ulcers can present as a significant problem in children with short bowel syndrome (SBS). They are typically a late complication occurring years after creation of an ileocolonic anastomosis. As the mucosa becomes inflamed and ulcers form complications of GI blood loss (gross or occult), iron deficiency anemia, chronic diarrhea, and feeding intolerance may occur. The purpose for this study is to identify a most common etiology of anastomotic ulcers and best treatment options in patients with SBS.

A retrospective chart review of intestinal rehabilitation patients was completed, and was limited to pediatric patients (<19 yo) with diagnoses of SBS, gastrointestinal bleeding, and endoscopic evidence of ulcers during a 10 year period of time (2006-2016). We collected basic data, including the age, sex, diagnoses, past medical and surgical history, post surgical anatomy, endoscopic findings, small bowel aspiration culture results, laboratory findings, and GI bleeding management and response. Data were analyzed using descriptive statistics and processed to find trends for clinical interpretation.

14 patients met inclusion criteria. The average intestinal length was 40 cm (11/14 ≤70 cm), and remaining colon median was 50% (9/14 ≤50%). Serial Transverse Enteroplasty (STEP) procedures performed on 9/14. Average age of anastomosis at first step was 2.9 yrs. Of the patients that had a STEP procedure, the median number of procedures was 1 (range 1-5). The median age of surgical anastomosis where ulcer was detected was approximately 3 years. On reviewed laboratory data, 11/14 patients required transfusions. Of the 11 that required a transfusion, the median number of transfusions was 3. The median number of procedures was 6 (range of 1-19). When treated for SBBO 3/7 showed improvement of ulcers with antibiotics alone. Stopping enteral iron therapy was successful in 2 cases. Surgical intervention was required in 6/14 cases.

Anastomotic ulcers are viewed as multifactorial problem. Factors that seemed to contribute include; past medical and surgical history, ischemic changes, medication exposure (ferrous sulfate), exposure to colonic bacteria and bile acids malabsorption. The one universal factor was the absence of an ileocecal valve. A systematic approach started with antibiotics, cholestyramine and/or steroids should be utilized and consider avoidance of enteral iron therapy. Early consideration of surgical intervention may be necessary.

Patient	SB legnth (cm)*	Colon (%)*	ICV	STEP	STEP#
1	32	25	No	Yes	5
2	27	75	No	No	0
3	60	50	No	Yes	1
4	70	50	No	Yes	1
5	35	50	No	Yes	2
6	143	33	No	Yes	1
7	23	50	No	No	0
8	20	67	No	Yes	2
9	100	75	No	No	0
10	35	33	No	Yes	1
11	65	50	No	Yes	2
12	40	67	No	No	0
13	54	67	No	Yes	1
14	50	33	No	No	0

Table 1: Intestinal anatomy: The median intestinal length was 40 cm, and the median percentage of remaining colon was estimated to be 50%. All patients included in this study had an enterocolonic anastomosis, and as a result there were none with preserved ICV.

Patient	Failed management	Period of time	Number of procedures	Resolution of ulcers/symptoms
1	steroids and antibiotics, resection of anastomosis, repair of stricturted anastomosis	2010-2014	16	Unknown Treatment after final scope demonstrating ulcers included oral steroids, 6MP for 3 months, antibiotics for SBBO, change from oral to IV iron, and he participated in a trial for teduglutide
2	budesonide and sulfasalazine Surgical resection	2014-2016	5	Change from oral to IV iron
3	cholestyramine and antibiotics	2010-2013	7	Change from oral to IV iron
4	Previous resection and reanastomosis (2011) and trial of mesalamine	2010-2015	8	Surgical resection
5	trials of entocort, and enteral gentamicin for SBBO	2013-2014	6	Surgical resection
6	sulfasalazine, mercaptopurine, and even infliximab	2008-2015	15	Enteral budesonide and sulfasalazine
7	cholestyramine	2015	2	SBBO antibiotics with Bactrim, flagyl (no duodenal aspirate).
8	antibiotics for SBBO and cholestyramine without improvement	2012-2014	6	prednisone taper and transitioned to budesonide and sulfasalazine
9	None	2012-2013	4	Surgical resection
10	Trials of entocort, cholestyramine, rifaximine/metronidazole/ nitazoxanide	2010-2014	7	Surgical resection
11	None, primary surgical problem identified	2015-2016	3	Surgical resection
12	None	2016	3	Enteral steroids and cholestyramine
13	Enteral steroids, sulfasalazine, Mesalamine, and Infliximab. He had 2 prior surgical resection and repair of entrocolonic anastomosis	2013-2016	19	Surgical resection
14	None	2016	1	None

Table 2: comparison of management options, period of time ulcers and bleeding was treated, and the ultimate resolution of ulcers. Estimated number of procedures required to diagnose and treat bleeding and ulcers had range of 1-9 with average of 7.3 per patient. Surgical resection was most successful in management of ulcers (6/14 cases).

P1.05 - Human Intestinal Transplant: is IL-22 stimulation of Intestinal Stem Cells a new partner for immunosuppressive therapies?

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Acute cellular rejection (ACR) is leading cause of graft loss and death in intestinal transplant (ITx) patients. ACR promotes intestinal injury, disruption of the mucosal barrier, organ dysfunction and bacterial translocation. Epithelial regeneration is critical to reverse the situation. The intestinal stem cell (ISC) provides signals supporting normal epithelial maintenance. It has been shown that innate lymphoid cells 3 (ILC3), potent producers of IL-22 after intestinal injury, increase proliferation and expansion of the ISC in an IL-22-dependent fashion. Therefore, we aimed to evaluate the immunological status during the ACR focusing on the axis ILC3/IL-22/IL22R/ISC. To do this, lamina propria cells of biopsies were isolated from ITx [Non-rejection (NR)=17; Mild rejection (MR)=4] and non-transplant patients (NITx)=7. Enrichment of ILCs and CD4 population was done using MACS technology. ILC3 were determined by flow cytometry. CD4 T cells were isolated and the expression levels of functional markers of Th1 (Tbet, IFN-γ), Th2 (GATA3, IL-13), Th22/17 (RORC, IL-22, IL-17A), Tregs (Foxp3, TGF-β) were evaluated by qPCR. Total levels of IL-22 in biopsies [NR=5 and Moderate rejection (MoR)=6] were measured by qPCR. ISC IL-22R+ were detected by immunohistochemical staining [NR=13; MR=9, MoR=12, Severe rejection (SR)=5]. The results showed that during ACR the expression of Tbet, GATA3, RORC, Foxp3 were significantly decreased (P=0.05). Although the total percentage of ILC3s was not impaired (P=0.47); a reduction of ILC3 NCR^+/NCR^- ratio was observed. ISC $IL\text{-}22R^+$ number was similar in all groups studied (P=0.21) while IL-22R expression showed a trend to be increased (P=0.06). Levels of IL-22 in ITxMoR were lower than in NRITx patients with normal biopsies (P=0.063) and NITx biopsies. In conclusion, during rejection CD4 population (TH1, TH2, TH17/22, Tregs) and ILC3/IL-22/IL-22R axis are affected. In this context ISC number not only is unaffected, but also is able to increase IL-22R expression. Finally, the variation in the ILC3 NCR^+/NCR^- ratio observed during ACR could explained, in part, the impairment in the epithelial regeneration observed during this process. Thus, our findings reveal that IL-22 can potentially be uses as a new therapeutic approach to be used in conjunction with immunosuppressants in order to promote mucosal regeneration. Due to the small number of patients evaluated, this preliminary study is currently being extended with a larger population.

P1.06 - Preserved renal function in children with intestinal failure on long-term parenteral nutrition

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Introduction: Chronic treatment with parenteral nutrition (PN) has been associated with renal complications, including hypercalciuria, nephrocalcinosis, glomerular proteinuria and reduced glomerular filtration rate (GFR). Some pediatric studies reported high prevalence of proteinuria and renal complications, but evidence is scarce and mostly short-termed. Thus, our aim was to evaluate renal complications in children with intestinal failure, receiving long term treatment with PN.

Methods: A cross sectional retrospective study was performed (in the period of 5.2017 until 12.2018), using electronic medical records of patients treated in our pediatric intestinal failure clinic for more than 1 year. Data was collected regarding medical background, anthropometric measurements, blood and urine tests and abdominal sonography.

Results: Complete data was available for 15 children (67% males), with median age of 6 years (ranged 1.5 to 15 years). Median duration of PN treatment was 4 years (IQR 1.5-6 years). All patients had normal blood pressure for age and height. Low grade proteinuria was identified in 61% and mild albuminuria in 30% of the cohort. Hypercalciuria was present in 50% and hyperoxaluria in 46% of the patients. Only one patient had nephrocalcinosis as noted on renal sonography. Estimated glomerular filtration rate (eGFR) was normal in all but one patient, who had preexisting renal disease.

Conclusions: Pediatric patients with intestinal failure can present with preserved kidney function after years of PN treatment. Among this age group, eGFR is normal in the absence of preexisting kidney disease. Despite high prevalence of hypercalciuria, nephrocalcinosis is rare. Continued monitoring of renal function, urinary protein excretion and metabolic urine parameters, and examining larger long-term cohorts are essential in order to characterize effects of prolonged PN on different kidney functions in pediatric patients.

P1.07 - The Effects Of Minimizing Phlebotomy Blood Volume On Anemia In Pediatric Home Parenteral Nutrition Patients

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Background & Objectives

Anemia is a common morbidity in pediatric patients who require home parenteral nutrition (HPN). One factor that increases the risk for anemia in this patient population is frequent phlebotomy as part of routine monitoring. At Loma Linda University Children's Hospital (LLUCH), the majority of pediatric patients on HPN have monthly labs drawn as part of the standard monitoring protocol. In June 2016, LLUCH began using micro-tubes for routine blood sampling. Traditional phlebotomy tubes require 15-20 mLof blood. Micro-tubes require less than 2mLfor the same tests. The purpose of this study is to understand the effects of phlebotomy blood volume minimization strategies in reducing anemia in our pediatric patients requiring HPN.

Methods

This study was IRB-approved and retrospective in design. Since June 2016, the HPN program at LLUCH began using micro tubes for routine laboratory monitoring. Standard clinical data (age, gender, weight) and laboratory data (CBC, ALT, bilirubin, albumin) were collected prior to June 2016 and after September 2016. The primary outcome of this study was to compare the change in hemoglobin concentrations before and after the use of micro-tubes. The secondary outcome was to estimate the prevalence of anemia for age before and after use of micro-tubes for phlebotomy. Statistical analyses were performed including standard descriptive analysis, t-tests, and bivariate analysis. P-value of <0.05 was considered statistically significant. The sensitivity and specificity of red cell mean corpuscle volume (MCV) and red cell distribution width (RDW) in detecting anemia for ages were also calculated.

Results

N = Thirty-eight subjects. Mean age = 6.1 years (SD +/- 4.2y). Prevalence of anemia for age before micro-tube implementation = 22% Prevalence of anemia for age after micro-tube implementation = 14% Mean difference in the hemoglobin of before and after implementation = +0.62g/dL(CI=0.21 to 1.02; p=0.004)

Secondary bivariate analysis:

No correlation between anemia for age and the following factors: age, gender, weight, ALT, and albumin level.

Conclusions

Strategies such as micro-tubes to reduce the volume of routine blood draws in pediatric patients requiring chronic HPN may reduce the prevalence of anemia and improve hemoglobin levels. Age, weight, and liver enzyme levels were not found to be independent risk factors for the presence of anemia for age.

P1.08 - Risk factors for copper deficiency in children with intestinal failure receiving long-term parenteral nutrition

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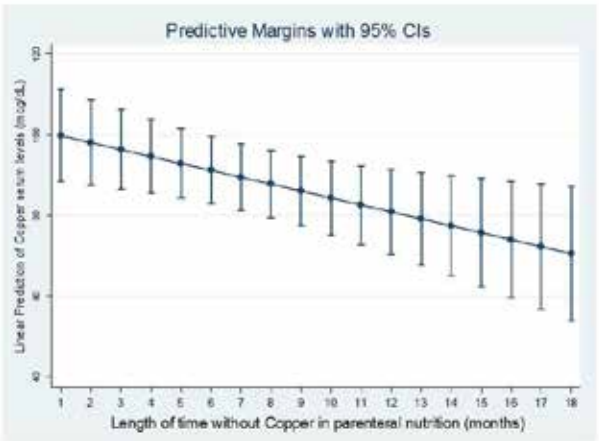
Introduction: Copper is necessary for normal function of hematopoietic, cardiovascular, connective/skeletal and the central nervous systems. A >50% prevalence of copper deficiency has been reported in retrospective case series of children with intestinal failure (IF) during transition from parenteral to enteral nutrition (Yang CJ et al, 2011; Namjoshi SS et al, 2017). We sought to determine the frequency and factors associated with copper deficiency in children with IF who had their copper plasma levels monitored according to a standard protocol.

Methods: Prospective cohort study in children with IF followed-up at an intestinal rehabilitation center between July 2015 and November 2018 and who were receiving home parenteral nutrition (PN). Patient's micronutrient status was routinely monitored at 3-month intervals or once a month when deficiency was detected. Copper was given at a standard dose of 20 mcg/kg as part of a trace-element solution, and was omitted in the PN if the patient developed intestinal failure liver associated disease. The outcome variable was copper plasma level during the follow-up period. The effect of the exposure variables (length of time on PN, prematurity, serum direct bilirubin levels, C-reactive protein, length of remnant small bowel and ostomy) on the outcome was analyzed by generalized estimating equations.

Results: Thirteen patients aged 34.2 months (IQR: 25.3; 41.1) were included; median time on PN was 26.4 months (IQR: 15.2 to 32.9). An average of 7 (range 2 to 15) copper measurements/patient were performed; 53.8% of patients had at least 1 copper measurement below normal during the follow-up. Eight patients who had cholestasis had trace elements of PN discontinued for 4 months (IQR: 1.6 to 12.2); from June 2017 these patients began to receive copper solution separately in doses to achieve basal requirements or to correct deficiency. Direct bilirubin levels (β coeff. -5.9, 95% CI: -9.0;-2.7, p=0.04), time on PN without copper (β coeff. -1.7, 95% CI: -3.2;-0.2, p<0.001) and ostomy (β coeff. -20.3, 95% CI: -37.6;-2.9, p=0.02) were associated with decreased copper levels in multivariable analysis. The figure shows adjusted predictions and marginal effects of the length of time without copper on copper serum levels.



The figure shows adjusted the predictions and marginal effects of the length of time without copper on copper serum levels.

Conclusion: Direct bilirubin levels, length of time on PN without copper and ostomy are independently associated with the high frequency of

decreased copper plasma levels in patients with IF receiving long term PN.

P1.09 - Donor's graft ex vivo T cell depletion with fludarabine reduces GvHD signs and improves survival after intestine transplantation

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Introduction: Intestine passenger T leukocytes are responsible of graft versus host disease (GvHD) in intestine transplantation (ITx). These lymphocytes are known to have inferior tolerogenic qualities compared with leukocytes in the liver, other solid organs and bone marrow. Fludarabine is a routinely used anti neoplasic agent with high cytotoxicity against T cells. We hypothesized that ex vivo fludarabine treatment of the bowel graft could diminish the risk of GvHD and improve post Tx overall survival.

Methods: We performed isolated heterotopic ITx from Lewis (LEW) to Brown Norway (BN) rat strains. The grafts of one of the experimental groups were imbided and sealed in Celsior preserving solution with 1000 µM fludarabine during surgery (1 h), before its implantation into recipient animals.

We compared a group of untreated (n = 7) vs a group of fludarabine-treated bowel recipients (n = 5). The mixed hematopoietic chimerism was determined by flow cytometry using strain-specific anti HLA antibodies. Clinical signs of GvHD or as well as post-Tx overall survival were also monitored.

Results: One hour fludarabine treatment of the bowel grafts induced specific apoptosis of its passenger T cells at concentrations from 100 µM while no histological signs of intestinal tissue alterations were observed after 1000 µM fludarabine treatment.

After heterotopic LEW -> BN ITx, untreated intestine recipients showed GvHD signs from the fourth day post-Tx (n = 7). These symptoms include: rash (n = 4), weight loss (n = 3), piloerection (n = 2) and diarrhea (n = 1). The chimerism or percentage of donor's lymphocytes in the recipient rat, determined in peripheral blood, reached 6.61% (range 1.7-10.8%) at day 3 post-Tx and 2.56% (range 0-9.8%) at day 7 post-Tx **(Fig. 1)**.

Rats transplanted with a fludarabine-conditioned intestine showed statistically signifcant later and milder clinical signs of GvHD. Additionally, fludarabine treatment reduced total donor cells chimerism at day 7 and the percentage of chimeric T cells at days 3 and 7 post-Tx **(Fig. 2)**.

Both experimental groups died showing clinical signs of graft rejection. Untreated bowel grafts recipients died within 9.2 days ± 0.3 days, while fludarabine-treated graft recipients showed prolonged survival (13.5 days ± 0.3 days).

Conclusions: Graft immunosupresion with fludarabine during surgical procedure protects bowel recipients of GvHD risk and improves post-Tx overall survival.

Figure 1

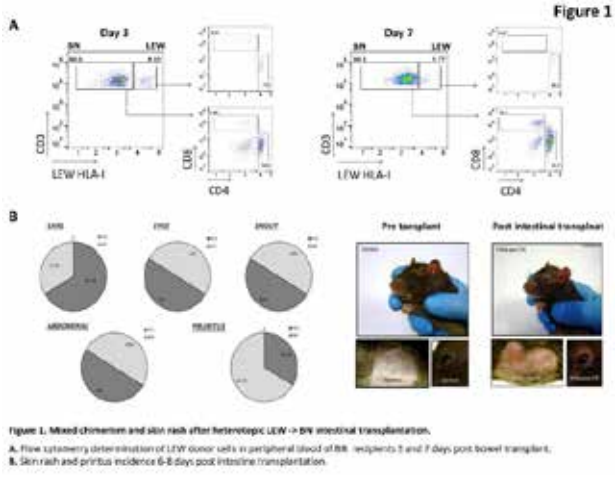
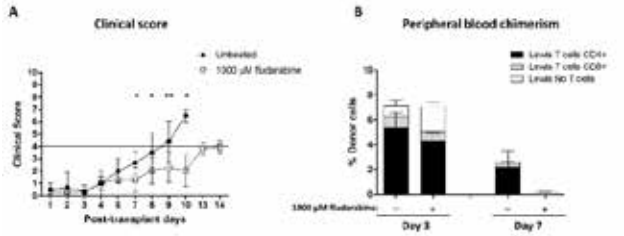


Figure 2



P1.10 - Mucosal Repair After Small Bowel Transplantation In The Rat: be quick or be dead

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Introduction: Graft cold storage and subsequent reperfusion during small bowel transplantation result in various degrees of mucosal injury ranging from mild edema to extensive mucosal loss. Mucosal barrier impairment favors bacterial translocation and fluid loss and raises nutritional challenges. Moreover, injured enterocytes can produce and release proinflammatory mediators and upregulate various epitopes towards an inflammatory phenotype. We studied the process of mucosal injury and repair during the early period after intestinal transplantation from a histological and molecular standpoint.

Methods: Three months old, Sprague Dawley male rats were used as donors and recipients. Donor intestines were perfused and stored in saline for 3 hours, then transplanted heterotopically using microvascular anastomoses. Small bowel graft segments were obtained after preservation, and at 20 minutes, 12 hours and 24 hours after reperfusion. Histology studies (Chiu score, Goblet cell count, morphometry, immunohistochemistry) and ddPCR for tight junctions (tricellulin, claudin-3), apoptosis (Bax, Bcl-2) and inflammation (IL-6, ICAM-1, TLR-4, TLR-9) were performed.

Results: Cold storage lead to extensive epithelial detachment (corresponding to Chiu grade 3) and reperfusion lead to extensive villus loss (about 50 % of the initial villus length, Chiu grade 5). Goblet cells showed a significant reduction ($p<0.01$). All these parameters ceased to differ significantly compared to normal intestines after 24 hours of reperfusion. However the villi appeared shorter and broader than in normal intestines and total mucosal voljme was reduced. Bax, Bcl-2, IL-6, ICAM-1 and TLR4 mRNA levels were lower after 24 hours compared with immediately after reperfusion. mRNA for tight junction proteins tricelllulin and claudin-3 remained lower than in normal intestines.

Discussion: The current data suggest that early mucosal recovery after intestinal transplantation is mainly due to cell migration and lamina propria remodeling rather than enterocyte proliferation. This rapid phenomenon seems to be accompanied by a local downregulation of the inflammatory response. The very rapid recovery of the rat intestine following moderate / severe reperfusion injury needs to be considered when designing intestinal transplant experiments and choosing sampling and end points.

P1.11 - A Unique Presentation of Pediatric Intestinal Failure: Familial chronic intestinal pseudo-obstruction occurring with diffuse intracranial vasculopathy - a systemtic smooth muscle disorder

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Introduction:

We present a unique case of familial intestinal failure secondary to chronic intestinal pseudo-obstruction (CIPO). Our patient is a 7-year-old male with longstanding feeding intolerance secondary to distension and vomiting that has required TPN. Additionally, he has a severe intracranial vasculopathy and a history of recurrent strokes. He had a sister who required TPN due to nonobstructive feeding intolerance, who passed away of complications related to stroke. While this association has been described in ACTA2 gene mutation disorders affecting systemic smooth muscle, our patients do not have an identified ACTA2 mutation. Therefore, we suspect a novel genetic mutation causing this phenotype of multi-system smooth muscle dysfunction. This unique case report expands the spectrum of disorders that should be considered in the evaluation of children with intestinal failure and suspected visceral myopathy.

Case Description:

This is a 7-year-old male with long standing history of vomiting, abdominal distension, and feeding intolerance, required parenteral nutrition for several years. Contrast imaging studies demonstrate diffuse small bowel dilation and slow colonic transit time, without evidence of anatomic obstruction. He also has a history of recurrent urinary tract infection, and markedly distended urinary bladder with bilateral hydronephrosis. These findings are highly suggestive of visceral myopathy. He has an established CNS vasculopathy with a Moyamoya-like presentation, with a history of chronic CNS infarction.

Family history is significant for a sister with similar gastrointestinal symptoms, requiring TPN. This sibling died following complications of a stroke.

Our patient and his sister had undergone genetic testing. ACTA2 mutation was not found. Other investigations are in progress to identify a causative mutation that might offer genotype-phenotype information.

Discussion:

An alpha-actin smooth muscle mutation can affect all smooth muscle in the body, leading to multi-system myopathy that may cause both intestinal failure and severe CNS vasculopathy. ACTA2 mutation disorders have been described in this presentation, although this spectrum of disorders is rare and not considered in the standard evaluation of patients with myopathic CIPO.

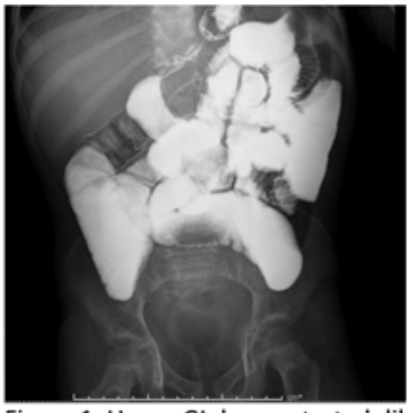

Figure 1. Upper GI demonstrated dilated small bowel

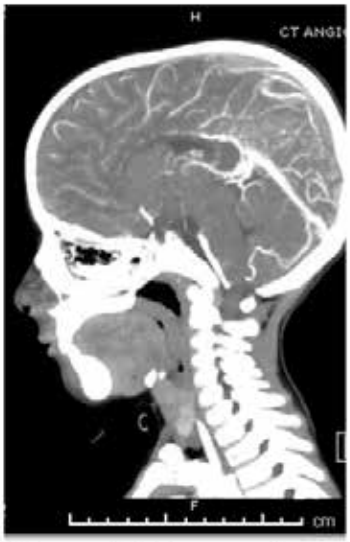

Figure 2: Abnormal cerebral vasculature

Conclusion:

This case illustrated the importance of multidisciplinary care when treating highly complex patients with intestinal failure, and the role of genetic testing within our field.

P1.12 - Surviving more than 10 years after intestinal transplant. First cohort of patients transplanted at a single centre.

Mariana Doeyo, Hector Solar, Carolina Rumbo, Maria Ines Martinez, Diego Ramish, Julio Trentadue, Adriana Crivelli, Adriana Fernandez, Gabriel Gondolesi

Hospital Universitario Fundación Favaloro

Introduction: Intestinal transplant (ITx) remains the last therapeutic alternative for patients (pts) with intestinal failure (IF). Although pt and graft survival have improved overtime, there are few reports of the long term outcomes of individual pts surviving more than 10 years with functional grafts; there is no long term results report from Latin-America.

Aim: to describe the outcome of those pts underwent ITx at our center and have more than 10 years survival with functional graft.

Materials and methods: This is a retrospective analysis of ITx long term survivors starting in May 2006. Diagnoses, ITx indications, incidence of acute and chronic rejection, complications related to immunosuppression (IS) and social reinsertion over time are reported.

Results: 5 / 49 (10.2%) ITx done at our center, have more than 10 year survival with a functional graft. Four of them are currently adults, but 3 were less than 18 years of age at the time of ITx; 3 are male. All pts had Short Bowel Syndrome (SBS). The indications for ITx were intestinal failure associated liver disease (40%), lack of central venous accesses (40%), and recurrent line sepsis (20%). The mean duration of hospital stay after ITx was 39.6±18.02 days (4 isolated ITx, 1 combined Liver-ITx). All pts presented at least 1 episode of acute cellular rejection (mean 2.8±1.78); 11 mild, 1 moderate, 2 severe. 7 episodes occurred during the first year post ITx and the rest occurred between the first and the fifth year post ITx. None of the pts developed chronic rejection. Complications related to IS therapy are chronic renal failure requiring kidney transplant (1); diabetes (1); bilateral aseptic necrosis of the femoral head (2) The 5 patients suffered infectious complications episodes (8 viral, 16 bacterial, 1 mycotic, 1 parasitic). One pt had visceral Kaposi's sarcoma. All the long term survivors were able to resume their social and labour activities (3 are students, 1 is a nurse, 1 is a builder); one pt had a child after ITx.

Conclusions: ITx has become feasible option in the Latin- American region with long term survival under the care of a multidisciplinary comprehensive team. Early diagnosis and aggressive management of post ITx complications is required in order to increase the long term survival with a functional graft.

P1.13 - Comprehensive guideline for the management of mesenteric ischemia

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Introduction: Concerning that the leading cause of short bowel syndrome in Asian countries is vascular events, unlike western countries which Chron's disease lies at the top of the list, and also considering that most of these patients would die without proper management and planning, we had decided to design an algorithmic approach for managing these group of patients including years of experience in our country and also other pioneer studies of the field in other countries, by which we have fortunately come into promising results. Due to limited options and lacking HPN most surgeons in our country prefer resection and anastomosis, which had lead to an unfavorable result during past years. So we as the first small bowl rehabilitation and transplantation center in our country decided to design a comprehensive management guideline for this entity and having a categorized approach which includes, what should the first surgeon confronting this situation do at a local hospital and what would the next treatment plan be in a referral hospital, whether the patient needs more complex procedures as small bowel transplantation or reconstructive surgeries, or not.

Methods: A study group of the Intestinal Rehabilitation Unit (IFU) of Shiraz University of Medical Sciences, Iran was formed in 2018 with the aim of developing guidelines for the management of AMI. The evidence was then reviewed to answer these questions, and recommendations formulated.

Results: Regarding what mentioned in the article, mortality will decrease and a considerable number of patients will survive and by performing AGIR surgeries possible need for bowel transplantation will become less. The resultant recommendations are presented in this paper.

Conclusion: The aim of these guidelines is to provide recommendations for practice that will lead to improved outcomes for patients.

P1.14 - Acquisition of food allergy by multivisceral transplantation

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Introduction: Adoptive transfer of food allergy by transplanted organs has been reported after most solid organ transplants. Here we describe two cases of multivisceral transplantation where the recipients acquired the food allergies of their donor.

Methods: Case note review

Results: Case 1 – A 62 year old male with cirrhosis secondary to NASH was dependent on parenteral nutrition for two years prior to decompensation following small bowel resection for intestinal obstruction. The donor was a young adult female with food allergies to peanut, shellfish and baked beans who died of anaphylaxis after eating a cereal bar. Intestine, liver, pancreas and colon were transplanted . The donor serum demonstrated a total IgE of 1059 u/l, and specific IgE positivity to peanut (32.6kua/l), Ara h1, h2 and h3. Following transplant the recipient avoided all nuts, shellfish and baked beans for 6 months. Specific IgE was positive to peanut and ara h1-3 but became negative after one month, and negative to shellfish and tree nuts. Skin prick tests were positive to peanut and grass pollen but negative to other allergens which were subsequently re-introduced. Skin prick positivity to peanut persisted beyond three years post transplant. He avoids peanuts and carries an adrenaline auto-injector.

Case 2 – A 29 year old female who underwent liver transplantation for alpha-1 antitrypsin deficiency at the age of 3 years became parenteral nutrition-dependent following intestinal resections for adhesional obstruction. She underwent liver, intestine, pancreas and colon transplant from a paediatric donor with a history of food allergy who died of anaphylaxis. The donor serum revealed strong specific IgE positivity to cow's milk (14.9kua/l), whey, casein and hazel nuts and ara H8 peanut allergen only. Total IgE was 301. Post transplant the recipient demonstrated brief IgE positivity to cow's milk only. Skin prick tests were positive only to cow's milk and remain positive at 5 months. The patient has reintroduced all other foods with the exception of hazel nuts without incident but continues to avoid milk.

Conclusions: Food allergy transfer by intestine containing grafts may persist longer than with other solid organ transplants, presumably due to persistence of sensitised passenger lymphocytes in the graft . Skin prick tests may be more accurate than specific IgE antibodies and patients should carefully avoid known allergens and take precautions against anaphylaxis.

P1.15 - Paediatric domino liver transplant following multivisceral transplant (liver-inclusive) with splenic preservation – A case report

Hector Vilca-Melendez [1], Amir Nawaz [1], Carly Bambridge [2], Miriam Cortes [1], Jonathan Hind [2], Anil Dhawan [2], Nigel Heaton [1]

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Introduction: A multivisceral transplant followed by domino implantation of the resected liver to another patient was first reported by Tzakis in 1999. Since then there has not been much development in this technique and its implications for both recipients. We present a paediatric multivisceral transplantation with native spleen preservation followed by the use of the recipient's liver as a domino graft for another child.

Patients and Methods:

Multivisceral donor: 3 year old boy with hypoxic brain damage, blood group O+, weight 14kg.

Multivisceral recipient: 7 year old boy, blood group A+, weight 24 kg, with severe intestinal failure (Neuropathic intestinal dysmotility). No enteral feed and 24-h PN, with persistent central line infections. Listed for multivisceral transplant seeking immunological advantage. At transplant, normal native liver (mild portal fibrosis at biopsy) preserved for domino transplant. Splenic artery and left gastric artery were preserved. Pancreas removed leaving splenic vein. Spleno-caval shunt performed preserving native spleen. Native liver perfused with UW solution and stored. Multiorgan graft implanted (liver, stomach, duodenum, pancreas, small bowel and right haemicolon). CIT: 10h.

Domino liver recipient: 3 year old boy, blood group: A+, weight 12 kg, with cholestatic liver disease. Domino liver transplant (graft weight: 484 g, CIT: 10h, duct-to-duct anastomosis).

Results: Multivisceral recipient had bowel obstruction (day 3 post-transplant) that required laparotomy. No acute cellular rejection and no serious infections post-operatively. Stoma reversed at 5 m. He remains on enteral feeding and PN support due to rapid bowel transit. The domino liver recipient had acute cellular rejection (day 8 post-transplant). Anastomotic biliary stricture corrected with biliary reconstruction (6 m post-transplant).

Conclusion: A liver-inclusive intestinal transplant seems to give an immunological advantage to the recipient by decreasing rejection episodes but make them vulnerable to lethal infections (Wu & Cruz, 2018), which is maybe worsened by native splenectomy at transplantation. Preserving the native spleen may reduce the incidence of PTLD, GVHD and risk of infections. The above case could be a better option than a modified multivisceral transplantation and using the multivisceral recipient's liver as a domino graft will decrease the impact on the donor pool. More cases are required to establish the advantages of these surgical techniques.

P1.16 - Chyme Reinfusion As Treatment Of Temporary Intestinal Failure Type 2 Related To High-Output Double Enterostomies Or Entero-Atmospheric Fistulas.

Sabrina layec, marie carsin, laurence dussaulx, eloi seynhaeve, florence trivin, denis picot

Clinique saint yves

Introduction: Temporary double enterostomy (DES) and entero-atmospheric fistulas (EAF) may lead to a type 2 intestinal failure by short bowel syndrome type I. The reinfusion of chyme (CR) from the afferent small bowel to the efferent ileum (EI) restores the intestinal functions until the surgical reestablishment of continuity (SR). Retrospective observational study of 306 patients with CR hospitalized in our centre for 19 years.

Methods: Data from 01/2000 to 12/2018. CR was made with automates and portable pumps with batteries. Height, weight, albumin (Alb), daily intestinal output (IO), nitrogen and lipid absorption (NA, LA), plasma citrulline (Cit) and liver enzymes (ASAT, ALAT, Alcaline phosphatases (AP), γGT were recorded before and during CR. BMI, Nutritional Risk Index (NRI) were calculated. Durations as medians ± IQ, other data as means ± SD. Student's t- test, χ^2 Fisher's tests.

Results: 185H/121F, 64±15 y. DES 266, EAF 40. CR began 5±8d after admission and was pursued 62±41d until SR, at home for 31% of DES patients. The intestinal function improved: IO (2378±775 ml/d - 325±320), NA (51±18 % - 81±12 %), LA (41±22 % - 87±9%), Cit (17.5±6.9 µmol/l – 32.2±17.4). Nutritional status: BMI 24.9±6.5 – 25.1±5.4, Alb 28.2±5.6 – 33.9±5.0 g/l, patients with NRI<83.5 (68% – 27%).The % of patients with plasma liver tests > 2N: ALAT 26% – 13%, ASAT 28% – 10%, AP 42% – 14%, γGT 78% – 38%.Oral feeding was exclusive (n= 194), with an enteral complement "en Y" in EI (n=75). The intravenous supplementation (IVS) requirements were nutritional (n=161) or hydration alone (n=44). They were stopped in 189/205 cases, 2±8d after the beginning of the RC. ($p<0.001$ in all results).

Conclusion: In cases of high-output DES or EAF, the CR reestablishes the continuity of the bowel, restores its functions and adaptes the downstream small bowel and colon before SR. Some postoperative complications are prevented. Patients are fed with what they eat, their nutritional and liver status improves, IVS are stopped in 92% of the cases, reduced otherwise. CR is feasible at home. CR is much less expensive and avoids complications related to IVS and central venous catheters. This enteral technic was recently recommended by special interest groups of ESPEN and ASPEN.

P1.17 - Hypomagnesaemia and Long-Term Outcome after Isolated Intestinal Transplantation- Taiwan experience

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Introduction: Hypomagnesaemia is a frequent complication in the early post isolated intestinal transplantation period and particularly associated with the use of calcineurin inhibitor(CNI) which impair renal tubular function causing tubular magnesium loss. Intestinal transplant recipients are at risk of hypomagnesaemia due to the high dosage of immunosuppressant post transplant than other organ transplantation. And we initiated an intestinal transplant program in Taiwan since 2007. We check the magnesium serum level regally after intestinal transplantation and provide magnesium supplement when the level below normal level to prevent hypomagnesaemia.

Methods: Twenty-two isolated intestinal transplantations were operated in 21 patients (6 children and 15 adults) with one re-transplantation. Immunosuppression protocol included tacrolimus with combination of low-dose steroids and MMF in some cases. Infectious complications were monitored over CMV and EBV titers. Scheduled biopsy of the graft and biochemical analysis of blood samples were used for the surveillance on the patient condition and graft function. Magnesium level was monitored weekly to monthly and Mg Sulfate 10-20mg was provided according to the level. We analyzed the cases with graft above 1-year survival and calculated the percentage of magnesium supplement among these patients.

Results: The causative factors for intestinal failure in these 21 patients include short bowel syndrome (16 / 21, 80%) and motility disorder (5 / 21, 24%). Indications for intestinal transplantation were repeated catheter-related sepsis (4 / 21, 20%), liver function impairment (1 / 21, 5%), major vein thrombosis (5 / 21, 25%), and ultra short bowel (11 / 21, 55%). The survival rates for 1-year, 3-year, and 5-year are 87%, 75%, and 65% for patients. In the 13 grafts that survive longer than 1 year, we found more than 90% patients had hypomagnesium and received supplement with 20meq Mg Sulfate everyday to maintain their Magnesium level around the lower normal limit of 1.6 mg / dl in early period after isolated intestinal transplantation.

Conclusion: Isolated intestinal transplantation is promising and high prevalence of magnesium deficiency was reported in the early post transplant period. Monitor magnesium level and supplementation after intestinal transplantation was essential.

P1.18 - Setting up a transition service for intestinal transplant patients

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Introduction: Improving survival of intestinal transplantation resulted in an increase in number of young people surviving into adulthood. The prospect of transition is exciting but “scary” in the words of our young people requiring the development of a service which meets their unique needs. It is vitally important that a robust supportive transition process is established for young people and families.

Method: Transition is discussed from 12 years with the family at their annual anniversary admission, introducing the concept and describing the process. Young people meet with the transition nurse, youth worker and psychologist. We use a transition programme called Ready, Steady Go and the HEADSS document to support transition.

Families first have the opportunity to meet the adult team at our biannual family day. The adult team consisting of the Lead Consultant, Specialist Nurse and Dietician contribute to the information session during the day. These can be a talk or information boards / posters. This allows families to gather information to make informed choices about their young person’s future care.

The adult team join us in the outpatient clinic at the children's hospital to meet the young person and their parents / carer. It is the start of the formal transition. The Paediatric Consultant and Specialist Transition Nurse attend the adult clinic. The adult consultant will lead the consultation with the Paediatric Consultant contributing.

Results :Ten young people have been transitioned and care handed over to the adult multidisciplinary team. The emphasis is very much on the young person and the time scale will be driven by their needs.

Retrospective review of the medical notes shows that young people are seen once in the paediatric clinic with the adult team, seen two / three times in the adult clinic with the paediatric team in attendance prior to formal handover. Formal handover can take two / three years.Six young people are in the process of being transitioned.

Conclusion :Feedback from families has shaped the service. Communication between paediatric and adult teams has highlighted differences in protocol processes.This has helped us prepare the young people to cope with the differences. Healthcare professionals need to therefore work collaboratively with young people to ensure they have all the information and resources to engage with the service. This will help to ensure a good long term outcome in young people undergoing transition.

P1.19 - Top-ten research topics in paediatric chronic intestinal failure, on behalf of the European Reference Network for rare Inherited and Congenital Anomalies(ERNICA) – Intestinal Failure working group*

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Introduction: Chronic intestinal failure in children is a rare and heterogeneous disease for which high-quality evidence is lacking to guide clinicians in daily practice. The European Reference Network for rare Inherited and Congenital Anomalies (ERNICA) has installed an intestinal failure working group with the aim to improve the care and treatment for these patients. One of the working group's strategies is to combine the knowledge on intestinal failure in the European expertise centres united in ERNICA. Areas of research interest and plans for future studies have been discussed in January 2019 during a two-day meeting in Amsterdam, the Netherlands.

Methods: Healthcare professionals from each participating centre as well as patient representatives presented a top-5 of research questions they deemed most important. The resulting top-10 research questions were discussed, after which a final consensus list of research topics was drawn up.

Results: Twenty-five healthcare professionals from nine countries as well as three patient representatives presented a total of eighteen top-5 research questions. Twelve healthcare professionals were specialized in paediatric gastroenterology and nine in paediatric surgery. Furthermore, three healthcare professionals specialized in adult intestinal failure and one dietician were present. Table 1 shows the final consensus list of research topics, to which was added the need for a joint European paediatric intestinal failure patient registry.

Development of a **patient registry**	
Efficacy and safety of **bowel lengthening procedures** for treating short bowel syndrome	The role of **(altering) the intestinal microbiota** in treating chronic intestinal failure
The efficacy and safety of **growth factors** for the treatment of short bowel syndrome	To evaluate **weaning strategies** and to standardize follow-up after weaning into adulthood in children with IF
The **quality of life** in patients suffering from chronic intestinal failure as well as their parents and siblings	To evaluate the management of patients suffering from **paediatric intestinal pseudo-obstruction syndrome**
The prevention and treatment of **central venous catheter related infection and thrombosis**	Development of a webpage to enable patients to contact expert centres for emergency care when they are on **holiday**
To assess the role of **genetics** in chronic intestinal failure	To evaluate **the body composition and bone mineral density** in patients suffering from intestinal failure

Table 1. the eleven research topics deemed most important by consensus of the working group

Discussion: Subgroups were formed to address these different research topics and develop a research strategy for future projects. The ultimate goal is to increase the standard of care for children with chronic intestinal failure.

P1.20 - Quality of life in children after intestinal transplantation: comparison with liver transplantation and home parenteral nutrition

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Introduction: Home parenteral nutrition (HPN) and intestinal transplantation (ITx) are efficient techniques of the management of intestinal failure (IF).We realised that duration of life may not always equate to child and parents' health related quality of life (HRQOL).The aims of this study are to evaluate the HRQOL in children after ITx with a validated questionnaire, and to compare this population to patients after liver transplantation (LTx), and to patients withIF on long term HPN.

Methods: It is an on-going prospective study including patients between 10 and 18 years old, receiving ITx at Necker-Enfants Malades Hospital, with at least 2 years graft survival. We compared them to patients who underwent LTx or receiving HPN, paired on age, delay from transplantation, diagnosis for children on HPN. We used the Child Health Questionnaire, child report form (CHQ-CF87) and parent report form (CHQ-PF 50), including 13 HRQOL domains: physical functioning, social emotional status, social behavioral status, social physical status, bodily pain, general behavior, mental health, self-esteem, general health perceptions, parental impact, family activities and family cohesion. Mean values for each item will be calculated and converted to percentages. Two-tailed Student t-test will be used to compare the mean scores of subjects.

Results: We enrolled 48 children: 16 after ITx (mean age 14.9 ± 2.7), 16 after LTx (mean age 14 ± 2.9) and 16 on long term HPN (mean age 13.8 ± 3.7). The study just started, with a good participation and feedback from patients and parents. 12 patients and 20 parents already answered. We already observed that in the same subcategory patients and parents scores often differed.

Conclusion: We expect to gain important information about the HRQOL of children after ITx compared to other chronic diseases, to improve the early and long term psychological care of these patients. We hope that better understanding of the impact of these procedures on the child as well as the family's QOL will assist them in the care.

P1.21 - Cmv Pan-Drug- Resistent Infection In Multivisceral Transplant Recipient: A Case Report Of Successfull Treatment

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Introduction: CMV infection is one of the more frequent infection after solid organ transplantation. Several specific antiviral therapy are nowadays available with success in most cases.

Methods: A 38 years old woman underwent total enterectomy due to severe tertiary peritonitis with multiple intestinal perforation. In may 2016 she undewent multivisceral and abdominal wall transplantation from the same donor. She underwent regular antibiotic, antifungal and antiviral profilaxis as universally described. Her CMV serological status wasD+ / R+.

Results: During post operative course a severe abdominal wall infection occurred and vacuum assisted closure needed to avoide abdominal wall graft removal. Despite minimization of the immunosuppressive regimen due to severe abdominal infection and despite antiviral profilaxis, in july 2016 the patient developed a CMV reactivation. Ganciclovir treatment was unsuccessfully attempted and a drug resistence test showed M460V mutation on UL97 gene which gives ganciclovir / valganciclovir resistence. Foscarnet treatment was tried,initially successfully, then CMV viremia increased again. A new drug test resistence showed a viral strain with multiple mutations: M460V on UL97 gene (as the previous test), Q578H and E756D on UL54 gene to confer a pan-drug-resistence (PDR) profile towards all drugs anti CMV available (ganciclovir,valganciclovir,foscarnet,cidofovir). Meanwhile the patient developed CMV disease with intestinal and retinal involvement. After multidisciplinary discussion and literature review,a rescue treatment with leflunomide was started. This is a rheumatoid and psoriatic arthritis drug with known anti CMV activity. With the combination of leflunomide and anti CMV immonoglobulins we obtained a complete response of CMV viremia. Leflunomide was discontinued after 1 year of treatment (due to lower limbs side effects) and anti CMV specific immunoglobulins was continued with progressive dosage descalation.

Conclusion: Leflunomide can be considered a rescue therapy in the cases of pan drug resistant CMV infection. The patient is nowadays stil alive,with residual blindness but with functioning graft,without parenteral or fluid support and with constantly negative cmv viremia.

P1.22 - Intestinal failure in a tertiary children's hospital before and after the establishment of a national intestinal failure service; incidence, aetiology and outcome.

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Introduction: Establishment of a formal intestinal rehabilitation service is associated with improved outcomes for intestinal failure (IF) patients. We compared incidence, aetiology and outcomes of inpatients with IF at the only tertiary children's hospital in New Zealand, before and after the establishment of the New Zealand National intestinal Failure Service (NZ NIFS).

Method: A retrospective review of intravenous nutrition (IVN) records identified patients with IF aged 0–18 years, admitted to Starship Child Health between July 2010 and October 2018. IF was defined as inpatients receiving IVN ≥21 days as per the NZ NIFS criteria.

Medical records were reviewed to identify demographics, indication for IVN, biochemical markers for intestinal failure-associated liver disease (IFALD) and clinical outcome. Indication for IVN was defined as per NZ NIFS pathological classifications (adapted from 2016 ESPEN guidelines for chronic IF in adults): extensive small bowel mucosal disease; mechanical obstruction; intestinal dysmotility; intestinal fistula; short bowel syndrome and other diagnosis. IFALD was defined as peak bilirubin >34mmol / L, for at least 2 weeks, in the absence of another cause.

Results: 882 children received IVN during the 8 year period. 19% (171 / 882) were classified as having IF. The IF patients came from 17 of NZ's 20 health care districts. There was no significant increase in patient transfers between the time periods. Three quarters of IF patients came from three of 11 referring teams; oncology 33% (51 / 171), gastroenterology 28% (48 / 171) and ICU 19% (32 / 171).

Common indications for IVN were extensive small bowel mucosal disease (46%), short bowel syndrome (15%) and mechanical obstruction (13%).

IFALD occurred in 9% (15 / 171), there was no difference between the time periods. There was a slight excess of patients with mechanical obstruction (17%, 4 / 23) but this was not statistically significant.

73% (125 / 171) had successful intestinal rehabilitation to enteral autonomy. 6% (10 / 171) were established on home IVN and existing home IVN patients accounted for 9% (15 / 171) of IF admissions. Intestinal transplantation was necessary for only one patient. No mortality related to IFALD was identified, however 12% (20 / 171) died from their underlying diagnosis.

Table 1: Intestinal failure pre and post the establishment of NZ NIFS

Starship Child Health admissions	Pre NZ NIFS 2010-2015	Post NZ NIFS 2015-2018
Total number on IVN (average per year)	572 (114)	310 (103)
Total number with IF (%)	101 (18)	70 (23)
Indications for IVN		
Extensive small bowel mucosal disease (%)	51 (50)	28 (40)
Intestinal dysmotility (%)	12 (12)	9 (13)
Intestinal fistula (%)	2 (2)	0 (0)
Mechanical obstruction (%)	8 (8)	15 (21)
Short bowel syndrome (%)	18 (18)	8 (12)
Other (%)	10 (10)	10 (14)
Outcomes		
Total number with IFALD (%)	9 (9)	6 (7)
Death from underlying diagnosis (%)	10 (10)	10 (14)
Enteral autonomy (%)	72 (71)	53 (76)
Existing home IVN (%)	11 (11)	4 (6)
New home IVN (%)	7 (7)	3 (4)
Intestinal transplant (%)	1 (1)	0 (0)

Conclusion: Since the establishment of NZ NIFS in 2015 our inpatient IF demographics have remained broadly the same, the incidence of IFALD remains low and inpatient numbers have not increased.

P1.23 - Use of Pureed Green Beans Through a G-tube in Pediatric Patients with Short Bowel Syndrome – A Single Center Experience

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Background: Pectin and other water-soluble fibers have been used in certain patients with short bowel syndrome. Fermented fibers may provide energy contribution via short chain fatty acids produced by colonic bacteria, while soluble fibers that retain a gel may improve the consistency of watery or loose stools and thus decrease stool output. At our institution, we aimed to study the effects of pureed green beans, a good source of pectin, given in a reliable and easy manner, through a G-tube.

Methods: Pureed green beans administered via syringe directly into the G-tube was prescribed in a handful of patients with short bowel syndrome. Dose of green beans was adjusted at regularly scheduled clinical visits. Patients and their stools were closely monitored.

Results: Of the 71 intestinal rehabilitation patients at our center, 7 are currently receiving pureed green beans through G-tube. All patients experienced a decrease in stool frequency and 6 of them experienced improvement in stool consistency. Over half of the patients also tolerated a decrease in loperamide. Of the 6 patients receiving either TPN or IV hydration, 5 tolerated a decrease in the overall volume. One patient was weaned off of IV hydration fluids entirely. Please refer to Table 1.

Conclusion: Overall, our cases highlight the improvement in stool frequency and consistency, TPN volume requirements, and loperamide administration following the administration of pureed green beans into a G-tube. For our patients with G-tubes and difficult to manage loose stools, the introduction of pureed green beans is now being considered more frequently. Potential future research may include: examining if higher doses of green beans increase the risk of malabsorption of certain nutrients (such as magnesium, zinc, and iron), monitoring the incidence of central line infections following stool normalization, and studying the effects of specific fibers or foods on the microbiome in patients with short bowel syndrome.

P1.24 - Vascular stenting for mycotic aneurysm in multivisceral transplant recipients

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Introduction: Severe graft pancreatitis (GP) although uncommon after multivisceral transplantation (MVT) may be associated with necrosis of the gland, infection of necrotic debris and bleeding secondary to erosion of infected necrosis into surrounding vasculature. For MVT the anatomic proximity of graft pancreas to the aortic conduit (AC) poses unique challenge when affected by infection and necrosis as local control of a mycotic aneurysm (MA) by embolization or surgical ligation would lead to ischemia of the transplanted viscera.

Case 1: A 40 year old female underwent MVT. Postoperatively, she developed severe GP and intra-abdominal abscesses and had persistent bacterial and fungal sepsis. On day 28, she developed massive intra-abdominal bleed. At emergent laparotomy, aortogram showed irregularities in the AC concerning for MA. An intra-aortic balloon was placed to control hemorrhage with excision of the involved area and primary anastomosis of the conduit. Three days later she had recurrent massive bleeding from multiple sites along the remaining length of the AC which could not be controlled and the patient succumbed.

Case 2: 44 year old male received MVT. His early post operative course was complicated GP and infected peripancreatic collections. On day 26 he developed massive intra-abdominal hemorrhage which on exploration was noted to be coming from the donor AC. The AC appeared thinned and had blackish discoloration consistent with MA. Vascular surgery colleagues deployed 2 endovascular stents in the celiac axis and superior mesenteric artery to bypass the weakened segment while maintaining blood flow in both the major graft vessels. The space between the stents and wall of the AC was then filled with coils. He had no graft dysfunction although further aneurysmal changes of the proximal AC (Fig1) a few weeks later required extension of the stents from the previously placed stents all the way to his native aorta. He is now more than 1 month after the revision without evidence of infection or extension of the MA, with resolution of the GP and good graft function.

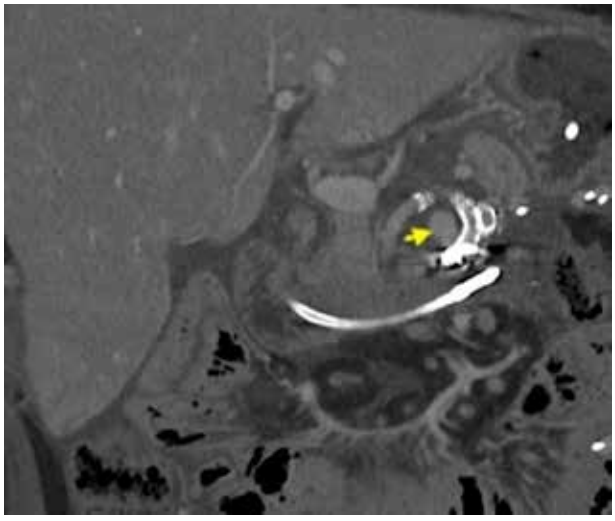

Table1: Recipient and donor data

Recipient Data	Case 1	Case 2
Age (years)	40	44
Sex	F	M
MELD	26	30
Organs transplanted	Liver, pancreas, small bowel	Liver, pancreas, stomach, small bowel, ascending colon
Explant duration (min)	420	490
CIT (min)	557	474
WIT (min)	30	36
Preoperative embolization	yes	yes
EBL (ml)	6000	7000
PRBC (units)	22	16
Pancreatitis	Yes, POD3	Yes, POD5
Aneurysm presentation	POD28	POD26
Infection	Bacterial, fungal	Bacterial, fungal, mycobacterial
Intervention	Surgical excision of involved segment and primary re-anastomosis of aortic conduit	Endovascular stenting of Celiac axis and SMA with coil embolization of conduit surrounding the stent
Outcome	Expired	Alive
Donor Data		
Age	*24*	*45*
Sex	*F*	*F*
Ht/Wt/BMI	*157/56.2/22.8*	*167.6/69/24.5*
Cause of death	*Anoxia*	*Cerebrovascular stroke*
Other findings		*Hypertension*

MELD, model for end-stage liver disease; CIT, cold ischemia time; WIT, warm ischemia time; EBL, estimated blood loss; PRBC, packed red blood cells; POD, post operative day; Ht, height; Wt, weight; BMI, body mass index

Conclusion: Graft pancreatitis following MVT can lead to fatal hemorrhage from erosion of infected necrosis into the vascular inflow to the graft. Endovascular stenting of the AC vessels (celiac and SMA) offers a potential treatment option in this situation. This is likely a safer and durable solution than attempt at surgical revision of the anastomosis in the presence of infection.

P1.25 - Importance Of Enteral Nutrition In Intestinal Rehabilitation. National Hospital Guillermo Almenara Irigoyen. Lima Peru.

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Introduction: Patients with short bowel syndrome (SBS) due to massive intestinal resection due to mesenteric ischemia or surgical complications, require parenteral nutrition (PN) for long periods until the residual intestinal length (RIL) adapts. This depends on age, RIL, underlying intestinal pathology. The adaptation can take two or more years; however, enteral nutrition (EN) can be an essential element by decreasing the time of intestinal adaptation and periods of PN.

Patients and methods: Prospective case series (2015 to 2017). Patients with intestinal failure associated with SBS were given an enteral access type gastrostomy or naso-jejunal tube during the autologous gastrointestinal reconstruction (AGIR), then they were administered polymer enteral nutrient by infusion pump, using the tolerance protocol (Denver) and then maintenance until you achieve EN total and leave the PN.

Results: 10 patients, 7 men and 3 women, between 30 and 68 years old, 5 with gastrostomy tube, when the RIL after the AGIR was less than 100 cm or naso-jejunal tube when the intestinal length was longer. Periods of intestinal rehabilitation were achieved, with withdrawal of PN and oral feeding, between 6 to 12 months. In all patients, the follow-up was performed for 1 year.

Discussion and conclusions: The results show the main advantage of the use of polymer enteral nutrition is the reduction of time to intestinal rehabilitation. These results would be associated to the physiological changes produced by the enteral stimulus and the utilization of the circadian rhythm of intrinsic secretion of Growth Hormone during nocturnal EN. The diagnosis and treatment of the underlying disease, as well as the preparation and protocolized execution of AGIR are important elements that allow to install a therapy of intestinal rehabilitation with EN.

P1.26 - The impact of advances in intestinal rehabilitation strategies and PN management on the outcome of children with Chronic Intestinal Failure

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Background: Recent advances in the management of children with chronic intestinal failure have presented new therapeutic options for treatment in this complex patient group. To help inform future therapeutic strategies, we assessed the outcome of children with chronic intestinal failure managed by a multidisciplinary intestinal rehabilitation program over a 27-year period.

Methods: A retrospective longitudinal review of children with chronic intestinal failure assessed for home parenteral nutrition (PN) therapy at the Royal Children's Hospital Melbourne from 1991 to 2018.

Results: A total of 64 children with chronic intestinal failure due to short bowel syndrome [SBS: median bowel length 33.5cm] (n=51, 80%), chronic intestinal pseudo-obstruction (n=5), congenital enteropathy (n=4) and other genetic abnormalities (cystic fibrosis n=1, megacystitis microcolon syndrome n=1, immune deficiency n=2) were included. The overall survival was 57 (88%), with no deaths attributed to intestinal failure or its management in home PN patients in the past decade. Weaning from PN was successful in 31/45 (69%) of SBS survivors after a median of 18.5 months. Longer residual small bowel length and the presence of the ileocaecal valve (ICV) and colon were predictors of success. The frequency of central line associated blood stream infections has fallen dramatically from ~7.3 episodes/1000 line days in 1991 to 2011, to ~0.5 episodes/1000 line days in 2018. Eight patients transitioned to an adult Home PN program and two patients have undergone successful liver-intestinal transplantation.

Conclusion: Advances in the management of children with chronic intestinal failure have had a significant impact resulting in improved outcomes. Children with SBS, even in the presence of small residual bowel length have a good prospect of weaning from PN, particularly if the ICV and colon are preserved. The survival rate and frequency of central line associated blood stream infections have dramatically improved. Targeted individualized therapy and care by a multidisciplinary team expert in intestinal rehabilitation and nutrition can optimize outcomes in children with chronic intestinal failure.

P1.28 - What do patients with short bowel syndrome eat in real life?

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ESPEN has elaborated guidelines for management of patients with short bowel syndrome (SBS). Those one include dietary recommendations that are difficult to put into practice. Our aim is to evaluate on a cohort of short bowel syndrome the real life food intakes in terms of quality and amount.

It is a prospective study including the consecutive adult patients with short bowel syndrome (remaining small bowel length ≤ 200 cm) who had their outpatient visit for regular nutritional monitoring between February 6th, 2018 and May 29th, 2018. As usual, oral intake was evaluated by one of the experimented dietitians involved in our multidisciplinary team. Sixty nine patients (M: 39%; F: 61%), with a mean age of 58.8 years (±19.4) were included. The mean BMI was 22.6 kg/m2 (±5.1). The mean remaining small bowel length was 99.4 cm (±54.4). Thirty nine patients (49%) require Home Parenteral Nutrition. Oral intake was evaluated using three days food diary. Total oral intake (percentage of carbohydrates, proteins and lipids), oral rehydration solution (ORS) consumption and amount of fibers were analyzed. The energy expenditure was calculated with Harris and Benedict formulae.

Patients with intestinal failure (n=39) required 4.6 ± 1.9 infusions per week, with a volume of 10 909 ± 9 187 ml per week and 7 030 ± 4 559 kcal per week. Six/15 patients with jejunostomy consumed ORS regularly with a mean intake of 9 041 ± 3 572 ml per week. Oral proteins/glucids/proteins(%) intake is respectively for patients with jejunostomy and patients with anastomosis 16.9/ 57/ 34.7 and 15.2/51.5/33.1. Guidelines recommende 20-30% of proteins for all patients, 40-50% of glucids for patients with jejunostomy and 50-60% for patients with anastomosis and 40% of lipids for jejunostomy and 20-30% for patients with anastomosis.

In a large SBS cohort patients with intestinal failure or intestinal insufficiency, even with dedicated dieticians, patients whatever the intestinal anatomy have the same profile of ingesta in terms of quantity and amount of macronutrients. Interestingly, in our population, 40% of patients with jejunostomy have a regular and consistent ORS intake. That's probably due to a very important engagement of dietician and physician to explain the importance of drinking specific beverage in these patients. So, we can suppose, that a more adapted, dietetic training program could improve the global adhesion of recommended diet for SBS patients.

Table 1: Oral intake evaluated in SBS population in comparison to expert recommendations

P1.29 - The impact of a nutrition multidisciplinary team

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Introduction: The evidence-based standard for optimal nutritional support is the Multidisciplinary team (MDT) approach of a Nutrition Support Team (NST). Our hospital team was established in 2015 after a 3 year pilot 2012-2014. The nurse-led team review new parenteral nutrition (PN) referrals and continue to visit assess and advice twice weekly. The aims of the team are to:

- Improve the safety and adequacy of PN delivery to patients
- Provide high quality nutritional outcomes via enteral and PN
- Deliver significant cost savings
- Improve hospital wide nutrition education (nursing, medical and allied health professional)

Aim: To assess improvements in clinical care and financial benefits associated with the NST before and after the service was established looking at:

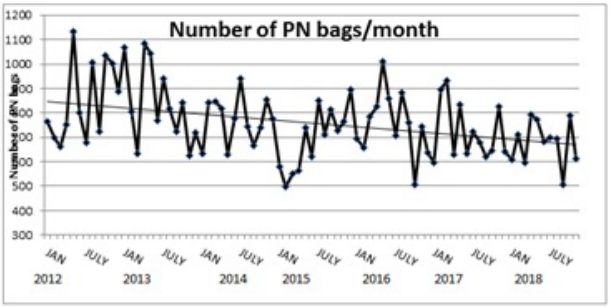
1) PN bag usage

2) Standard bag usage

4) Wastage

Method: The PN usage pre and post the NST was collected from a pharmacy database. A new NST database collected prospective data on the activity of the team. Data collected included: clinical speciality, recommendations, abnormal blood results, time on PN and refeeding risk. This data was analysed as part of this audit process.

Results:



There has been a 20% reduction in the number of total PN bags / year (fig 1).

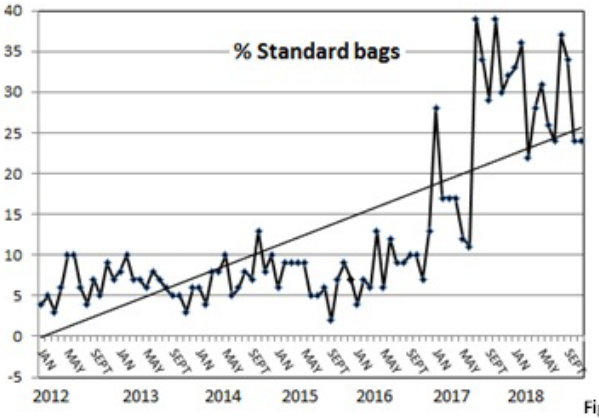


Fig 2

Standard bag usage increased from 6% to 30% between 2012 and 2018 (fig 2) .

Reduction in PN usage and increased % of standard bags has reduced cost of PN provision between 2012 and 2018 by approximately €230,000 / year.

Wastage of PN bags reduced from 4% to 3.7% between 2012 and 2018. Reasons for wastage include full enteral nutrition, patient deceased and transfer to another hospital.

NST recommendations for changes in PN prescribing and monitoring were made in 70% of contacts in a 12 month period.

57 patients in a 12 month period were considered at risk of refeeding, 56% of patients showed metabolic signs of refeeding and their plan of care was adjusted accordingly. There were no cases of unanticipated refeeding.

Conclusion: Regular patient reviews, forward planning and education has improved the safety of PN delivery, decreased the total number of PN bags used and contributed to increased standard bag usage. Choosing other available standard bags to suit our population of patients has also been a contributory factor for this significant increase.

Wastage of PN has shown a modest decrease during the study period. Anticipating weaning of PN and patient transfer is an area of focus for the team.

P1.30 - Teduglutide: the new weapon in pediatric short bowel syndrome

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Introduction: Short bowel syndrome (SBS) is generally defined as the loss of an extensive length of the small intestine resulting in an inadequate absorption of enteral nutrients. Teduglutide is a recombinant analog of native human GLP-2 with resistance to in vivo degradation, enhanced intestinal adaptation and increased the absorptive capacity of the remnant intestine in patients with SBS.

Methods: A premature girl (33 weeks) with necrotizing enterocolitis (NEC) underwent extensive intestinal resection (only 30 cm of jejunum anastomosed to the sigmoid colon preserved). Intestinal dilation and the need for PN forced to perform an intestinal lengthening with a modified serial transverse enteroplasty procedure (STEP) twice, at 19 months and 3.5 years (final small bowel length 175 cm).

At the age of 7 years old, the patient still required PN 25 Kcal/kg and high volume of iv fluids (2300 ml; 85 ml/kg) administered for 17 hours/day. She had 7-8 semiliquid bowel movements/day (output 2000 ml/day) and frequent hospital re-admissions owing to catheter-related infections. She only had a single central venous access for PN administration. The written informed consent of the parents was obtained for the administration of teduglutide and the hospital approved its subcutaneous administration in a dose of 0.05 mg/kg/day.

Results: The evolution of PN volume, calorie requirements, days of PN administration and plasma citrulline, before and during teduglutide treatment are shown in Table 1.

Table 1. Monitoring teduglutide administration

Teduglutide treatment (weeks)	PN volume (mL)	PN calories (Kcal/kg)	PN Days/week of PN	Plasmatic Citrulline (µmol/L)
0	2300	25	7	14,7
4	2000	20	7	31,6
8	1000	10	7	51,3
12	1200	10	6	-
16	1200	7	4	64,3
20	1200	5	3	-
24	1200	3,5	2	52,1
30	0	0	0	-
60	0	0	0	56

Prior to treatment, weight, height and body mass index (BMI) were 27.2 kg (+0.86 SD), 135 cm (+2.04 SD) and 14.9 (-0.39 SD), respectively. After 4 weeks of treatment, less frequent bowel movements, change in stool form (more consistency) and increased urine output were noted, weaning off PN support was initiated. At 22 weeks, the patient only required PN 2 days/week which was stopped at week 30 of treatment. In parallel, a rise in serum citrulline was observed.

After 18 months of treatment we decreased dose to 0.025 mg/Kg/day and after follow-up of 24 months, the patient remained free of PN at this daily dose. Nowadays, bowel movement frequency is 2-3 per day (type 5 on the Bristol scale). Weight (31.6; -0.24 SD) and BMI remain stable (14.8; -0.85 SD), while her height has increased to 146 cm (+1.5 SD).

Conclusions: Teduglutide has allowed this child, a candidate for intestinal transplantation, to achieve complete PN-free status with a great improvement in her quality of life.

P1.31 - Salvage therapy with Infliximab for anastomotic ulcers- a potential treatment for a challenging complication

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Background:

Children with short bowel syndrome (SBS) may require bowel lengthening procedures such as the Serial Transverse Enteroplasty (STEP) procedure. STEP may be associated with severe complications such as anastomotic and staple line ulcers with gastrointestinal (GI) bleeding. These complications pose a therapeutic challenge and are often refractory to medical therapy. We present a child with recurrent GI bleeds from staple line ulcers responsive to treatment with Infliximab (IFX).

Case:

An 11 year old male with SBS and intestinal failure secondary to gastroschisis with midgut atresia underwent STEP procedures at 4 months of age and again at 4 years. He developed recurrent GI bleeds and was found to have multiple ulcers along staple lines on repeat endoscopies. Initial treatment included mesalamine (65mg / kg / day), oral budesonide (9mg), pantoprazole, omega-3, and cycling antibiotics with no improvement. Due to failure of all treatment attempts by 8 years old, he was started on IFX (6.5mg / kg / dose at week 0, 2, and 6 weeks then every 8 weeks). IFX level at dose #4 was <0.035ug / mL, anti-IFX antibodies <2AU / mL. Almost complete mucosal healing was found on endoscopy after dose #4. At infusion #6, anti-IFX antibodies were 70AU / mL, the child developed a rash and fever during the infusion and IFX was stopped.

Other bioplogic therapies attempted included Adalimumab and Golimumab, not effective in preventing recurrent GI bleeding. The failure of medical therapies led to massive small bowel resection with removal of all areas involved with the previous STEP procedures. The most proximal staples were left in situ. Despite resection, new ulcers and GI bleeding occurred at the remaining staple site and in the duodenum. As a result IFX was reintroduced with methylprednisolone for premedication. The patient received IFX (10mg / kg / dose, week 0 and 2), repeat induction at week 4 due to low levels of IFX <0.035ug / mL. Follow up endoscopy showed excellent mucosal healing after 3 doses of IFX. Due to high anti-IFX antibodies, 190AU / mL, IFX was held at dose #4.

Conclusion:

Anastomotic and staple line ulcers post-STEP procedures were responsive to treatment with IFX in this case. Development of anti-IFX antibody can be a barrier for a successful outcome and should be monitored. The response to IFX suggests a potential role for innate immunity and TNF alpha in the pathogenesis of anastomotic ulcers.

P1.32 - Concordance of Fibroscan and Biopsy for monitoring liver fibrosis in patient undergoing long term parenteral nutrition.

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Department of Gastroenterology

Background: Home parenteral nutrition (HPN) associated liver disorder remains a major metabolic complication that may requires liver-intestine or multivisceral transplantation in some cases.The decision about the timing and the type of transplantation depends on the degree of liver fibrosis, whose evaluation requires liver histology. Although hepatic biopsy is the gold standard for detecting liver fibrosis, it is an invasive procedure with some complications. Therefore, noninvasive methods as a Fibroscan were developed to assess liver fibrosis. The goal of this study was to compare liver biopsy and Fibroscan in the evaluation of liver changes in patients with intestinal failure in HPN.

Methods: Inclusion criteria:Patient with short bowel syndrome using HPN for at least six months who underwent liver biopsy.In each patient we evaluated: characteristic of HPN, underlying disease, gut anatomy; clinical assessment; biochemical work-up; liver biopsy; Fibroscan assessment (score of liver stiffness).Liver histologic fibrosis was scored according the Brunt classification (grade: 0 to 4).

Results: Eighteen patients were enrolled (07 women / 11 men, mean age: 37y.). Reasons for liver biopsy were altered hepatic enzymes (n =18). The median duration of HPN was 31 months (range 11-133). Indication for HPN was short bowel disease (chronic mesenteric ischemia n = 4; Crohn's disease n = 4; complications of bariatric surgery n = 4; volvulus n = 3) and chronic intestinal pseudobstrution (n = 3).Liver histology showed severe fibrosis (Brunt stage > 2) in 5 patients (28%) Abnormal Fibroscan score (F >3) was observed in 5 patients (28%). The results of liver disease graduation are presented in Table 1.Statistical analysis by Concordance Kappa was evaluated and no correlation was observed between Fiboscan and liver biopsy (p <0,238).

PATIENT	FIBROSCAN	BRUNT
1	F1	F1
2	F1	F1
3	F3	F2
4	F3	F2
5	F2	F1
6	F1	F1
7	F1	F1
8	F2	F1
9	F1	F1
10	F1	F1
11	F3	F2
12	F1	F1
13	F4	F4
14	F4	F2
15	F1	F1
16	F1	F1
17	F2	F1
18	F2	F1

Table 1.*Comparison between the Fibroscan and the Brunt stage.*

Conclusion: No correlation was observed between Fiboscan and liver biopsy in patients on HPN due to short bowel disease.

P1.33 - Is there a role for ultrasound in the evaluation of graft small bowel ?

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Introduction: Intestinal graft recipients are subjected to often significant doses of radiation. MRI studies may not be feasible acutely. Endoscopic examination of the intestine is usually limited to small sections of the graft. Ultrasound (US) is an established technique in the evaluation of disease extent in patients with small bowel Crohn's. We have utilised US for several years to evaluate the graft small bowel and have retrospectively reviewed our findings.

Methods: This is a retrospective review of small bowel US studies performed post operatively for our cohort of 97 patients receiving an intestine-containing graft between 2007 and 2019. Imaging interpretation was made on the basis of grey-scale images and Doppler imaging. US images were reviewed with subsequent clinical, imaging, endoscopy and histology findings

Results: 97 patients received an intestine-containing transplant between 2007 and 2019. There were 45 US studies undertaken in 27 patients. The majority of studies (23 studies in 9 patients) were undertaken in those with biopsy-proven acute cellular rejection (ACR). Imaging findings of mural thickening, loss of mural stratification, reduced peristalsis and mesenteric hypervascularity were observed in 7 patients with ACR. 2 patients with a history of ACR had normal US appearances at follow up, which correlated with endoscopic findings of recovery.

Of the US performed for ACR, concurrent endoscopy (within 1 week) occurred in 11 US studies. 8 endoscopies demonstrated features related to rejection confirmed at histology. 3 demonstrated recovery.

5 patients underwent US immediately post surgery with normal findings consistent with concurrent CT or endoscopy findings.

17 US studies were undertaken for 12 patients for a range of clinical indications : 5 studies were normal, 4 consistent with clinical / imaging findings. 1 patient had drug related ulceration at endoscopy. 11 studies in 6 patients demonstrated minimal mural thickening but no further features to suggest rejection, 4 were followed with endoscopy with no features of rejection . The remainder were followed clinically and radiologically. 1 US demonstrated features suggesting rejection but normal endoscopic findings. An internal hernia was found at surgery.

Conclusion: Small bowel US is a useful technique in establishing normal appearances of the bowel. When interpreted in conjunction with clinical and endoscopic findings in patients with ACR it may have a potential role in surveillance.

P1.34 - Multivisceral transplantation in the Czech Republic- 4years single-center experiences Kudla M., Wohl P., Janousek L., Honsova E., Fronek J.

Michal Kudla

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Introduction: Intestinal / multivisceral transplantation (IT / MVT) is the gold standard treatment for patients with intestinal failure and complications related to total parenteral nutrition, gastrointestinal inoperable indolent tumors, or diffuse portal trombosis.

Methods: Since 2004 we performed 7 full multivisceral transplantation between December 2014 and May 2018. Indications for transplantation were multivisceral thrombosis (n=5) and desmoid tumours (n=2). Immunosuppression was based on induction with alemtuzumab (followed by tacrolimus and steroids) in the first period and infliximab and basiliximab (followed by with tacrolimus and steroids) in the last case.

Results: Four patients are alive. All these patients are without parenteral nutrition. Mortality rate was 43% due to sepsis in 2 cases and in 1 case to cardiac faillure in the first day after transplantation. In all patients we diagnosed acute cellular rejection. Graft-vs.-host disease was seen in 1 case.

Conclusion: Intestinal transplantation is a suitable treatment for highly selected patients with intestinal failure who meet specific listing criteria.

P1.35 - Spectrum of major abdominal surgical procedures within a pediatric intestinal rehabilitation (IR) program

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Background: Surgery plays a key role for the intestinal rehabilitation (IR) of children with short bowel syndrome or chronical intestinal failure. Whereas single procedures – especially for intestinal lengthening - are regularly being evaluated and described, the whole spectrum of surgical procedures within large IR programs in children is often difficult to assess. Our aim was to analyse the complete spectrum of major abdominal surgical procedures in a pediatric IR program.

Methods: We retrospectively analysed patients' data from our pediatric IR program with special focus on all patients undergoing major abdominal surgery. Patients characteristics as well as surgical data were evaluated.

Results: The study period ranged from 2013 until 2018. During that period 184 patients were treated within our IR program. Of these children, 58 (31,5%) underwent major abdominal surgery. There were 35 male and 23 female patients. Diagnoses were anatomical short bowel syndrome (gastroschisis, atresia, volvulus on others) in 40 patients, hypoperistaltic conditions (aganglionosis, hypoganglionosis, MMIHS) in 17 patients and malabsorption (Microvillus Inclusion Disease) in one patient. Ten children originated from our own area, whereas 48 children were referred to us from different national or international regions. Mean number of operations prior to referral to us in those patients coming from other sites was 2.6 (0-7). In the 58 patients, 107 operations were performed (median 1.5, range 1-6). One operation was performed in 29 children, 19 children underwent 2 operations, 6 children underwent 3 operations, 2 children received 4 operations and 2 children underwent 6 operations. The types of surgical procedures were mostly reconstructive (n=100), while lengthening procedures were performed on 7 occasions (6.5%). Mean operating time was 145.2 minutes (range 31-1356). One child died in the early postoperative phase because of SIRS and two children died independently from the surgical procedure because of the central line sepsis.

Conclusion: The spectrum of surgical procedures in a pediatric IR program displays a wide variety of indications; reconstructive procedures are predominant. The procedures are complex and time consuming and require a comprehensive management including preoperative workup and indication, intraoperative surgical and anaesthesiological care as well as postoperative intensive care treatment.

P1.36 - Essential fatty acids profile in pediatric patients receiving an intravenous lipid emulsion containing 15% fish oil

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Composite intravenous lipid emulsion (ILE) containing soybean (30%), medium chain triglycerides (MCT) (30%), olive (25%) and fish (15%) oil (SMOFlipid®) is now widely used in the world for prematures, newborns and children on parenteral nutrition (PN). Long-term use in children on home-PN (HPN) is not documented. The aim was to assess the fatty acids (FA) profile of such HPN children.

Population: 26 children with chronic intestinal failure (CIF) were assessed [SBS = 10, congenital enteropathy = 9, total aganglionosis = 4, CIPOS = 3] aged 6 months-16 years on home-PN for 12 months-16 years, highly dependent on PN (low plasma citrulline levels and high PN intake). All received SMOFlipid® as source of ILE for 12 - 38 months at the dose of 2.1 ± 0.39 g/kg/day, 6.7 ± 0.7 days/week. They were compared to 26 SBS children aged 7.8±3.9 years, weaned off PN for > 2 years.

Methods: Sampling performed after ≥ 24h fat free PN and 6-8h after PN discontinuation. Red blood cell (RBC) fatty acids (FA) profiles were established by using gas-chromatography. Citrulline plasma levels, ratio non protein energy PN-intake(NPE)/resting energy expenditure (REE) - Schofield equation-, growth parameters in Z-score and total bilirubin were assessed.. FA profiles and Holman ratio (triene/tetraene) were compared to those obtained from the control group.

Results:

	SMOF (n=26)	Control (n=25)	P values
Citrulline mean µmol/l	5.9 ± 2.8	27.0 ± 7.8	P < .0001
NPEI/REE (%)	130 ± 20 %	0	
Total bilirubin µmol/l	11.3 ± 7.0	6.4 ± 3.0	NSD
Body weight (Z-score)	- 0.1 ± 1.4	- 0.2 ± 1.0	NSD
Body size (Z-score)	- 0.3 ± 1.5	+ 0.1 ± 1.2	NSD
C16: 0; Palmitic Ac	26.3 ± 1.7	24.5 ± 2.0	NSD
C18: 1n-9; Oleic Ac	15.8 ± 1.6	13.8 ± 1.1	NSD
C18: 2 n-6; Linoleic Ac	7.8 ± 3.4	9.6 ± 1.6	NSD
C20: 4 n-6; ARA	8.5 ± 1.4	14.7 ± 1.7	P < .0001
C20: 5 n-3; EPA	3.8 ± 1.4	0.84 ± 0.52	P < .0001
C22: 6 n-3; DHA	10.1 ± 1.9	6.56 ± 2.30	P < .0001
Holman ratio	0.029 ± 0.014	0.026 ± 0.005	NSD

NSD : No significant difference.

Conclusion: Long-term administration of an ILE rich in fish oil (15%) in highly PN dependent children (PN/REE:130±20 %) is well tolerated. Bilirubin plasma levels remained low and growth was normal. The RBC-FA profile, reflects the n-3/n-6 FA acid composition of this new fish oil rich ILE, without EFA deficiency as assessed by the Holman ratio. This "new" RBC-FA profile, followed on the long term, is not accompanied with any harmful clinical effect and can be considered as safe and probably beneficial for preventing IFALD.

P1.37 - Incidence and outcomes of exfoliative rejection at a UK transplant centre

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Introduction: Exfoliative rejection (ER) of the intestinal graft is associated with significant fluid and electrolyte losses, recurrent sepsis due to microbial translocation and often leads to graft enterectomy, re-transplant or death. The majority of previously reported cases or case series of ER are in paediatrics.

Methods: We present here a case series of ER in adults from a single centre in the UK over the time period 2007-2018. This is a retrospective review of a database containing patient demographics, endoscopy and histology findings and outcomes. ER was diagnosed based on endoscopic findings of widespread areas of denuded mucosa.

Results: 84 patients were transplanted in the specified time period: 34 MVT, 13 Liver / Intestine, 11 MMVT, 25 Intestine only. 7 patients (8.3%) experienced an episode of ER. Precipitating reasons for ER were immunosuppression switch (2), non-compliance (2), low immunosuppression levels because of comorbidity (2) and in one case the patient had concurrent severe adenovirus infection. It is not clear whether the viral infection triggered rejection.

All patients received pulsed steroids. 4 / 7 patients received second line treatment with Alemtuzumab (1) or Anti-Thymocyte Globulin (3). 3 patients underwent repeat transplant of which one had graft enterectomy 3 weeks prior to the second transplant. 2 further patients had limited graft resection due to strictures and had subsequent full graft function. The only death related to ER occurred in the patient with concurrent adenovirus who developed a recurrence of this following re-transplant. All patients required parenteral nutrition and often additional fluids and electrolyte replacement due to the large volume stomal losses (often in excess of 5 litres per day) until recovery or re-transplant.

Conclusion: Exfoliative rejection in this case series frequently occurred in the setting of overall lower immunosuppression than would be desirable. In some cases this was unavoidable, but every effort should be made to support patient adherence to treatment and to provide general psychological support. Historically, switching immunosuppression has been a potential trigger for severe / exfoliative rejection in our unit. Protocols are now in place for managing switches and since these have been instigated, no episodes of rejection have occurred in this context. Reducing immunosuppression due to co-morbidity is always a difficult decision and should be made within a full multidisciplinary setting.

P1.38 - The Dental Health of patients referred for Small Bowel and Multivisceral Transplantation to a UK transplant centre

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Introduction: Dental care during pre-transplant workup is important to reduce potential sources of infection, following immunosuppression to prevent graft rejection. This study documents the prevalence of oral abnormalities and recommended treatment of patients assessed for small bowel and multivisceral transplantation.

Methods: We present a case series of 57 patients who underwent assessment for small bowel and multivisceral transplantation in a single centre in the UK (Cambridge) over the time period 2015-2018. This is a retrospective review of their formal assessment in a maxillofacial clinic and subsequent outcomes.

Results: Of all patients assessed, 18(32%) required no treatment or crown and polish only; 12(21%) required at least one filling; 27(47%) required at least one tooth extraction and 6(10.5%) required full dental clearance. Of the 28 patients accepted and listed for transplantation, 11(39%) required no treatment or crown and polish only; 4(14%) required at least one filling; 13(46%) required at least one tooth extraction and 4(14%) required full dental clearance.

Conclusion: This is the first reported study of the dental health of patients referred for small bowel and multivisceral transplantation. Overall these patients have poorer dental health compared with published data for patients referred for liver transplantation1 and over half of those accepted for transplantation required procedural intervention prior to listing. Many patients have intestinal failure at the time of referral. We hypothesise that long-term use of hypertonic fluids may partly account for the poor results described and that patients with intestinal failure should be considered for regular dental review and timely intervention.

1 J Appl Oral Sci. 2012 Mar-Apr;20(2):241-5.

P1.39 - Clinical characteristics of 16 cases of gastrosquisis accompanied at a reference hospital in northeastern of Brazil.

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Instituto de Medicina Integral Professor Fernando Figueira - IMIP

Introduction: Gastroschisis is a rare congenital abdominal wall defect. Other associated malformations are not commom occuring in 5-35% of cases. However, these patients can present infections, failure to thrive and intestinal failure. This study described a group of patients with gastroschisis and their evolution umtil hospital discharge born at reference hospital of Northeastern of Brazil.

Method: this is a study of case series of 16 pediatric patients with a diagnosis of gastroschisis accompanied at a reference hospital during a year (2017-2018).The birth weight, surgical approach (in one or two times with silo use), associated malformations, parenteral nutrition time (considered to be prolonged when greater than 14 days), time to onset of enteral diet (considered early if less than or equal to 7 days), presence of neonatal cholestasis , confection of ostomy, intestinal resection, and death were evaluated. The data evaluated were selected according to the characteristics and risk factors already described at the literature.

Results: sixteen children were evaluated and 6 / 16 (37.5%) patients had birth weight less than 2,500 g; 11 / 16 (68.7%) had single-time surgical correction; 3 / 16 (18.7%) had other associated malformations (2 intestinal atresias, polydactyly). All patients required prolonged parenteral nutrition (NP); 13 / 16 (81.2%) had onset of diet in more than 7 days of life. The mean time of central venous access were 26.8 days and 12 / 16 (75%) patients progressed with cholestasis and 2 / 16 (12.5%) patients needed ostomies. One patient didn't used antibiotic and the maximum time of antibiotic use was 70 days in one patient. Only one patient had intestinal resection and 2 / 16 (12,5%) children died in the first 48 hours of life after the surgical correction.

Conclusion: The most patients described had presented adequate birth weight and surgical repair in a single time without silo utilization. Associated malformations were not frequent. All patients used NP for a long time and they had had late onset of diet. Two deaths were observed few hours after the surgery correction. The patients presented similar characteristics to those described in the literature and required multidisciplinary team and specialized care for a long period of time.

P1.40 - Impact of residual bowel length on cost of home parenteral nutrition for short bowel syndrome

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Introduction: Key determinants of costs associated with home parenteral nutrition (HPN) among patients with short bowel syndrome (SBS) are unknown. The aim of this analysis was to examine how charges associated with HPN relate to residual bowel anatomy.

Methods: We conducted a retrospective cohort analysis of medical history and charges for patients with SBS treated at a large Danish referral center. Clinical characteristics for SBS patients from 2006-2016 were obtained from a longitudinal database (LD). Charges assigned to patients for transport, PN, drugs, admissions, and ambulatory care visits were available from hospital databases for the year 2011. The LD contained 210 patients, while the 2011 sample contained a subset of 105 patients. For this analysis, we focused on patients with jejunostomies and ileostomies (2011 n=79). Charges are reported in Danish Kroner (DKK). We used linear regression to assess the relationship between anatomy (length of remaining bowel in cm) and 2011 charges.

Results: Patients in both the 2011 cohort and LD averaged 6.5 days of HPN per week. The 2011 sample had an average of 283 HPN days per year (275 in LD), and an average of 5.27 years since HPN initiation (5.9 years in LD). Patients in 2011 received an average 2690.6 mL of HPN fluids per day (2803.8 mL in LD). Sample characteristics were similar across demographic and disease characteristics when comparing 2011 patients to the LD of patients in the 10-year cohort. Among patients with jejunostomies and ileostomies, those with the most severe SBS had higher charges compared to those with greater length of residual bowel. Linear regression demonstrated a significant relationship (b=-82657, p<0.001) between anatomy type and total annual charges, with decreasing remnant bowel length resulting in increasing charges

Conclusion: This study aimed to evaluate costs associated with caring for SBS patients while considering 5 main factors – HPN, hospital admission, ambulatory care visits, transport, and drugs. Our data indicate a linear inverse relation between residual bowel anatomy and costs of care. The potential impact of PN complications and their relation to anatomy merits further study. Improved understanding of these costs will allow more nuanced cost benefit analysis of emerging novel treatments that may allow some patients to be partially weaned off PN.

Table 1. Sample Characteristics

	2011 Only, All Patients, N=105	2006-2015, N=210
	Mean (SD)	Mean (SD)
Demographics		
Age	51.5 (16.5)	51.3 (16.6)
BMI (kg/m)	22.7 (3.9)	22.5 (3.9)
Time since HPN Initiation (years)	5.27 (6.8)	5.9 (7.0)
Disease Characteristics		
Remaining Bowel Length		
Ileum (cm)	5 (20.0)	5.1 (21.5)
Jejunum (cm)	88 (48.8)	92.8 (52.6)
Colon (%)	14 (31.9)	14.6 (31.9)
Anatomy, N (%)		
Type 1: Jejuno/ileo-stomy		
Ia (<50 cm)	16 (16)	29 (13.8)
Ib (50-99 cm)	24 (24)	47 (22.4)
Ic (100-149 cm)	31 (31)	62 (29.5)
Id (150-200cm)	12 (12)	45 (21.4)
Type 2: Jejuno-colonic anastomosis 2	15 (15)	24 (11.4)
Type 3: Jejuno-ileo-colonic anastomosis 3	2 (2)	3 (1.4)
HPN		
HPN Days/Week	6.5 (1.3)	6.5 (1.2)
Total Annual HPN Days	283.0 (122.0)	275.0 (131.4)
Average HPN Volume/day (mL)	2690.5 (1338.8)	2803.8 (1397.6)
Average HPN Energy/day (kJ)	4943.9 (2875.6)	5049.2 (3082.0)
2011 Charges (in DKK)		
Total 2011 charges	409449.89 (292841.07)	
Total Admissions charges	197469.39 (206497.38)	
Total Ambulant care charges	7507.54 (4618.54)	
Total HPN charges	121211.30 (97828.43)	
Total Drug charges	46785.91 (44611.10)	
Total Transport charges	36475.74 (23893.25)	

Table 2. Total charges (DKK) assigned to patients in 2011 (includes HPN, Admissions, Ambulatory visits, Transportation, Drugs)

Remaining bowel length	N	Min	Max	Mean (SD)	Median
(<50 cm)	18	236780.02	695322.80	442640.62 (133611.65)	426252.68
(50-99 cm)	20	39168.77	745972.60	380666.28 (221825.69)	337720.42
(100-149 cm)	31	39178.26	554360.42	274178.40 (104742.06)	273956.23
(150-200cm)	10	93628.24	306449.82	209179.35 (75609.78)	212812.84

P1.41 - Double balloon enteroscopy reliably directs assessment for patients with short bowel syndrome.

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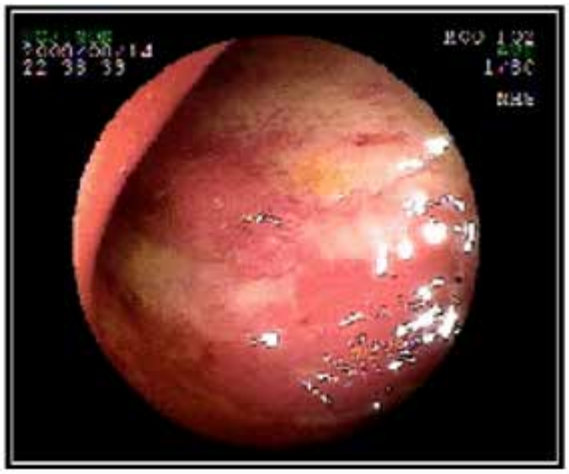
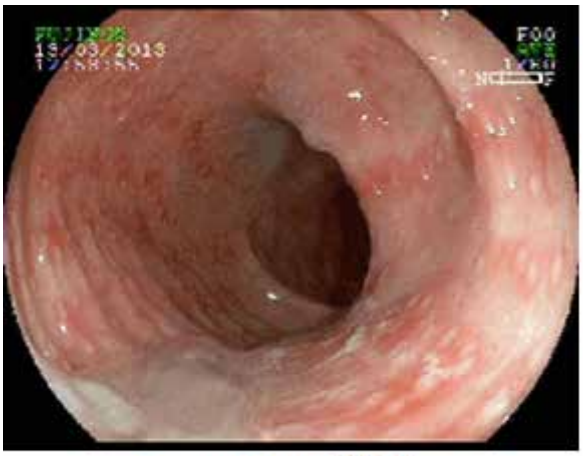
Aim: To evaluated patients with short bowel syndrome(SBS) for determining extension of remnant intestine and aspect of the intestinal mucosal

Methods: We retrospectively reviewed 20 patients who are at least 12 months in Home Parenteral Nutrition(HPN), included type III of intestinal failure characterized chronic condition, metabolic stable Of these patients divided in three groups: Nine had ultrashort bowel syndrome (USBS) characterized type I of SBS, nine had type II of SBS and two presented "no gut syndrome" We considered type I, patients with end-terminal jejunostomy and complex intestinal fistula as the same group. In case of the intestinal dilatation we collected intraluminal fluid for culture to diagnose bacterial overgrowth

Results: The nine patients SBS type I group, the enteroscopy show us in the proximal intestinal mucosa with normal aspect and distal stump of the closed transverse colon, show severe ischemic colitis, except in one patient with mucosal fistula of colon The other nine patients of SBS type II group was observed intestinal stretching and dilatation, which caused difficulty in evaluating the length of the remnant intestine. In this group we diagnosis four cases of bacterial overgrowth and two cases of anastomotic ulcers in jejunum / transverse colon For the two cases of " no gut syndrome" they have the fourth duodenal stumps closed with gastrostomy, we just observed the duodenum dilatation with some food waste



Jejunum Ulcers (SBS)



Ischemic Colitis (USBS)

Conclusion: Double balloon enteroscopy is a safe, reliable modality for determining changes in the intestinal mucosal and monitoring the intestine adaptation in SBS This technique can be used to direct selective surgical reconstruction of intestinal transit in pre-operative time

P1.42 - Nutritional, metabolic and hepatic impact associated with HPN use on stable patients undergoing Home Parenteral Nutrition (HPN)

Andre Lee, Mariana Hollanda Martins da Rocha, Maria Carolina Dias, Tatiana Rana, Lara Lordello Melo, Gabriela Oliveira Lemos, Yassmin Syagha, Flavio Galvão, Dan Waitzberg

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Intestinal Failure is a severe condition defined as the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required. Patients with Chronic Intestinal Failure despite being metabolically stable patients, require intravenous supplementation over months or years.

Objectives: The aim of this study was to describe the nutritional, metabolic and hepatic impairment associated with HPN use of sixteen adult patients treated at an outpatient clinic of intestinal failure (AMULSIC – Multidisciplinary Ambulatory of Short Bowel Syndrome) located in a public tertiary referral hospital in São Paulo, Brazil. The patients were stable and undergoing Home Parenteral Nutrition (HPN) for at least 12 months.

Methods: Patients were evaluated according to criteria for liver disease progression related to long term parenteral nutrition therapy. The parameters utilized were: elastography (fibroscan), liver biopsy, laboratory tests (AST, ALT, alkaline phosphatase, γ-GT, ferritin, bilirubins, activated partial thromboplastin time, total proteins and fractions), body mass index (BMI), body composition by electrical bioimpedance and also by indirect calorimetry for the accurate determination of individual caloric demands.

Results: Sixteen patients with a mean age of 38.5 years diagnosed with chronic intestinal failure undergoing HPN were followed up for at least 12 months and a maximum of 144 months (mean of 53 months). Fibroscan analysis revealed liver fibrosis grade I in nine patients, grade II in three patients and grades III/IV in four patients. Two patients presented grade III fibrosis in liver biopsy. Three patients had excessively elevated levels of ferritin. Eleven patients present a normal range of weight, three patients presented a BMI ≥ 24 (owerweight) and two patients presented BMI ≤ 18,5 (underweight). Ten patients out of this group [PM1] showed muscle mass reduction in electrical bioimpedance. Indirect calorimetry had a 0.8 (SD:± 0,079) mean respiratory coefficient.

Conclusions: In the population studied, there was no direct correlation between fibroscan results and liver biopsy and there was not a home parenteral nutrition time direct correlation with hepatic impairment. It was also observed an association between parenteral nutrition associated liver disease and high levels of ferritin, previous history of morbid obesity and intestinal pseudo-obstruction.

P1.43 - Use of transient elastography to determine liver fibrosis in pediatric intestinal failure

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Introduction: Intestinal failure associated liver disease (IFALD) is a significant complication in pediatric intestinal failure. Liver fibrosis with or without cholestasis is a frequent occurrence in IFALD. However, the diagnosis of fibrosis in IFALD is challenging and currently limited to liver biopsy. Our objective was to evaluate the use of transient elastography (TE) in pediatric IF patients to determine its efficacy for monitoring liver fibrosis as an alternative to liver biopsy.

Methods: A retrospective cohort study of IF patients between January 1, 2015 to December 31, 2017. The study cohort included a sample of patients who had a routine liver biopsy during an operative procedure and completed transient elastography at the same time. Liver biopsies were evaluated for stage of fibrosis using the modified Scheuer score. Statistical analysis included univariate analysis and Chi-square methods. High (grade 3-4) versus low (grade 0-2) fibrosis and TE scores were compared to determine sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Receiver operating characteristic (ROC) curves were also used to determine the ability of TE to discriminate various stages of fibrosis. Data is presented as medians with interquartile ranges and frequencies.

Results: 30 patients (21 male [70%]) with a median age at biopsy of 320 days (154-1776) were evaluated. Majority of patients had an etiology of abdominal wall defects (12[40%]) and necrotizing enterocolitis (9[30%]). Median length of PN therapy was 190 days (120-789). All TE measurements were completed within a median of 8.5 days (5.0-13.3) of the liver biopsy. Individuals with histologic fibrosis scores of 0-1 (n=18) had a median TE score of 4.9 (3.9-7.1), fibrosis scores of 2 (n=5) had a median TE of 6.7 (4.4-11.4) and those with a fibrosis score of 3 (n=7) had a median TE of 12.1 (6.3-14.6). No patients had grade 4 fibrosis. Dichotomous evaluation of the fibrosis scores (low vs high grade) compared to the chronic cholestatic scale for Fibroscan demonstrated 95.7% sensitivity, 57.1% specificity, 88.0% PPV and 80.0% NPV for low grade fibrosis. The c-statistic for the ROC curve was 0.764.

Conclusion: Fibrosis in patients with IF is often difficult to assess without liver biopsy. TE has only been evaluated in small cohorts but shows potential as a non-invasive method to monitor low vs high grade fibrosis in children with IF. Further studies in a larger cohort are required.

P1.44 - Exploration of factors impacting on eating in paediatric intestinal transplant recipients: a mixed methods study

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Introduction: The transition to eating after intestinal transplant (IT) can be difficult for some children. Children may have had little experience of eating before IT. Studies suggest that disruptions to the process of learning to eat in early childhood may be implicated in eating difficulties but there is no empirical data in IT recipients regarding factors associated with this. Identifying factors that may influence eating after IT could help manage caregiver expectations and plan targeted interventions. The aim of this study was to describe the nutritional intake and eating behaviours of IT recipient children and to explore factors impacting on eating.

Methods: This mixed methods study consisted of quantitative self-completion questionnaires and a three-day food diary followed by a semi-structured telephone interview. Caregivers of the entire UK paediatric IT population were invited to participate. The questionnaires included the Children's Eating Behaviour Questionnaire and 26 demographic items. Analysis was by descriptive statistics using SPSS. Semi-structured telephone interviews explored caregiver perceptions of their child's eating, analysed thematically.

Results:The survey response rate was 26% (n=9) with 89% (n=8) of respondents also being interviewed. Of the nine respondents, two were discharged on an exclusive oral diet following IT with three able to wean off tube feeding after between one and five years. Median energy intake was 93% (range, 61-137) of the Estimated Average Requirement and 56% (n=5) were categorised as food avoidant. Transitioning to an oral diet after IT without home tube feeding was statistically significantly associated with complementary foods being introduced at the recommended age, learning to eat, having significant practice and positive eating experiences before IT. The qualitative data supported this as well as providing explanations in relation to three themes: medical, caregiver and child influences.

Conclusion: The study findings present a picture of a complex interplay of factors that can influence eating in IT recipients. This study, although small, provides the first empirical evidence of an association between pre and post-IT eating. The findings suggest that promoting pre-IT eating may be beneficial and indicate that there may be predictors for eating difficulties that could be used to facilitate targeted interventions - further research is required.

P1.45 - Mycotic aneurysm after Liver and Small Bowel Transplantation.

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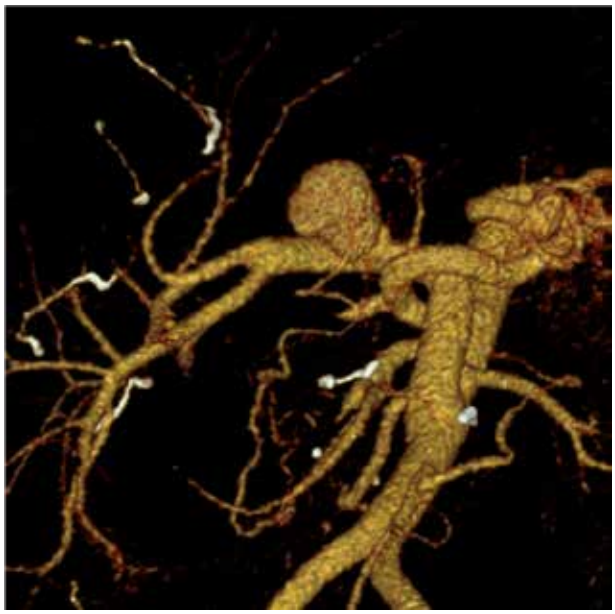
Mycotic aneurysm is a much-feared complication of vascular surgery. Management in the non-transplant situation often utilises placement of an endovascular prosthetic graft and long-term antibiotics. In formally immunosuppressed patients the ongoing likely infection of the prosthesis is of great concern.

We describe the case of a 29-year-old recipient of a liver small bowel transplant who developed a mycotic aneurysm of the donor aortic conduit two months after transplantation.

She had undergone an isolated liver transplant at the age of two for alpha 1 antitrypsin deficiency. This was complicated after transplantation by a volvulus of her small bowel, leaving her with 30 cm of jejunum and dependent on parenteral nutrition till the age of 13. Graft failure, 27 years later, necessitated the need for re-transplantation and at this stage a liver small bowel transplant was performed.

Four weeks post-transplant, she developed a pyrexia of unknown origin and at that stage cross sectional imaging was unremarkable. This was repeated two weeks later and still no source of sepsis could be determined. A Further CT two weeks later demonstrated a 2 cm mycotic aneurysm in the mid portion of the donor aortic conduit, (Image 1).

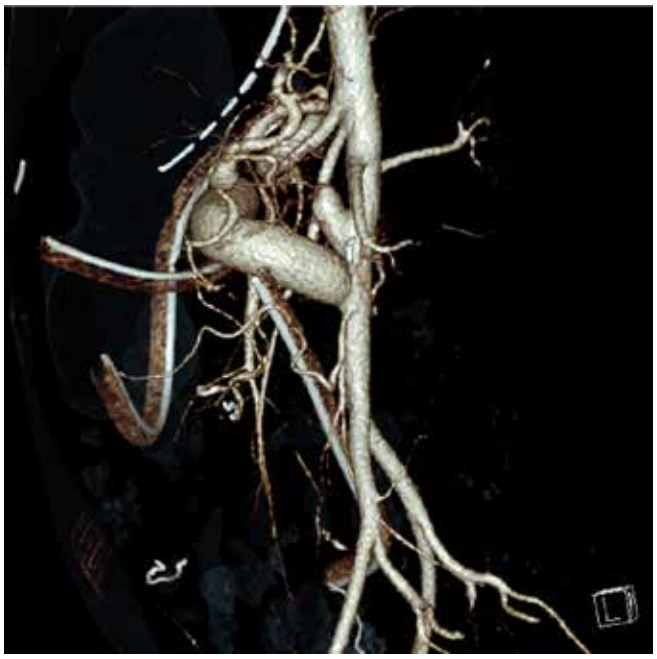


Initial management involved endovascular stenting and antibiotics to gain immediate control, followed by a definitive surgical intervention.

A third-party donor thoracic aortic conduit was acquired (blood group compatible) and at laparotomy the infected graft and stent were removed and replaced with the new conduit. Culture of the stent and aortic tissue grew vancomycin resistant enterococci (VRE) and Candida glabrata, necessitating six weeks of antimicrobial treatment (linezolid and liposomal amphotericin).

Five and a half weeks after initiation of linezolid therapy the patient developed profound lactic acidosis and severe pancreatitis requiring ICU admission and haemofiltration for the symptomatic lactic acidosis. Following discontinuation of linezolid, the pancreatitis and lactic acidosis resolved.

She is now four months after the vascular reconstruction and is well with no evidence of recurrence of the aneurysm (Image 2) and no recurrent VRE.



She has developed CMV disease from the third-party tissue. This is an important consideration when considering matching for third party tissues and prophylaxis must be reviewed.

P1.46 - Home Parenteral Nutrition : training of the adolescents

Catherine Poisson, Amelia Rocha, Christelle Alliot, Julie Ollivier, Isabelle Eicher, Cécile Talbotec, Cécile Lambe, Olivier Goulet

Home-Parenteral Nutrition Division. Hôpital Necker Enfants Malades ; Université Paris-Descartes

The Necker-Enfants Malades Hospital Home Parenteral Nutrition (HPN) program was certified in 1984. It is the largest in France with ~ 40% of the 380 children currently on HPN. More than 800 infants and children have been enrolled in the Necker program since 1984. In 2018, it supported 156 children (age range : 3mths-7yrs) : short bowel syndrome (SBS)(n=78), congenital enteropathy (CE) (n=28), total intestinal aganlionosis (TIA) (n=22) or chronic intestinal pseudoobstruction (CIPOS) (n=17); miscellaneous (n=11), > 60% presenting with irreversible intestinal failure (IF) : In order to prepare the transition to adulhood and to offer more freedom for leaving the family nest, we train the adolescents (ado) for self cares. In that view, we designed a training program.

Methods: Training involves nurses, MD, pharmacists, psychologist, social worker…. It requires time for the team as well as for the adolescent. It is organiszed during the school vacation in 3 steps each lasting 5 days. Step 1 :Line disconnexion & illness knowledge; Step 2 : Line connexion & body control; Step 3 :CVC dressing & information on adult transition. Training also includes an approach focused on their physical and psychological well-being to understand their body and their illness.

Results: In 2018, Z adolescents (age range :13-17 years) were trained : SBS (n=2), CE (n=2), TIA (n=1) and CIPOS (n=2). Children received PN 3 to 7 nights a week with bags from the french provider Baxter-Faconnable. At the end of the training program, 4 ado can be considered as fully autonomous on daily basis, 2 are partially (for disconnexion only) and 1 failed to finish the training program.

Conclusions: Autonomy is acheived for the majority. However, gaining autonomy does not mean accepting illness or being ready to move into the adult world. It seems that this multidisciplinary approach and the effect of group teaching are beneficial to them. We do continue to adapt the program according to the ado feeling and feedback.

P1.47 - Evaluation of central venous catheters in hospitalized pediatric patients with intestinal failure from a brazilian gastroenterology reference center

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Introduction: Intestinal Failure (IF) is a debilitating condition, defined as the need for parenteral Nutrition (PN) for more than 60 days. One of the most important IF complication is central catheter-associated bloodstream infection (CCABSI). The Taurolidine line prophylaxis seems to be a promising measure for the prevention of these infections.

Materials and Methods: retrospective study, evaluating 89 catheters used by 18 pediatric patients with IF from 2015 to 2017 at a center in the Southern Brazil.

Results and Discussion: Most patients (61%) had short bowel syndrome, and prevalence of CCABSI was higher in this group of patients (P=0,036). Of the 18 children studied, 14 (77,8%) had at least one CCABSI. A total of 89 catheters were used by these children – mean of 4,95 / patient. CCABSI occurred in 27 catheters (30,3%). 66.3% of the total number of catheters were non-tunneled and 32,6% were tunneled. 35,6% of the non-tunneled CVC had CCABSI compared to 20,7% of the tunneled (p=0,289).34,8% of the catheters were removed due to mechanical problems and 18% were removed due to CCABSI. The frequency of CCABSI was 5.7 per 1000 catheter days. The taurolock line prophylaxis has been used in our hospital since march / 2016 and this paper included patients before this period. We found a statistically significant association between CCABSI and death (p=0,01). Patients with at least one CCABSI needed to change the CVC more often (x= 4 catheters) than children that did not presented infection (x= 2 catheters) (p=0,035). The use of taurolock improved catheter survival from 20 days to 26 days (p=0,032).

Conclusions: CCABSIs was the main cause of death in this group of patients and frequency of CCABSIs is still high among our population. The use of taurolock helped to increase the days that the CVC remained in the patient, but more data is necessary to correlate this lock with an improvement in infection rate in our population.

P1.48 - Long term follow up of cord blood followed by intestinal transplant in patient with immunodeficiency and intestinal failure

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Introduction: There are limited case reports regarding patients who have received solid organ and hematopoietic cell transplant (HCT). Herein we describe the case of a now 20-year-old female with combined immunodeficiency and intestinal atresia who underwent a cord blood transplant, followed by an intestinal transplant(ITx). Our patient had gastroschisis with resultant short-gut syndrome. She developed lymphopenia and hypogammaglobulinemia with absent response to pneumococcal antigens, low number of T-cell receptor excision circles, and recurrent infections. Given these findings, she was diagnosed with combined immunodeficiency. ITx was deemed too risky due to her recurrent infections and immunodeficiency. Thus, she was evaluated for HCT.

Methods: She received a conditioning regimen of hydroxyurea, alemtuzumab, fludarabine, melphalan and thiotepa, with GVHD prophylaxis of tacrolimus (TAC) and mycophenolate mofetil (MMF). One month after HCT, MMF was discontinued. She received a 6/6 antigen-matched unrelated umbilical cord blood transplant in May of 2013. Nineteen months later, she received a 3/6 HLA matched intestine and colon allograft from a deceased donor. She was maintained on TAC and steroids, and also received basiliximab.

Results: One month post-HCT, she had ~50% donor cells in her blood. Her TAC dose was decreased and she received a cryopreserved fraction of her umbilical cord blood graft, with significant improvement. She developed acute GVHD limited to the skin, which was successfully treated with topical creams. Six weeks following her ITx, she was found on surveillance endoscopy to have mild ACR. This resolved with steroid therapy and the addition of MMF. Six months after her ITx, was noted to have an 8.5 mm pulmonary nodule on surveillance CT scan. Pathology revealed EBER+ PLTD. She underwent successful resection of the lesion and her immunosuppression was decreased with no evidence of recurrence. Most recent peripheral blood studies in December 2018 show she is 86-93% donor engrafted. Her immune profile remains normal, she's had no recent infections, and her only immunosuppressant is TAC with troughs in the 2-3 ng/mL range.

Conclusion: To our knowledge, this is the only reported successful case of a patient who received HCT followed by ITx. Despite not having a perfect HLA match between the HCT and intestinal donors, the patient achieved prope immune tolerance with the need for very low level immunosuppression and no significant GVHD

P1.49 - Tuberculosis Infection after Intestinal Transplantation.

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Aim / Background: High levels of immunosuppression required for intestinal transplant patients makes us alert for potentially serious infections. We present 2 patients who developed tuberculosis (TB) infection along the follow-up.

Case reports:

Patient 1: This is a 30-year-old male who presented a volvulus at 16 yo and became anenteric. Few months later, he was succesfully transplanted with an isolated intestinal graft. He was converted to Sirolimus (SRL) due to renal insufficiency and hypertension one year after transplant. Twelve years later, he was readmitted due to crhonic rejection, and was retransplanted with a multivisceral graft, with no spleen preservation, receiving Alemtuzumab for induction. He developed rejection during the postoperative period being treated with steroid bolus and higher doses of Tacrolimus. Later, he presented persistent bilateral pleural effusion requiring thoracocentesis, being positive for Adenovirus, and was treated with Brincidofovir. Three months later cultures were positive for Aspergillus and Acinetobacter refractory to medical treatment. Finally PCR for Mycobacterium TB was positive in the bronchoalveolar lavage, so quadruple therapy was initiated (Isoniazide-Rifampicin-Pyrazinamide and Etambutol) and the pleural effusion disappeared. Two months after the diagnosis, he is still on treatment and requires occasional hospital admissions to manage the mutifactorial respiratory problems.

Patient 2: This is a 28 yo female who received a modified multivisceral transplant at 17yo because of a desmoid tumor in the context of a Gardner Syndrome. She received Alemtuzumab as induction and posteriorly to manage immunological complications. She had a difficult postoperative course with severe hemolytic anemia, graft versus host disease and several episodes of acute rejection which could be succesfully managed with immunosuppressants and splenectomy. She was converted to SRL because of renal insufficiency one year after transplant. One year later, she was diagnosed of miliary TB by bone marrow punture in the context of fever of unknown origin, with no evidence of pulmonary or cerebral infiltration. Triple therapy (Isoniazide-Pyrazinamide and Etambutol) was given for several months with no recurrences until today.

Conclusions: Clinical evidence suggests to rule out subclinical Tuberculosis infection prior to intestinal transplant as part of the routine work-up in order to optimize treatments and admissions.

P1.50 - Finacial hardship faced by our patients and their families Road to Recovery

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Cambridge University Hospitals NHS Foundation Trust

Introduction: Many advances have been made in the field of intestinal / multivisceral transplant over recent years and favourable outcomes are now the expectation, rather than the exception. Despite this, life after small bowel / multivisceral transplants can be unpredictable. Healthcare professionals often reflect on the physical and psychological 'costs' of undertaking this treatment, but rarely consider the financial costs involved.

Methods: Survey of a sub-group of post-transplant patients and their families for estimate of annual personal cost of transplant follow-up care, in a single UK centre performing adult intestinal transplants.

Results: Having surveyed a sub group of 9 patients we have interesting data which identifies that our patients travel significant distances and this has wide and varied travel costs to enable them to receive the required follow up in our hospital. This data doesnt reflect parking charges on site. Some patients / relatives stay in accomodation which is funded whcih varies from £19 per night to £55 per night if on site. Other accomodation would be considerably more and an average ini our area would be around £100 per night.

Conclusion: Some patients have not been able to work pre transplant and some cannot regain work post-transplant. This is partly due to physical problems, such as fatigue, difficulty concentrating, tremor. For many, the unpredictability and intensive surveillance requirements are also an anticipated or actual barrier. As a national service extending across the UK, our patients travel notable distances to attend follow-up and the cost of fuel and cost of living make coming here challenging.

To mitigate some of these costs, we offer on-site accommodation wherever possible, signpost patients towards charitable funds or organisations that can assist. We as specialist nurses write supportive letters for our patients to receive Personal Independance Payments / Employment Support Allowance(s).

Financial hardship is a real concern for many transplant patients and assistance / support with this should be part of holistic follow-up care, within the limitations of national social support agencies.

P1.51 - Five year survival of the first pediatric multidisciplinary intestinal rehabilitation program with home parenteral nutrition in the public health system in Brazil

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Introduction: Data on multidisciplinary programs dedicated to the care of intestinal failure (IF) patients on home parenteral nutrition (HPN) in middle-income countries from Latin America are scarce. This study described the results of the first Pediatric Multidisciplinary Intestinal Rehabilitation Program with HPN in the public Health System from a public tertiary hospital in Brazil.

Methods: We conducted a retrospective study that included all children who were referred to our institution with IF from 1-January-2014 to 31-January-2019. Inclusion criterion was the use of parenteral nutrition (PN) for at least 2 months while in stable condition. We assessed the medical records of patients who were discharged while receiving HPN and those who were not discharged and received PN whilst in hospital. All patients who were not discharged on HPN had psychological or social impairments or did not reach a stable clinical condition. The following outcomes were analyzed: total PN period (HPN or PN in hospital period), full PN weaning off and causes of death.

Results: 49 patients were included, median age at onset of long-term PN was 4 months old (17 days-16 years). 15 (30.6%) were girls and 38 (77.6%) had short bowel syndrome, of whom 10 had remnant intestine <20cm. IF causes were: intestinal atresia 18(36.7%); volvulus 9(18.4%); gastroschisis 7(14.3%); necrotizing enterocolitis 6(12.2%); Hirschsprung's disease 2(4.1%); pseudo-obstruction syndrome 2(4.1%); other causes 5(10.2%). 35(71.4%) were discharged receiving HPN, of whom 9 weaned off HPN, 23 are currently on HPN (1 patient is on waiting list for multivisceral transplant) and 3 died [1 catheter-related bloodstream infection (CRBSI), 1 loss of venous access, and 1 intestinal failure associated liver disease]. Median period of HPN was 13.9 months (10 days–4.5 years). From the 14 patients who were not discharged from hospital, 7 weaned off PN, 2 are still receiving PN, and 5 died (3 loss of venous access and 2 CRBSI). Total weaning off PN rate was 32.7%. 5-year survival rate of all patients was 81.4% whereas 5-year survival on HPN was 90.4% (Kaplan-Meier).

Conclusion: Treatment of patients with IF by a multidisciplinary rehabilitation program with HPN is feasible and safe in the public health system in Brazil. The high survival rate supported the use of HPN as the primary treatment for IF.

P1.52 - Extended Hirschsprung's Disease: Our Experience And Literature Review

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Introduction: Extended Hirschsprung's disease (EHD) is a rare condition leading to intestinal failure (IF). Its impact in Latin America (LATAM) is unknown. The aim of this study is to review our experience and published evidence.

Methods: Case series. Inclusion criteria: patients < 18 ys. with EHD diagnosis, confirmed by full thickness biopsies during laparotomy, between 2009-2018. Residual intestinal length (RIL): measured from ligament of Treitz to enterostomy. Medical records and patients data base review, in addition to PubMed, Cochrane, Embase, Lilacs and Medline research, using "Hirschsprung's disease", "intestinal failure" and "total intestinal aganglionosis" as keywords, 1993-2018.

Results: N=5. Median age 42.2 m (r:4-108). Mean RIL: 54.6 cm (r:30-80). It took 3.2 surgical procedures (r:2-4) to perform a functional enterostomy. The distal aganglionic bowel was preserved in all cases. 5/5 with IF and mean parenteral nutrition (PN) dependance time of 46 months (r:10-114) . All received enteral nutrition by oral feeds and gastroclisis in 2 cases. 3 patients were listed for intestinal transplantation (ITx), 2 have already received an ITx. Follow up: 2.16 years (r: 0.75-4.25). 80% (4/5) overall survival on home PN, 1 death 9 months after ITx due to PTLD (off PN).

Literature review: 127 articles. No publications from LATAM. 120 excluded: 6 duplications, 114 do not fulfill inclusion criteria. 7 remaining articles, N 47: 0.49 mo.; mean 4.9 years follow up (r:2.67-7.3); 3.57 procedures (r:1.4-5.75) until reaching an accurate diagnosis; RIL: 44.7 cm (32.2-60); 7 had aganglionic bowel resection; 66% survival; causes of death: 3 after ITx, 1 listed for ITx, 11 due to PN complications. 18/47 patients received an ITx.

Discussion: EHD is an uncommon disorder leading to IF, and its prevalence in our continent is unknown. Our outcomes are similar to those published elsewhere. Home PN provides acceptable medium-term survival, although most patients will need an ITx in the long term.

	Our institution	LITERATURE REVIEW
N	5	47
RIL (cm)	54.6 (30-80)	44.7 (32-60)
PREVIOUS SURGERIES	3.2 (2-4)	3.57 (1.4-5.75)
AGANGLIONIC BOWEL RESECTION	0 (0%)	7 (15%)
ITx	2 (40%)	18 (38%)
FOLLOW UP (years)	2.16 (0.75-4.25)	4.9 (2.67-7.3)
SURVIVAL	4 (80%)	31 (66%)

P1.53 - Are Femoral Tunnelled Central Venous Catheters safe to use for HPN ?

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Background: Patients with Intestinal Failure (IF) require reliable intravenous access for provision of Parenteral Nutrition. Venous access for Home Parenteral Nutrition (HPN) patients with Type 3 IF can be compromised due to thrombosis of deep veins. Preferred choice of veins for central venous catheter are the supra cardiac veins. Femoral tunnelled CVC are avoided due to concerns of catheter related blood stream infection (CRBSI) and are considered as a last resort when all other thoracic CVC access is exhausted. We assess the outcomes of tunnelled femoral catheters in our cohort of HPN patients.

Methods: We did a retrospective analysis of a prospectively collected data of all HPN patients and venous access from January 2013 to December 2018 managed at a National HPN Unit. The details of venous access, complications of CVC, sex and details of stoma extracted from database.

Results: In a cohort of 9 HPN patients with tunnelled femoral CVC, 6 were females and 3 were males leading to a total of 8418 days. A total 3 episodes of CRBSI were recorded in 1 patient. All of the 3 episodes (methicillin – sensitive Staphylococcus aureus (MSSA), Escherichia Coli and CNS) were successfully salvaged. The average no of days for femoral CVC was 935 days. The rate of CRBSI was 0.35 per 1000 catheter days. 8 patients had stoma or open abdominal wound. There were no episodes of ipsilateral femoral DVT. The CVC was replaced for 2 patients due to fracture of CVC.

Conclusion: Tunnelled femoral CVC CRBSI rate (0.35)is comparable to thoracic veins CVC CRBSI rate(0.31) in our unit. Furthermore femoral access could be considered as a reliable access to provide HPN. It may be considered as an option if more than 2 thoracic deep veins are occluded to prevent complete occlusion of SVC. We feel tunnelled femoral CVC is a safe option to consider for HPN

P1.54 - Global gut dysmotility: Patient characteristics and unique clinical features

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Introduction: The pathophysiology and biogenetics of global gut dysmotility has yet to be fully defined. This abstract highlights the results of an observational study that is conducted at a tertiary center with high referral volume. The aim of this study is to define the clinical, neuropsychiatric, and socioeconomic status of this unique patient population.

Methods: A total of 175 patients were referred to our program with global gut dysmotilty for possible surgical management including reductive surgery and/or transplantation. The diagnosis of global gut dysmotility was made by exclusion of mechanical bowel obstruction, capsule endoscopy, and sitz marker testing.

Results: Most patients were female adults with a total mean age of 36 ± 14 (range: 5-70). The medical and surgical histories were significant for oral intolerance, constipation, abdominal pain, orthopedic procedures and cosmetic surgery. There was a common association between the disorder, bariatric surgery, and congenital anomalies. The major neuropsychiatric disorders were anxiety (70%), depression (64%), behavioral disorders (35%), abuse (32%), PTSD (15%), suicidal ideations (13%), and bipolar disorder (7%). The syndrome was associated with autonomic dysfunction (72%), autoimmunity (19%), and mitochodrial disease (3%). Most of the socioeconomic milestones including marriage, education, occupation, and daily activities were severely impaired.

Conclusion: The described herein clinical features may be a valuable tool to assess the spectrum of the disorder, guide therapy, and selection criteria for transplantion.

P1.55 - Does BMI Correlate with Enteral Autonomy Post Intestinal transplant?

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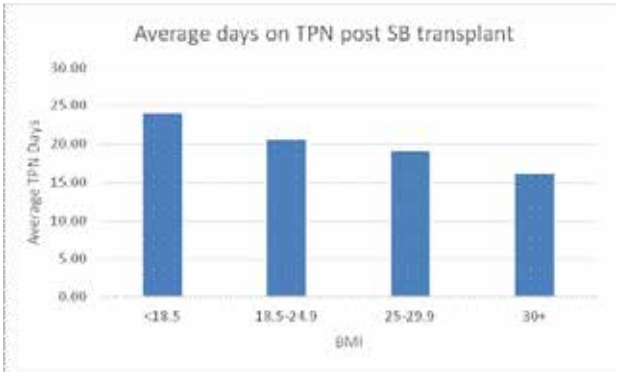
Georgetown University Hospital

Introduction: Intestinal transplant recipients often require total parenteral nutrition (TPN) support in the post-operative period until they achieve enteral autonomy. The time to enteral autonomy is a meaningful clinical outcome and indicator of successful graft function. Further, minimizing TPN exposure in the heavily immunosuppressed patient may mitigate infectious risk. TPN dependence after intestinal transplantation is variable and nutritional status at the time of transplant may be a determinant of the duration of TPN dependence. Body Mass Index (BMI) is one surrogate of nutritional status in the adult population. The aim of this study was to assess how BMI at the time of transplant impacts the duration of TPN after transplant.

Methods: Adult patients who received an intestinal transplant at Georgetown University Hospital from 2006 to 2018, and survived beyond one year after transplant were retrospectively identified. BMI at the time of transplant was categorized based on current definitions (<18.5 indicates malnutrition, 18.5-24.9 healthy weight, 25-29.9 overweight, and >29.9 obesity), and compared to duration of TPN dependence in days.



Results: 105 adult patients transplanted between 2006 and 2018 were included in the analysis. 51 of the patients were male and 54 were female. Median age was 43 years (range 18-66). Across all BMI categories the average days of TPN was 19.9 ± 12.6 days.

Patients with a higher BMI at the time of transplant had the shortest duration of TPN post-transplant. Patients with a BMI of >30 (n= 11) had a mean of 16.1 ± 7.2 days; patients between 25-29.9 (n = 21) had an average of 18.9 ± 9.2 days; patients between 18.6-24.9 (n = 63) had an average of 20.6 ± 14.8 days; lastly, patients <18.5 (n = 10) had an average of 23.9 ± 8.7 days. There was a significant difference in duration of TPN in days between the <18.5 BMI and >30 BMI category (p=0.05)

Conclusion: Achievement of enteral autonomy post-intestinal transplant is multifactorial. It is well established that post-transplant surgical and immunological complications are important factors that play a role in determining when TPN can be successfully weaned. Pre-transplant factors, however, may also contribute to enteral autonomy, such as recipient BMI at the time of transplant. Transplant practitioners should assist patients in avoiding a <18.5 BMI pre-transplant in order to potentially decrease the duration of TPN dependence post-transplant.

P1.56 - Colonic continuity and Incidence of weaning from PN by 5 years of age in children with onset of intestinal failure(IF) related to short bowel syndrome(SBS) by 3 months of age with chronic persistent dependence on parenteral nutrition(PN) at one year of age

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Great Ormond Street Hospital for Children NHS Foundation Trust

Objectives: To review 5-year outcome of children presenting in infancy with chronic intestinal failure (IF) associated with short bowel syndrome (SBS) who were still on parenteral nutrition (PN) treatment at 12 months of age.

Method: Medical records of patients with SBS related IF presenting in neonatal period and up to 3 months of age from 2007-2017 who were still on PN at 12 months of age were reviewed. Data obtained included small intestinal length at time of resection, aetiology, presence / absence of ileo-caecal (I-C) valve and / or colon and number of patients still on PN at 5 years.

Results: Twenty patients were identified. Eleven were male and 9 female. 14 / 20 were born prematurely. Diagnoses were necrotising enterocolitis (NEC) in 9, volvulus in 4, long segment Hirschsprung's disease in 3, gastroschisis in 2, and intestinal atresia in 2. The remaining small intestinal length at time of surgery ranged from 4.5cm - 120cm (median 18cm) in 19 cases (not measured in 1). Four patients had ultra SBS (length <10cm). Eleven patients weaned from PN by 5 years of age and 9 were still on PN. The median age at time of weaning (corrected for gestational age in premature infants) was 2 years 4 months (range 1 year 6 months - 5 years 9 months). Small intestinal length ranged from 7-120 cm (median 30cm) in the weaned group and from 4-90 cm (median 20cm) in the persistent IF group. Seven / 11 patients who weaned and 2 / 9 still on PN were female (p=0.09 not significant). 8 / 11 who weaned and 2 / 9 still on PN had NEC (p=0.068, not significant). 7 / 11 who weaned had an intact I-C valve compared to 3 / 9 on PN (p=0.6 not significant).

All 11 children who weaned had a colon present compared to 5 / 9 who remained on PN (p=0.026, significant). 11 / 16 or 68% with colon in continuity weaned.

Conclusion: Over 50% (11 / 20) infants with SBS and PN dependence for >12 months weaned from PN by or at 5 years of age. There was a statistically significant association with presence of colon with 68% with a colon weaning and even with some cases of ultra-SBS. Larger studies are needed to gain other predictors of weaning in this diverse group of patients.

P1.57 - Severe Late Onset Acute Cellular Rejection in a Pediatric Patient with isolated small intestinal transplant rescued with aggressive immunosuppressive approach

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Children Hospital Los Angeles. Keck School of Medicine. University of Southern California

Introduction: Small intestinal transplantation has been the standard treatment modality for pediatric patient with intestinal failure who failed other surgical and medical treatment. At its current stage, it carries its own risks including but not limited to acute and chronic cellular rejection, graft malfunctions, development of PTLD, viral and bacterial infections. Acute cellular rejection of the intestinal graft is an important and major complication secondary to its rich lymphatic supply.

It is usually results from sub therapeutic immunosuppression or non-adherence to medical management. The current management includes modifying the immunosuppression to achieve therapeutic level. Late severe acute intestinal allograft rejection is associated with increased risks of sepsis, bleeding and in the majority of cases with graft loss that ends up in graft enterectomy.

We present a case of a 20 year old patient who underwent isolated small bowel transplant for complete intestinal Hirschsprung Disease at age 7 years old, but due to medication non-adherence developed severe late-onset acute cellular rejection manifested by large ostomy OP, fever, weight loss. Underwent ileoscopy on presentation that showed complete loss of normal anatomical intestinal landmarks, bleeding, and ulcerated mucosa. Graft biopsies showed ulceration and granulation tissue with severe architectural distortion, and rare residual consistent with severe intestinal graft rejection. She initially received pulse doses of Intravenous corticosteroids and increased dose of tacrolimus without significant improvement. Her immunosuppression plan was escalated to include infliximab and finally had Antithymocyte globulin (ATG). Graft enterectomy option was entertained frequently during the treatment course; however clinical improvement was noted with evidence of histological improvement and salvage of the graft.

The aggressive anti-rejection treatment was complicated with the development of monomorphic, plasmacytoma (PTLD) that was managed with modifying her immunosuppression. Now her graft function is maintained on tacrolimus, oral prednisone, and routine Remicade infusion.

Conclusion:

1-Small bowel graft rejection is associated with increased morbidity and mortality, increased risks of sepsis, bleeding and graft loss. 2-We believe that prompt and aggressive immunosuppressive approach significantly increases the chance of rescuing small bowel transplant rejection.

P1.58 - Significance of the Extent of Intestinal Resection on the Outcome of a Short-bowel Syndrome in a Porcine Model.

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Background: Insufficient data are available to determine the most suitable extent of intestinal resection required to induce short-bowel syndrome (SBS) in pigs. This study aimed to compare the three main SBS-models published.

Methods: A 75%, 90%, or 100% mid-intestinal resection was performed in groups of n = 5 pigs each. Clinical (body weight, stool consistency) and biochemical (serum eletrolytes, citrulline, albumin, prealbumin, and transferrin) parameters were determined daily, functional (D-xylose resorption) and histological (intestinal villus length) parameters were determined after 2 weeks. A t-test and ANOVA were used for statistical analysis.

Results: Only in the 100% group, we observed a persistent weight loss (13.6 ± 3.8%) and diarrhea, as well as a decrease in prealbumin-levels (41%) and transferrin levels (33%). Serum electrolytes remained stable in all groups during the observation period. Citrulline stabilized at different levels (100% group 13.9 ± 1.0 µmol/L; 90% group 18.8 ± 1.0 µmol/L; 75% group 26.3 ± 1.4 µmol/L; all $p < .05$). D-xylose resorption was lowest in the 100%, followed by 90% and 75% group (100% group 32.8 ± 4.9 mg/L; 90% group 50.0 ± 19.6 mg/L; 75% group 57.8 ± 8.8 mg/L; $p = .393$). Intestinal villus length decreased in all groups (100% group 11.0%; 90% group 14.0%; 75% group 19.1%).

Conclusions: 75% intestinal resection is less suitable as an SBS model, as animals tend to recover remarkably. The 90% model is suitable for longer-term studies, as animals might survive longer due to partial compensation. Due to severe nutritional, biochemical, and physiological derangements, the 100% model can only be used for acute experiments and those immediately followed by small bowel transplantation.

P1.59 - Establishing the first national home parenteral nutrition program for paediatric patients with intestinal failure

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Introduction: Intestinal failure (IF) is a complex condition of severe intestinal malabsorption caused by short bowel syndrome (SBS), congenital diseases of enterocyte development, and severe motility disorders (total or subtotal aganglionosis or chronic intestinal pseudo-obstruction syndrome). Children with IF require long-term total or partial parenteral nutrition (PN) to preserve nutritional status and prevent complications. When a child depends on long-term PN, home parenteral nutrition (HPN) is the best alternative to prolonged hospital stay and is recognized as the best option for improving the quality of life of these children and their families. In our country, during many years all paediatric patients with IF were managed individually within the hospital setting of paediatric gastroenterology referral centres.

Methods: We present the process of developing the first national HPN program for paediatric patients with IF, and the current practice of establishing and managing children on HPN.

Results: Five patients were managed on HPN for prolonged period, four of those are currently on HPN. There is a multidisciplinary team involved in the process. With regards to the aetiology, three patients have SBS, one patient has tufting enteropathy and one total aganglionosis with severe dysmotility and postoperative SBS. For administration of HPN we place a tunnelled single lumen central venous catheter (CVC) surgically. We use commercial premixed PN solutions with individual adjustments. The regime, monitoring and prevention of complications follow the European HPN guidelines.

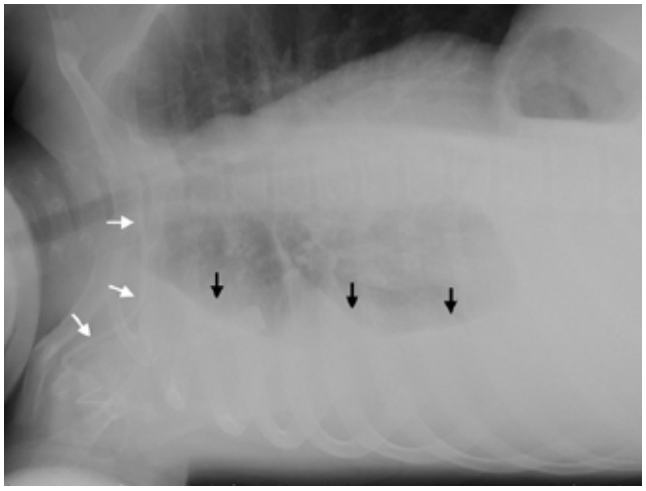
Conclusion: Although PN is a life-saving therapeutic option for children with IF, it is a high-risk therapy with potential acute and long-term complications. The rate of complications can be high, particularly in inexperienced hands. Management of HPN by centralised units with expertise in the investigation of IF rehabilitation and with a multidisciplinary team to support care at home would minimise complications and improve outcome. This program will continue to expand and to improve the management at all levels.

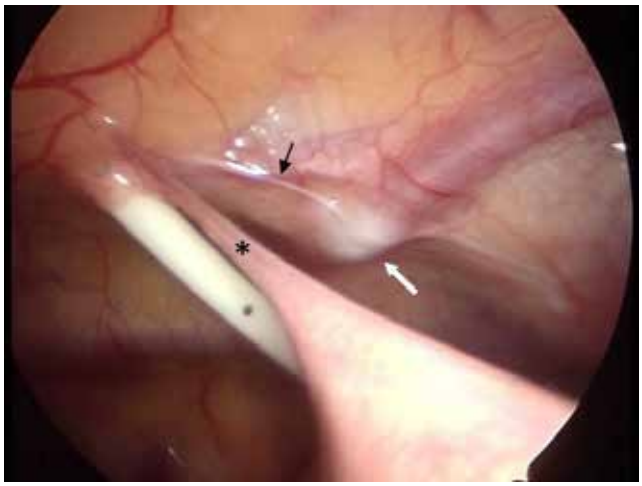
P1.60 - Hydrothorax following delayed extravascular migration of a totally implantable venous access device in a child

Yu-Tang Chang, et al.

Kaohsiung Medical University Hospital

Totally implantable venous access devices are widely used in nutrition. The authors encountered a 10-year-old boy with implantation of the device at the age of 7 years. In the recent half-year, the device was not used except for regular heparin flushing. However, hydrothorax occurred when fluid therapy was required from the device during this admission. Thoracoscopic approach showed extravascular migration and intrapleural malposition of the catheter. Intrapleural migration of the extravascular portion of the catheter owing to irritation and pressure necrosis of the pleura and gradual shortening of intravascular portion of the catheter when the child grew up may be the pathogenesis of delayed extravascular migration of the catheter.





POSTERS PRESENTED ON THURSDAY JULY 4, 2019

P2.22 - Oral Lactoferrin Increases Intestinal Regulatory T Cells And Decreases Th17 Cells Via Microbiome Alterations

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Background: Lactoferrin (LF) is a mammalian protein produced in all bodily fluids, with its greatest concentration is in colostrum and breastmilk. LF is a known iron-binding glycoprotein and iron transporter with both antimicrobial and anti-inflammatory properties, however its exact mechanisms remain unknown. LF likely impacts the intestinal immune system, both through direct effects on immune cell development and activity, and indirect effects mediated through the gut microbiome. Studies in mice demonstrate that the gut microbiome is critical for the development and evolution of gut-associated lymphoid tissues. Segmented filamentous bacteria (SFB), members of the Firmicutes, promote proliferation of gut inflammatory Th17 cells. In contrast, other commensals stimulate Treg differentiation. We hypothesize that recombinant human LF (rhLF) ameliorates inflammation via altering the composition and function of the intestinal microbiome, promoting the development and function of Tregs.

Methods: TNFΔAREmice were administered oral vehicle (PBS), IV anti-TNF antibody (Infliximab) or oral recombinant human lactoferrin (rhLF) for 14 days by gavage. After 14 days of treatment the mice were euthanized and intestinal tissues were isolated for evaluation by Flow cytometry, ELISA, and PCR.Cecal stool samples were collected and bacterial RNA was isolatedand sequenced.

Results: Treatment of TNFΔAREmice with orally administered LF decreased ileitis with a significant decrease in Th17 inflammatory cells (12.3%+/- .7% vs 8.2%+/- 1.2%) and a concominant increase in anti-inflammatory regulatory T cells (18.9% +/- 1.3% vs 28.1 +/- 3.2%). Upon evaluation of the cecal bacteria of treated mice we noted that lactoferrin (rhLF55 or rhLF500) altered both the composition (Figure 1A, B, C) and diversity (Figure 1D) of the cecal microbiota. The alterations in the microbiome correlated well with the changes in immune cell predominance and the increase in the the anti-inflammatory genus Faecalibacteriumand Treg-skewing SCFA-producing Firmicutes, along with decreased levels of Th17-skewing Segmented Filamentous Bacteria (SFB) (Figure 1C).

Conclusion: The above data demonstrates that rhLF treatment results in a shift of the balance of pro- and anti-inflammatory T cell populations to favor resolution of gut inflammation and identifies a plausible mechanism for this shift.

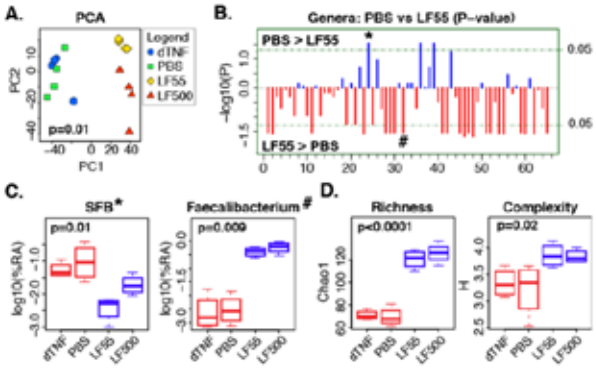

Figure 1: **Cecal microbiota in TNF$^{\Delta ARE}$ (dTNF) mice exposed to LF (500 or 55 mg/kg/day) or PBS by oral gavage.** A) Principal components analysis shows clear separation of LF-treated animals (LF55) and (LF500) compared to untreated (dTNF) and PBS-treated (PBS) animals. B) Multiple genera were altered by LF55 treatment compared to PBS. This Manhattan plot depicts log10 transformed p-values from Wilcoxon tests: blue lines indicate taxa that were more abundant in PBS animals while red lines indicate taxa that were more abundant in LF55 animals. Horizontal lines indicate p=0.05. C) LF treatment suppresses the relative abundance of Segmented Filamentous Bacteria and increases that of Faecalibacterium spp. D) LF treatment increases measures of biodiversity.

P2.23 - New alternative to antibiotics: 4% Tetrasodium EDTA is a non-antibiotic antimicrobial solution effective against Canadian microorganisms and associated biofilms found in central venous access devices of total parenteral nutrition patients

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Background information

Infections are problematic for total parenteral nutrition (TPN) patients with chronic central venous access devices (CVADs) prone to microbial colonisation and exposed to multiple antibiotic treatments. This catheter is supposed to provide life-saving treatment but makes them vulnerable to central-line associated bloodstream infections (CLABSI). The current standard of care for CVADs is saline or heparin which do not prevent CLABSI.

Objective

The objective of this clinical evaluation was to confirm the clinical safety and efficacy of a non-antibiotic antimicrobial catheter lock solution containing 4% Tetrasodium EDTA (T-EDTA) to eradicate clinically relevant microbes and associated biofilms colonising the lumen of CVADs of TPN patients.

Materials and Methods

Patients with CVADs were selected across Canada based on a high risk of complications: CLABSI and occlusions. The latter determined from the high use of alteplase. Selected TPN patients used a 4% T-EDTA lock solution as the sole lock solution rather than their standard of care. Main clinical endpoints included reduction of alteplase use and infection, and safety assessment. Before and during data were collected.

Results

Data collected over a 24-month period in 24 TPN patients show both a clinically relevant decrease in CLABSI by 50%, in-hospital days by 75%, catheter replacement by 68% and alteplase use by 100% when the standard lock solution was replaced by 4% T-EDTA. No adverse events including hypocalcemia was observed with its use over time. Findings correlate with previously published in vitro results and supporting a multicentre, randomized controlled clinical trial showing significant eradication of clinically relevant microorganisms by 87% within CVADs of hemodialysis patients by 4% T-EDTA compared to heparin.

Table 1 - Comparison of the number of catheter complications before and during the use of 4% T-EDTA as sole lock solution in 24 TPN patients during a 2-year period.

	Standard*	4% T-EDTA	% reduction
Number of catheter replacement	19	6	68
Number of catheter-related infections	16	8	50
Number of occlusions	11	0	100
Number of inpatient days	161	40	75

TPN: total parenteral nutrition; * saline, taurolidine, heparin

Conclusions

Intraluminal microenvironment of a CVAD is ideal for polymicrobial biofilm formation where quorum sensing promotes antibiotic resistance and provides the perfect hiding spot for superbugs. There is a close relationship between clot, bacteria and biofilm propagating CVAD complications: infections and occlusions. Results from this evaluation demonstrate clinically relevant reduction in CVAD complications with the use of a 4% T-EDTA lock solution. Routine use of an effective non-antibiotic antimicrobial solution is crucial in reducing the risk of CLABSI within Canadian hospitals and addresses the need to use alternatives to antibiotic agents.

P2.24 - Gothenburg Intestinal Transplant Endoscopy Score: A Prospective, Single Center Evaluation

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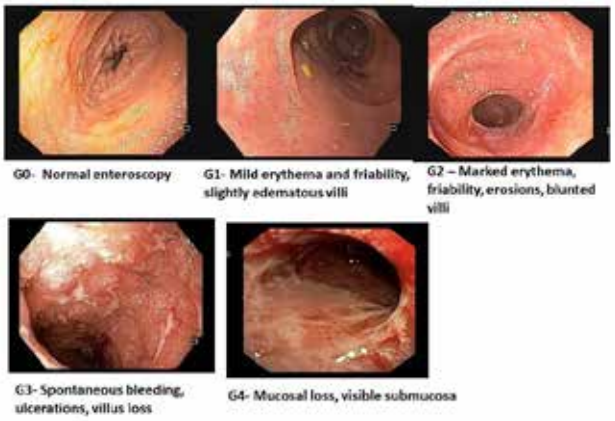
Introduction: The findings during endoscopy in acute cellular rejection (ACR) are well-known, but a grading system for its severity is lacking. Gothenburg Intestinal Transplant Endoscopy Score (GITES) is a novel, five-stage endoscopic score aiming to describe and categorize the endoscopic findings after intestinal transplantation. The aim with this study was to establish the usefulness of GITES in diagnosing acute cellular rejection. This could result in a more objective evaluation of the endoscopic findings and subsequently an earlier diagnosis of rejection

Methods: We prospectively graded the endoscopic findings with GITES in 13 adult patients (3 isolated intestinal grafts,10 multivisceral grafts) at one single center using white light high definition endoscopy systems. The scoring was performed at the time of endoscopy and later correlated to the histological findings.

Results: Eighty-five ileoscopies were scored. In 52 (61%) cases the endoscopic findings were normal. Twenty-three (69%) out of the 33 abnormal endoscopies revealed mild alterations represented by mild / moderate edema, erythema or blunted villi (GITES 1 and 2). Acute rejection was found in biopsies from 11 (14%) endoscopy sessions (4 mild & 7 moderate / severe) and in three specimens the biopsies revealed CMV enteritis. GITES above 1 (erythema, edematous villi) had 91% sensitivity and 94% specificity for ACR whereas positive (PPV) and negative predictive values (NPVs) were 78% and 98%, respectively. During moderate and severe ACR, GITES revealed an 87% sensitivity and 94% specificity whereas positive (PPV) and negative predictive values (NPVs) were 78% and 98% respectively.

Conclusions: These results suggest that evaluation of the endoscopic findings with GITES results in a satisfactory identification and stratification of rejection. A prospective, multicenter evaluation is needed to confirm these findings.



P2.25 - Effects of major liver allocation policy changes on waitlist outcomes in multivisceral transplantation in the United States

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Background: Organ allocation in multivisceral transplant (MVT; liver-intestine, liver-pancreas-intestine) is determined based on their ranking in the liver transplant waitlist. MVT candidates do not usually have high laboratory MELDNa (MELD) score and an exception point is given per the OPTN policy. Currently, their exception point is determined as "10% increase in mortality risk to their MELD score". Since 2013, an exception point of 29 has been applied to MVT candidates with approval by regional review board. As major revisions in liver allocation, Share 35 rule and MELDNa score were implemented in 2013 and 2016. The aim of this study was to evaluate effects of these updates in liver allocation policy on waitlist outcomes in MVT.

Methods: We examined adult patients who were registered for liver alone (LTA), liver-kidney (L-K), and MVT between 2011 and 2018 by using the UNOS registry. Registration periods were grouped according to the major revisions of liver allocation; 1) pre-Share 35 period (1/1/2011-6/17/2013), 2) post-Share 35 period (6/18/2013-1/10/2016), 3) MELDNa period (1/11/2016-3/31/2018). 90-day waitlist mortality in MVT candidates were evaluated in each period in comparison with those in LTA/L-K candidates who had similar MELD score (score categories of 20-28 and 29-34) to exception points for MVT candidates. Risks were adjusted by using Fine-Gray regression model.

Results: In MVT candidates, while there was no difference between the pre and post-Share 35 periods (HR, 0.96; P=0.29), 90 day-mortality significantly increased in the MELDNa period compared with that in post-Share 35 period (HR, 1.08; P=0.02). Mortality within 90 days in LTA/L-K candidates with MELD score of 20-28 continued to decrease over periods (hazard ratio [HR], 0.91 and 0.82; P=0.042 and <0.001 for pre vs. post-Share 35 periods and post-Share 35 vs. MELDNa periods). 90 day-mortality in LTA/L-K candidates with MELD score of 29-34 significantly decreased in the MELDNa period compared with the post-Share 35 period (HR, 0.78; P<0.001), whereas there was no difference between the pre and post-Share 35 periods (HR, 0.99; P=0.9).

Conclusions: While the recent revisions of liver allocation improved waitlist outcomes in LTA/L-K candidates, MVT candidates did not benefit from them and 90 day-mortality significantly increased in the MELDNa period. Exception point for MVT candidates may need to be reconsidered, given the increased number of high score patients.

P2.26 - Optimizing the Management of intestinal pseudo-obstruction with effective bowel decompression using a pan intestinal decompressive tube

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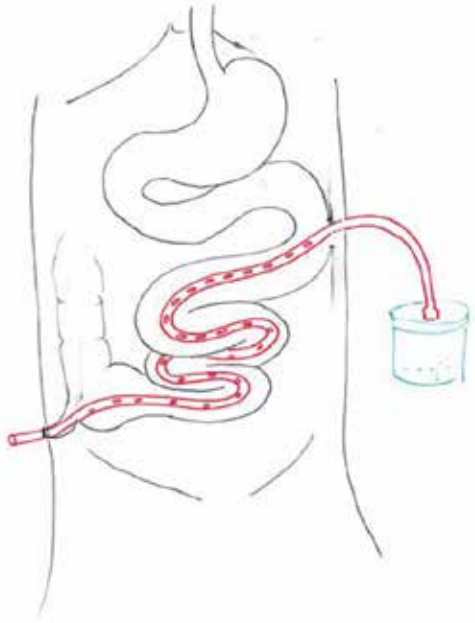
Children with intestinal psuedoobstruction are notoriously hard to manage. Refractory abdominal distension, small bowel bacterial overgrowth, inability to feed, frequent line infections, septic episodes and intestinal failure related liver damage are unfortunate realities in the management of these children. It's also hard to determine how contributory adhesive bowel obstruction is to the ongoing abdominal distension. One of the central factors contributing to all this is the inability to effectively decompress the inherently poorly peristaltic long tubular length of the intestine.

We devised a simple solution to effectively decompress the entire length of small bowel by passing a perforated decompresive tube all along its length that went from the DJ flexure to the caecum. Low profile devices at both ends ensured decompression into bags at both ends. The resulting decompressed bowel with reduced luminal calibre prevented stasis and promoted some peristalsis. In, addition it stented the bowel in a non-obstructive pattern in the abdomen.

8 children with intestinal pseudo obstruction had pan intestinal decompressive tubes placed. Ages ranged from 5 weeks to 16 years. All children had improvement in their abdominal distension, were able to take oral feeds and started stooling more frequently. 2 children with gastroschisis came off TPN after 4 and 6 months. Serum bilirubin improved initally in all children. In 2 children, after temporary relief, there was progression to liver failure and eventual death. In 3 children, additional procedures to reduce leakage around the tubes and skin excoriation were done. In 7 children, this reduced hospitalization significantly and allowed management to continue from home.

In children with intestinal psuedoobstruction, the placement of a pan intestinal decompressive tube can mitigate several of the problems associated with this condition. In gastroschisis with hypomotilitiy, it has the potential to restore motility and avoid the need for a transplant.



P2.27 - Bortezomib for refractory autoimmune hemolytic anemia after intestinal transplantation

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Introduction: Autoimmune Hemolytic anemia (AIHA) after solid organ transplantation is a relatively rare but severe complication. In contrast, after intestinal transplantation the incidence is up to 12.2% and generally occurs between 8-10 months after transplantation. Published therapeutic regimes include high-dose corticosteroids, intravenous immunoglobulin, plasmapheresis, rituximab and a switch of tacrolimus-immunosuppression towards other options, but the anemia can be refractory to this treatment. The overall mortality rate of AIHA is about 8%.

Bortezomib is a selective and reversible proteasome 26S inhibitor that directly inhibits antibody production through plasma cell depletion, it is registered as a treatment of multiple myeloma and chronic cold agglutin disease after allogenic hematopoietic stamcell transplantation (HSCT).

Methods: In this case-report we describe a 5-year old boy with microvillous inclusion disease who developed severe haemolytic anemia (Coombs negative) circa one year after multivisceral transplantation, which was unresponsive to conventional therapy with high dose steroids, IVIG and a switch from tacrolimus to cyclosporine. Plasmapheresis was not feasible due to circulatory instability. Because we ran out of therapeutic options a trial with bortezomib (Velcade®) at a dose of 1.0-1.3 mg / m2was given every 3 days, four times in total (with a second course 10 days later).

Results: We observed a rapid and sustained raise in haemoglobin within the first week after administration of bortezomib. During the treatment he developed a transient increased in stoma production, leucopenia and a raise in transaminase. Three years later he is doing well and never relapsed.

Conclusion: This is the first report to describe the use of bortezomib in the treatment of refractory autoimmune hemolytic anemia after multivesceral transplantation. In our case the therapy was relatively well tolerated and gave a fast and sustained favourable response with a long-term follow-up of over 3 years. The occurrence of AIHA and its treatment after multivisceral transplantation should be the subject of future registry studies to collect additional experience and explore the optimal therapeutic approach. Bortezomib should be regarded as an important therapeutic alternative for AIHA after solid organ transplantation.

P2.28 - Eosinophilic gastrointestinal disease following intestinal transplant

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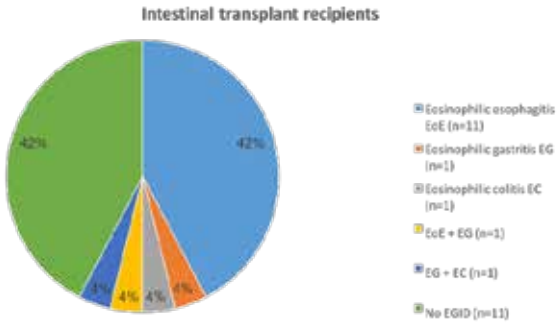
Introduction: Eosinophilic gastrointestinal disease (EGID) has been reported to be of higher incidence following solid organ transplantation than the general population. We reviewed the EGID incidence following single organ intestinal transplant or multi-visceral transplants at our institution.

Methods: We completed a retrospective chart review on twenty-six patients who were followed at our center after intestinal or multi-visceral transplant between the years of 2003-2016. Patients transplanted prior to age of 18 and followed at least 1 year from transplant were included. Histological criteria were used for EGID diagnoses. Eosinophil infiltration of the native gastrointestinal (GI) tract only was included and not the allograft. Comparisons were done using Fisher's exact test and Mann-Whitney two-tailed test.

Results: Of the 26 individuals followed for minimum of a year after intestinal or multi-visceral transplant, 15 (15 / 26, 58%) individuals were subsequently diagnosed with EGID. Twelve patients (12 / 26, 46%) were diagnosed with eosinophilic esophagitis (EoE), one of which also had eosinophilic gastritis (EG). One patient had EG and eosinophilic colitis (EC) and one each with EC and EG. The mean age at diagnosis of EGID was 7.56 ± 5.10 years and EGID developed on average 5.20 ± 3.59 years from transplant. There was no statistically significant difference between age at time of transplant in EGID vs non-EGID (2.35 ± 2.91 vs 4.08 ± 5.07). All (15 / 15) patients who developed EGID were on tacrolimus at the time of diagnosis and thirteen (13 / 15, 87%) underwent immunosuppression induction with anti-thymocyte globulin. Five (5 / 15, 33%) patients also developed food allergies post-transplant, including 2 (2 / 11, 18%) in the non-EGID group. Three patients (3 / 15, 20%) were diagnosed with PTLD prior to EGID diagnosis, while no (0 / 11) PTLD diagnoses occurred in the non-EGID group. Rejection occurred at a greater frequency in the EGID group than the non-EGID groups (13 / 14, 93% vs 7 / 11, 64%). Mean time from first rejection episode to developing EGID was 3.74 ± 2.74 years. Eleven (11 / 13, 85%) EGID patients we have data on were taking at least a partial PO diet at time of diagnosis, one each of PO formula and formula by G-Tube.

Column1	No EGID	EGID
Number of patients	11	15
Age at transplant in years (mean(SD))	4.08 (5.07)	2.35 (2.91)
Age at transplant (median)	1.46	0.97
Age at diagnosis of EGID (mean(SD))		7.56 (5.10)
Age of diagnosis (median)		5.35
Time from transplant to EGID (mean(SD))		5.20 (3.59)
Time from transplant to EGID (median)		3.63
Endoscopy indication		
Dysphagia		6 (40)
Diarrhea		2 (13)
Abdominal Pain		1 (7)
Concern for rejection		2 (13)
PTLD evaluation		3 (20)
History of ulceration		2 (13)
Elevated liver transaminases		1 (7)
Nausea		2 (13)
Bloody Stools		1 (7)
Rejection (number of patients with rejection(	7 (63.6)	13 (94)
Grade 1(total episodes of rejection)	7	5
Grade 2	5	13
Grade 3	3	4
Unspecified grade	5	1
Other Associations		
Food allergies post-transplant (n(%))	2 (16.7)	5 (35.7)
Time post tx to food allergies (mean(SD))	1.68 (0)	7.35 (6.79)
Peak AEC K/mcL post-transplant (mean (sd))	1.63 (1.56)	1.24 (0.89)
Diagnosed with PTLD (n(%))	0 (0.0)	3 (21.4)



Conclusion: The prevalence of EGID disorders in intestinal transplants is much higher than the general population and other single solid organ transplants. Close screening for EGID development following intestinal transplant is warranted.

P2.29 - IGL-1 solution for the preservation of human intestine: the first report in the literature

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Introduction: IGL-1 is a newer preservation solution largely resembling University Wisconsin (UW) solution in terms of ingredients but where the viscous starch has been replaced by polyethylene glycol resulting in lower viscosity. In addition, IGL-1 has low potassium and high sodium concentrations (extracellular-type solution). The solution has been used in several European countries for the preservation of kidneys, pancreases and livers with efficacy and safety comparable to those of UW or Custodiol. However, a systematic appraisal of the intestinal preservation injury using ILG-1 is missing.

Methods: Following aortic retrograde perfusion with 4 liters IGL-1, the ileum of fifteen deceased, brain dead multiorgan donors was retrieved and stored at 4C. Samples were obtained after 8h, 14h and 24 hours of cold storage. Histology (Chiu/Park scale), Goblet cells (GC) count, apoptosis (active caspase 3) and tight junction proteins claudin 3 and Zonula occludens (ZO)-1 were studied.

Results: Eight hours of cold storage resulted in a moderate epithelial detachment form lamina propria (median Chiu grade 2 (range 1-3) and minimal GC depletion. Preservation injury progressed to a median grade of 3 (range 2-5) after 14 hours and remained at similar levels at 24 hours. Active Caspase-3 was very low or absent at all time-points. After 8h ZO-1 expression was well preserved along the entire villus but became discontinuous after 14 hours of cold storage. Claudin 3 staining pattern remained well preserved throughout the entire cold storage.

Conclusions: The development of the preservation injury in the human intestine following perfusion and storage in IGL-1 appears similar with the other solutions. Interestingly, the structural preservation injury did not seem to continue to worsen after 14 hours while the injury at subcellular level advanced further.

P2.30 - Non-Transplant Strategy For The Management Of Short Bowel Syndrome In Children

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Aim: To present the results of multidisciplinary care for the children with short bowel syndrome (SBS).

Methods: A wide range of non-transplant options has been established in the Department of Pediatric Surgery at Russian Children's Clinical Hospital in Moscow. It includes home parenteral nutrition (HPN), autologous intestinal reconstructions (AIR), absorption-enhancing drug therapy etc.

57 patients with SBS aged 1 months to 17 years have been treated for the last 13 years. 40 patients underwent serial transverse enteroplasty (STEP) with our own modification, five children went through repeated STEP procedure. Spiral intestinal lengthening and tailoring (SILT) has been introduced and is considered over STEP in certain cases. Techniques of mechanical intestinal lengthening that can be applicable for SBS care are being studied. Four patients with complicated forms of SBS continue to receive GLP-2 analog - teduglutide (TED) with promising effect.

Results: Fifteenn children remain off PN 32 months after surgery. Twenty children who underwent intestinal reconstruction continue to receive reduced PN 2-4 times a week - all with reassuring growth and nutritional status. For the past year at least 20 new primary patients with SBS have been hospitalized and were introduced to HPN program. In four patients receiving TED-therapy for the past 12 months PN haven reduced by 50 to 75%. Preliminary trials with the device for distraction enterogenesis have been conducted on animal models showing promising effect that poses new solutions for extreme forms of SBS once implemented in clinical practice. Applying routine preventive therapy for all patients with SBS, we were able to minimize the number of complications such as central line-related occlusion / thrombosis, intestinal failure-associated liver disease, gallbladder sludge and stone formation, renal failure and metabolic bone disease. All fatal outcomes (8,7%, n=5) were caused by central line-related infections.

Conclusions: Pediatric SBS is a diverse clinical issue requiring coordinated multidisciplinary care. Modern strategies for SBS management help to reduce PN, regain enteral autonomy and avoid bowel transplatation. New non-transplant options need to be investigated to find solutions for most complicated forms of SBS.

P2.31 - Isolated liver transplant in children with intestinal failure-associated liver disease – a life-saving option in the current parenteral nutrition era

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Introduction: Children who develop intestinal failure-associated liver disease (IFALD) may be referred for combined liver intestinal transplantation with an aim to becoming parenteral nutrition (PN)-independent and free from liver disease. Isolated liver transplantation (ILT) in these patients is avoided, as most patients who had this procedure developed disease in the graft liver due to the ongoing need for PN. However, with the current paradigm of successful long-term PN managed in an expert centre, ILT may be an option for children at risk of death due to end-stage IFALD where no intestinal graft is available.

Methods: A retrospective review of case notes of three patients with IFALD who underwent ILT in a single centre between 2014 and 2018.

Results: Case 1 is an 8 year-old with short bowel syndrome (SBS) secondary to gastroschisis. Following resection she had 21cm of small bowel, and developed life-threatening IFALD. She was referred for combined liver intestinal transplant, but her parents declined the small bowel so she underwent ILT at age 3. She remains PN-dependent, despite pre-transplant bowel lengthening surgery. She is well and growing along the <0.4th centile with no liver disease at 4 years post-transplant.

Case 2 also developed SBS secondary to gastroschisis, with 32cm of small bowel after resection. She was listed for combined liver intestine transplant at 9 months of age, but developed end-stage liver disease with severe stomal bleeding necessitating a life-saving ILT in 2015. Following transplant she remains PN-dependent with some oral feeds and no signs of liver disease at 2 years post-transplant[J1] [J2] .

Case 3 is a 2 year-old with SBS due to antenatal bowel perforation requiring removal of a large portion of small bowel as a neonate. He underwent ILT at 13 months due to development of end-stage liver disease and coagulopathy, with no available intestinal graft. Recovery was complicated with life-threatening line infections, but he has achieved stability, and is growing well with 70% of his calorie and fluid requirement coming from PN and no signs of liver disease at 9 months post-transplant.

Conclusion: In the era of successful modern PN, ILT in children with end-stage IFALD may be life-saving for patients in whom size-matched organs are not available, or intestinal transplantation is declined.

P2.32 - Dynamics of recipient-derived T cell populations infiltrating intestinal transplant mucosa, and their expression of gut-homing chemokines and integrins

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Introduction: Early infiltration of recipient-derived T cells into an intestinal transplant graft is associated with rejection, which can lead to graft loss and death[1]. However, the infiltration dynamics of different T cell subsets are poorly understood, as are the mechanisms of entry. With the development of anti-integrin and -chemokine therapeutics, understanding whether pathways involved in gut-homing could be targeted for the prevention or treatment of early rejection is of significance.

Methods: Adult intestinal transplantation recipients were identified via longitudinal cohort studies at Oxford University Hospitals NHS Foundation Trust. Fifteen samples of intestinal graft biopsies were obtained from ten patients (Table 1) at various times after transplantation (23 days to 5 years).

Donor- and recipient-derived T cells in intestinal transplant mucosa were identified using flow cytometry and antibodies to discordant HLA Class I proteins (Fig 1A)[1]. Gut-homing molecules CCR9 and β7 integrin, and markers of conventional and innate-like T cell subsets were examined.

Table 1: Demographics of study subject cohort.

Subject	Age (decade)	IF cause	Year of Transplant	HLA mismatch used	Number of samples
1	20s	Crohn's	2013	A2	1
2	30s	Ischaemia	2017	A2	2
3	50s	PMP	2017	A2	4
4	50s	NET	2013	A3	2
5	60s	Crohn's	2013	A3	1
6	30s	Desmoid	2014	N/A	1
7	40s	Crohn's	2017	A2	1
8	20s	Neuropathy	2018	A3	1
9	30s	PMP	2015	N/A	1
10	20s	Crohn's	2013	A3	1

IF – Intestinal failure; HLA – Human leucocyte antigen; PMP – Pseudomyxoma peritonei; NET – Neuroendocrine tumour; N/A – Not applicable as no suitable HLA mismatch for flow cytometry found.

Results: The relative frequencies of key T cell subsets altered following transplantation (Fig 1B & C). Early post-transplant, CD8 and non-Vδ2 γδT cells dominated (28% and 49%, respectively). These early non-Vδ2 γδT cells were predominantly donor-derived. Innate-like MAIT and Vδ2+ γδT cells were rare (<1%) early post-transplant but recovered with time (6% and 2%, respectively). The fraction of recipient-derived T cells in the graft increased with time, with highly variable kinetics between subjects.

Early post-transplant, expression of CCR9 and β7 integrin was low on recipient-derived T cells, with 29% of CD8 and 48% of CD4 T cells negative for both markers. In contrast, 52% of CD8 and 31% of CD4 donor-derived T cells co-expressed CCR9 / β7 (Fig 1D). CCR9 / β7 co-expression increased in recipient-derived T cells with time.

Conclusion: Following intestinal transplantation, the relative abundance of T cell subsets within the graft is dynamic. Innate-like T cells were near-absent in the first year post-transplant, whilst early post-transplant, donor-derived non-Vδ2 γδT cells were over-enriched. Fewer recipient-derived T cells infiltrating the graft expressed putative gut-homing molecules. This questions whether pharmaceutical targeting of these pathways is appropriate in graft rejection, but samples from a rejection episode are needed for validation.

1. Zuber J. et al. Sci Immunol 1, eaah3732 (2016).

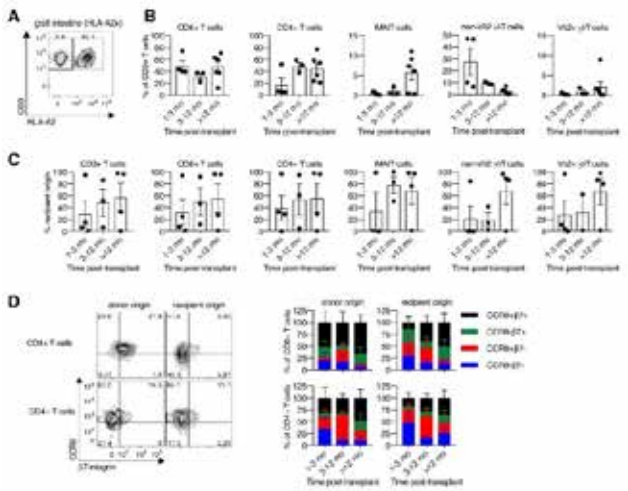

Figure 1. Dynamics of graft-infiltrating T cells and expression of gut homing markers.
(A) HLA genotype-specific antibodies can distinguish between recipient-derived gut-infiltrating and donor-derived gut-resident T cells within the transplanted intestine. **(B)** Frequency of major T cell subsets within the transplanted intestine. **(C)** Proportion of all CD3+ T cells and each major T cell subset that are recipient-derived gut-infiltrating T cells. **(D)** Representative flow cytometry staining (left) and group summary (right) for expression of the gut homing markers CCR9 and β7 integrin on CD8+ and CD4+ T cells of both donor and recipient origin.

P2.33 - Fish oil monotherapy for intestinal failure-associated liver disease on SMOFlipid in the neonatal intensive care unit

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Background: Management of IFALD using FO monotherapy with Omegaven has repeatedly been shown to be safe and effective in children and more recently, also in preterm neonates who are on dependent on long-term PN. In the present study we report the outcome of our expanded experience with FO monotherapy for IFALD on fish oil-based combination LE in the pediatric population, particularly in preterm low birth weight infants.

Methods: A diagnosis of IFALD was made when serum direct bilirubin levels were > 2.0 mg/dL in two consecutive measurements that were more than one week apart, without evidence of intrinsic causes of liver dysfunction. Management of IFALD was done by initially decreasing the total calories provided by PN, usually by lowering the amount of lipid to 2.0 g/kg/day. When calorie decrement did not result in alleviation of cholestasis, LE was switched from SMOF to Omegaven at 1.0 g/kg/day infused over 24 hours.

Results: Fifteen infants met the criteria for IFALD and received FO monotherapy during the study period from March 2017 to June 2018. Median gestational age was 27.5 weeks and median birth weight was 862.5 g. IFALD was successfully reversed in 10 infants (11/15, 73.3%). Four infants died of IFALD and resultant hepatic failure. Median direct bilirubin values were initially elevated and then steadily declined from the third week of treatment onward. Enteral tolerance increased in varying degrees in all but one patient during the treatment period. Mean weight gain was 26.0 g/day during FO monotherapy. Omegaven at a dose of 1.0 g/kg/day was well tolerated in these infants during the entire period of administration and no adverse events related to Omegaven use were seen. No signs of essential fatty acid deficiency (EFAD) were observed.

Conclusion: Fish oil monotherapy was safe and effective in the treatment of IFALD arising during SMOFlipid use in premature neonates on long-term PN.

P2.34 - Intestinal transplantation: GVHD and different induction immunosuppression protocols over 25 years at a single center.

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Background: Even though graft versus host disease (GVHD) occurs in 50% of patients receiving allogeneic hematopoietic stem cell transplantation, it is a rare complication after solid organ transplantation. Due to the large amount of lymphoid cells, intestinal and multivisceral transplantation triggers the bidirectional exchange of immune cells resulting in graft versus host and host versus graft interaction. Once it occurs, GVHD is associated with high morbidity and mortality after intestinal transplantation. We describe our center experience with GVHD over almost 25 years.

Methods: We retrospectively reviewed 442 intestinal transplants from 1994-2018 at Miami Transplant Institute and recipients were divided into 5 groups depending on the induction immunosuppression used; group 1 (44/442): high dose steroid (34/44), OKT3 (7/44), or cyclophosphamide (3/44); group 2: anti-CD25 (daclizumab or basilixmab) (159/442); group 3: alemtuzumab (113/442); group 4: rabbit antithymocyte globulin (rATG) (34/442); group 5: rATG and rituximab. Types of intestinal transplant included: isolated intestine (I) (n=124), liver-intestine (LI) (n=38), modified multivisceral (MMV) (n=39), and multivisceral (MV) (n=241) allografts.

Results: GVHD occurred in 8.6% (39/442). Actuarial estimates of GVHD free survival at 3, 6, 12, 24 and 60 months in the 5 induction groups were: 92% through all times in group 1; 94%, 88%, 87%, 86% and 86% in group 2; 99%, 99%, 97%, 96% and 96% in group 3; 88% through all times in group 4; 90%, 87%, 86%, 86% and 86% in group 5, respectively. MV and MMV allografts were associated with an increased incidence of GVHD (P= 0.00004) during 60 post-transplant months. Group 3 (Alemtuzumab) was associated with a decreased hazard rate of developing GVHD (P=0.004) but this effect lasted only during the 1st 6 post-transplant months. Graft loss due to GVHD occurred in 31.6% (12/38) with an increased risk in MV and MMV transplant recipients (P=0.05).

Conclusion: MV and MMV transplant recipients experienced increased risk of GVHD related morbidity and mortality while alemtuzumab induction immunosuppression protocol was associated with a decreased risk of GVHD during the 1st 6 post-transplant months.

P2.35 - Outcomes of children with phenotypic diarrhoea

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Introduction: Phenotypic diarrhoea (PD), also known as tricho-hepato-enteric syndrome, is a rare disorder with intestinal and extra-intestinal manifestations. Patients have low birth weight, facial and hair changes and a severe diarrhoeal illness, requiring parenteral nutrition (PN).

In this study, we reviewed outcomes for the largest UK cohort of patients with phenotypic diarrhoea born since 1996.

Methods: We reviewed the medical records of children with phenotypic diarrhoea cared for in our tertiary gastroenterology centre up to 31 December 2018.

Results: 12 patients (7 female, 5 male) were included. 2 patients died, one at age 2 years and one at 10 years, both due to respiratory complications secondary to infection. Median age of the surviving 10 patients was 12.6 years (range 3.7-22.2). Probabilities of survival based on the Kaplan-Meier method was 100% at 1 years, 92% at 5 years, 79% at 10 years and 79% at 15 years.

Median age of PD diagnosis was 11.6 months (range 2.9-114.8). Presenting symptoms included protracted diarrhoea (n=6), faltering growth (n=6), liver disease (n=3), choledochal cyst (n=1) and meconium ileus (n=1). 9/12 (75%) patients developed respiratory issues, including bronchiectasis (n=5). 1 patient had bronchiolitis obliterans, resulting in prolonged ventilation, intensive care stay and subsequent requirement for home oxygen. 9/12 (75%) patients had liver involvement, improving with age. 4 (33%) patients had cardiac abnormalities. All patients showed intermittently low immunoglobulin levels and suboptimal immune response to vaccines.

All 12 patients received PN, with 6/10 surviving patients weaned off. Median age PN stopped was 9.7 years (range 4.37-13.27); median PN length was 5.7 years (range 3.7-13.4 years). Probability of continuing PN based on the Kaplan-Meier method was 100% at 1 year, 80% at 5 years, 41% at 10 years and 21% at 15 years. Patients continuing PN receive it 3-4 nights/week. One patient restarted PN after 11.4 years to achieve pubertal growth. Patients had improved weight-for-age Z scores with PN but showed a decline (median -0.61, range -3.5 to -0.12) after PN stopped. The majority have short stature, following the lower centiles (0.4th-9th) for growth.

Conclusion: In our cohort, intestinal failure is temporary- half of our patients are off PN, with future plans to wean the remaining patients. Rather than intestinal failure per se, morbidity and mortality is largely caused by immune deficit and resultant infections.

P2.37 - Variance in peripheral blood absolute lymphocyte counts as a predictor of exfoliative rejection in small bowel transplant recipients

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Introduction: Exfoliative rejection (ER) following small bowel or combined liver/small bowel transplantation is an extreme form of graft rejection associated with significant morbidity and mortality with high rates of allograft removal. Re-transplantation after exfoliative rejection has demonstrated low success rates. During the outset of rejection episodes, few predictors differentiate between ER and non-exfoliative rejection. Aggressive immunosuppression with antibody based therapy and early surgical intervention remain the cornerstone of management. Our treatment protocol for acute cellular rejection requires failure of a steroid burst before antithymocyte antibodies are started, but excessive delay in initiation of antibody therapy may result in exfoliation and graft loss. Our objective is to determine if peripheral blood lymphocyte counts can predict progression to ER.

Methods: All patients undergoing a small bowel or combined liver/small bowel transplant at Cincinnati Children's Hospital Medical Center (CCHMC) were retrospectively reviewed for this study. All with biopsy proven acute cellular rejection and peripheral blood lymphocyte enumeration were included. The histologic severity of the rejection episode and lymphocyte counts prior to and during the rejection episode were collected.

Results: Electronic medical record changes permitted review of 38 of 55 transplants since 2003. Twenty-nine patients (76%) had histologic rejection greater than Grade 1. Of all patients, 5 (13%) had ER. Early biopsies eventually progressing to ER had higher peripheral blood absolute lymphocyte counts (ALC) prior to rejection than did biopsies diagnostic of rejection failing to progress (960 vs 600, $p = 0.02$). More importantly, peripheral blood lymphocyte counts also rose much more dramatically in those whose biopsies subsequently progressed to exfoliation than in those whose rejection did not progress (1179% vs 81%, $p < 0.001$).

Conclusion: Based on these data, absolute lymphocyte count, specifically, the variance in ALC is associated with progression from low grade rejection to ER. Although, there was a statistically significant difference in the ALC in patients with exfoliation, substantial variance from baseline may be more important than the absolute number in predicting ER, thereby justifying early use of antithymocyte globulin or alemtuzumab.

P2.38 - Contemporary outcomes of pediatric intestinal failure: a multicenter study

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Introduction: Important changes in the management of pediatric intestinal failure (IF) have been implemented over the last 15 years.

Objective: To assess the impact of those changes on the outcome of a contemporary cohort of pediatric IF patients from 6 IF programs, 5 of which offer intestinal transplantation.

Methods: Retrospective analysis of a multicenter IF cohort. Entry criteria included patients < 18 years of age receiving PN for more than 42 consecutive days, primary gastroenterological disorder and diagnosis of IF between 2010 and 2015. Primary outcome was death, transplant or enteral autonomy. Kaplan-Meier analysis was used for time-to-event and competing risk analysis for cumulative incidence rates. Comparisons were conducted with a log rank test and Cox regression analysis.

Results: 443 patients (male 61%) with a median gestational age of 34 weeks (29-37) and birth weight of 2.1 kg (1.2-2.8) constituted the study group. Patients were followed for 3.8 years (2.3-5.3). Median time on PN was 384 days (110-947). Patients had 40% (16-100) of expected small bowel length for age remaining and 250 (56.4%) patients had intact full colon in continuity. Main etiologies included necrotizing enterocolitis (29.3%), abdominal wall defects (30.5%), dysmotility disorders (7.2%), and mucosal enteropathies (6.8%). Eighty-one patients (18.3%) developed progressive intestinal failure associated liver disease (IFALD) with a bilirubin >75mmol/l. All patients were managed with hepatoprotective nutritional strategies (fish oil based lipids or lipid lowering strategies). The presence of IFALD impacted negatively on transplant free survival (P<0.001) and achievement of enteral autonomy (P<0.01). Overall, 213 (48.1%) patients achieved enteral autonomy, 137 (30.9%) remained on PN, 53 (12%) were transplanted and 40 (9%) patients died. Achievement of enteral autonomy was associated with short bowel syndrome (P<0.01), NEC (P=0.026), intact colon (P<0.01), and ileocecal valve (P<0.01).

Conclusions: This contemporary cohort achieved a significantly lower incidence of death and transplantation compared with previous multicenter reports. However, the number of children achieving enteral autonomy has not changed while a larger number of patients remain PN dependent. Although this cohort may represent a more complex group of patients due to potential referral bias, these findings suggests a shift in outcomes and a need for new strategies for the achievement of enteral autonomy.

P2.39 - Visceral Transplantation in megacystis microcolon intestinal hypoperistalsis syndrome

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Introduction: Megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS) is a rare congenital disorder with poor prognosis. It is associated with intestinal pseudo-obstruction and urinary system problems secondary to dilated bladder. MMIHS patients usually have multiple surgical interventions related to pseudo-obstruction episodes and become TPN dependent due to surgical or functional short gut syndrome. We aim to analyze patient and graft characteristics including early and late post-transplant complications in patients with MMIHS with visceral transplantation (VT).

Methods: Data of all patients with MMIHS receiving visceral transplantation between 1990 and 2019 were reviewed retrospectively.

Results: Six MMIHS patients underwent VT at our institution. One had prior isolated small bowel transplantation at another facility and had allograft failure. Transplantation was with multivisceral (MVT) in 5 and modified multivisceral (MMVT) in one patient with good liver function. Pancreaticoduodenal and splenic complex was preserved in MMVT. Allograft included colon and pyloromyotomy was performed in last 4 patients. Thymoglobulin was administered as induction agent and tacrolimus and prednisolone were given as maintenance immunosuppression. Median age at transplantation was 4.3 years (range=1-18.6 years) with a M/F ratio of 5/1.Overall patient and graft survival is 100% at median follow-up of 3.8 years (range=1.2-15.4 years). Acute cellular rejection was the most frequent early post-transplant complication (83%) and 2 patients had EBV associated post-transplant lymphoproliferative disorder during the follow up period. One patient needed kidney transplantation because of IgA nephropathy. Two patients currently have end ileostomy and 3 have end colostomy after closure of loop ileostomy. One patient is awaiting ileostomy closure. Five patients have attained nutritional autonomy and were weaned-off TPN and intravenous fluids. One of these 5 patients is on jejunostomy tube feeds due to oral aversion. One patient is still on tube feeds and TPN due to esophageal stricture caused by perforation after myotomy for achalasia diagnosed at post-transplant 8 months.

Conclusions: Visceral transplantation for MMIHS patients is a lifesaving procedure with excellent patient and allograft survival. Timing, thorough pre-transplant work-up and appropriate allograft selection are keys for good outcomes.

P2.40 - Visceral Transplantation in Pediatric Patients with Intestinal Failure: Report from a Large Academic Transplant Program

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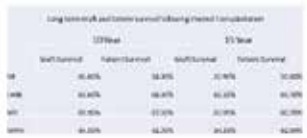
Objective: Visceral transplantation (VT) is indicated in patients who have failed intestinal rehabilitation and have complications related to parenteral therapy. VT outcomes from an academic center over a 20-year period were studied.

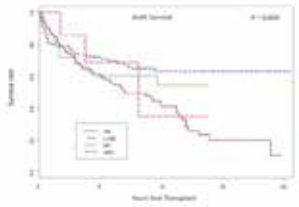
Methods: Between 1/1996 and 12/2015, 212 pediatric patients underwent 235 VT. There were 23 re-transplants. Index VT included isolated small bowel (SB n=90); liver, pancreas, small bowel (L+SB n=86); liver, stomach, pancreas, small bowel (multivisceral MVT n= 28); or stomach, pancreas, small bowel (modified multivisceral MMVT n=7) with or without colon. M/F ratio was 125/87. Immunosuppression was antibody induction, tacrolimus and steroids. VT indications were gastroschisis (n=52), intestinal atresia (n=21), volvulus (n=49), necrotizing enterocolitis (n=24), pseudo-obstruction (n=27), Hirschsprung's disease (n=17), microvillous inclusion disease (n=12), others (n=11).

Results: 140 patients are alive between 2 and 23 years after transplant (mean 12.8 years). 31 of these underwent allograft enterectomy for rejection (n=26), technical (n=3), primary nonfunction (n=1), PTLD (n=1), and are on parenteral nutrition. 11 in this group were re-transplanted.

77 patients died between 4 days and 20.5 years following visceral transplant (mean 44.5 months). Infection and multisystem organ failure was the leading cause of death (n=26, 31%). Maximum 10 and 15-year graft and patient survival were observed in LB recipients confirming liver's protective role in sustaining small bowel grafts (table and graph; p=0.009).

Conclusions: Visceral transplantation is a viable option for patients with intestinal failure and offers long-term benefit and freedom from parenteral nutrition. Infection continues to be a major factor responsible for graft loss. With careful patient selection and comprehensive management by multidisciplinary team prolonged nutritional autonomy can be restored.





P2.41 - Gastrointestinal outcomes of gastroschisis in and around Osaka, Japan

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Introduction: According to the Intestinal Transplant Registry report 2018, gastroschisis was the most frequent indication (21%) for pediatric intestinal transplantation. However, in Japan, none of the pediatric intestinal transplant candidates has gastroschisis. The purpose of this study was to analyze gastrointestinal outcomes of gastroschisis in and around Osaka, Japan.

Methods: One hundred and nine patients with gastroschisis were treated between January 1982 and December 2018 at our three hospitals. The patients' gender, gestational age at birth, birth weight, Apgar Score, delivery route, fetal diagnosis, gastrointestinal complications of gastroschisis, surgical treatment, and outcomes were analyzed.

Results: Mean gestational age at birth of the 109 patients (males: 57, 52%) was 36.3 ± 2.1 weeks. Mean birth weight was 2159 ± 441 g, mean Apgar Score (after 1 minute / after 5 minute) was 6.9 ± 2.3 / 8.4 ± 1.2, and 38 patients were delivered by Cesarean section. Fetal diagnosis of gastroschisis was made in 78 (72%) cases. All 109 patients were operated for gastroschisis, with primary repair in 63, silo repair in 23, and silo placement with delayed abdominal closure in 23. Eight patients (7%) had the gastrointestinal complications: seven had atresia of the intestine or colon, one had intestinal perforation. Closed gastroschisis was detected in three patients after birth. The patients with gastrointestinal complications were treated concurrently by intestinal anastomosis or enterostomy at the initial operation. Three of the eight patients underwent massive intestinal resection, resulting in short bowel syndrome (SBS), and required total parenteral nutrition (TPN) for about a year. Two of the three patients with SBS survived weaning off TPN. However, the other baby with SBS died of intestinal failure-associated liver disease. The other two patients without gastrointestinal complications died, one was an extremely low birth weight infant and the other with thrombosis in the lower extremities. Eventually, the remaining 106 (97.2 %) patients with gastroschisis have been surviving without TPN.

Conclusion: Gastrointestinal complications are rare in Japanese patients with gastroschisis. One of the factors contributing to this might be the low incidence of closed gastroschisis and low prevalence of SBS and complications secondary to intestinal failure after repair of gastroschisis.

Ethical approval: The hospital research ethics committee (reference number H30-36).

P2.42 - Vascularized composite allografts as immunological monitors

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Introduction: Abdominal wall transplantation (AWTx) offered a potential solution to the often-challenging closure of the abdominal wall at the time of intestinal transplantation (ITx). However, besides facilitating closure, the AWTx has been proven a promising asset for early, patient led rejection monitoring. We have therefore also used sentinel skin grafts for solely graft monitoring purposes when there was no clinical need for AWTx.

Methods: We performed a retrospective analysis of all patients undergoing intestinal and vascularized composite allograft (VCA) transplantation. Clinical presentation of rejection was correlated with histology, stoma output, citrulline levels and endoscopy findings.

Results: From October 2008 to October 2018, 45 patients underwent ITx. Ten underwent a modified multivisceral transplant and 35 an isolated small bowel transplant. Mean age was 42.6 years (range 23-73). M/F: 27:18. Median follow up was 1031 days (range 14- 3651). All patients had Campath induction (30 mg iv) followed initially by Tacrolimus based maintenance (trough level of 8-12 ng/ml). Thirty one patients received a VCA in addition to ITx. Twenty two of these were AWTx.

There were 5 intestinal biopsy proven rejections in the IT alone group (36%) and a further 5 patients in the same group were falsely treated for rejection, as this was later labelled as infection.

There were 10 patients with rejection in the VCA part of the IT+ VCA group (11/31, 35%). These patients presented with a rash limited to the VCA. Of those 11 patients, there were 5 with concurrent intestinal rejection (5/31, 15%) with a lead-time of 5- 7 days between VCA and ITx.

Conclusion: We report on a series of combined VCA and ITx. The skin component has been utilized as a dynamic canvas for remote immune monitoring of visceral grafts. It has so far been useful for patient led monitoring of the ITx graft since it is visible and presents the earliest and only sign of rejection.

P2.43 - Impact of a new Nordic waiting list algorithm for patients awaiting intestinal transplantation in Sweden and Norway

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Introduction: Since 1998, Swedish and Norwegian patients are transplanted in Gothenburg, Sweden. Initially, our institution managed the organ allocation of intestinal grafts for all patients. From 2010, due to a high mortality on the pediatric waiting list (WL) (70%), candidates were listed separately to increase awareness. From 2013 onwards, a joint Nordic shared waiting list (WL) was implemented for children listed for a liver transplantation and both pediatric and adult patients in need of an ITx; Herein, we describe and assess whether the change in WL algorithm implemented in 2010 has had an impact on WL dynamics for Swedish and Norwegian patients.

Matreials and methods: Retrospective review of the Nordic Liver Transplant Registry.

Variables studied: Comparison between (ERA 1: 1998-2010) and (ERA 2: 2011-2018). WL dynamics, organ donor characteristics, donor to recipient body weight ratio, cold ischemia time, mortality on the WL, proportion of grafts being shared between Swedish and Norwegian patients as well as the number of grafts imported from other Nordic and European countries.

Results: 35 ITx have been performed in 34 patients; pediatric (9), adults (25). Isolated ITx (6) and MV grafts (29). Median time on the WL decreased when comparing ERA 1 and 2 but was not statistically significant (Table 1). Median waiting time for the pediatric recipients was longer than for the adults during both Eras. There were no mortalities on the WL after 2010. The proportion of grafts imported from other countries increased from 28% to 43% and the number of Swedish patients receiving grafts from other countries increased from 15% (n=3) to 33% (n=5). Eight Norwegian patients received 4 Swedish grafts and 4 Norwegian grafts. One isolated intestinal graft was harvested outside the Scandiatransplant procurement area (Switzerland).

Table 1. WAITING LIST CHARACTERISTICS FOR INTESTINAL ORGAN ALLOCATION IN SWEDEN

	ERA 1 (n= 21)	ERA 2 (n=14)	
Median (range, days) waiting time (all patients)	211 (1-1130)	159 (1-1102)	
Median (range, days) waiting time (pediatric)	990 (220-1102)	362 (216-874)	
Median (range, days) waiting time (adults)	89 (1-1130)	41 (1-854)	
Median (range) D/R body weight ratio	0.8 (0.3-1.2)	0.9 (0.4-1.8)	
Median donor age (years)	26 (0,5-56)	16 (2-51)	
Median cold ischemia time (range, hours)	7 (1,5-12)	9 (3,5-15)	
Percentage of "imported grafts"	28% (6/21)	43% (6/14)	
Pediatric mortality on waiting list	(4/6) 70%	(0/5) 0%	

Conclusions:

Changes in our Nordic waiting list policy appears to have shortened the waiting times, most notably for pediatric ITx candidates. No further mortalities on the WL occurred, but this may be attributed to other factors such as earlier referral for transplantation rather than changes in the shared waiting list. These data suggest an optimized utilization of the donor pool. Broadening the geographic procurement area may explain the longer cold ischemia times. Although many of the studied variables showed clear tendencies as mentioned above, they were not statistically significant. This may be due to the low number of observations.

P2.44 - Vedolizumab for IBD-like inflammation after intestinal transplantation : does it work ?

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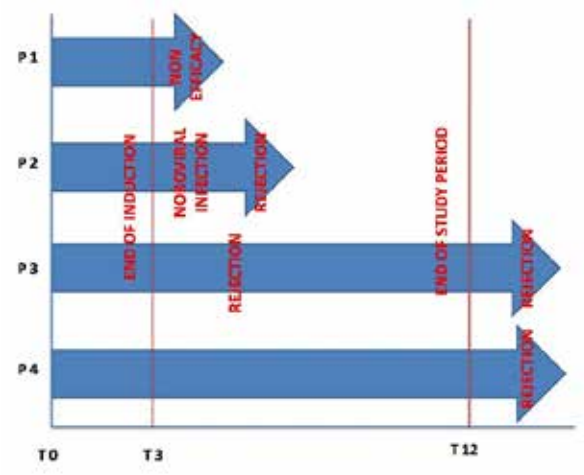
Introduction: Vedolizumab (VEDO) is a monoclonal antibody selectively blocking gut lymphocyte migration by blocking the $\alpha 4\beta 7$ integrin. VEDO has proven its efficacy in inflammatory bowel disease (IBD). Based on the selective mode of action we tested this molecule to control chronic IBD-like inflammation.

Methods: Between September 2016 and January 2017, four patients presenting with IBD-like inflammation of the small bowel / colon resistant to conventional treatment were started on VEDO (standard induction therapy at W0-2 6 (6mg / kg) followed by maintenance therapy every 4-8 weeks). Patients were followed one year after VEDO start.

Results: All four patients had received an isolated small bowel transplant for definitive intestinal failure. All four patients had failed conventional treatment for IBD-like ileocolic chronic inflammation Median age at Vedolizumab onset was 11 years (5-20).Three patients were on triple immunosuppression with steroids, tacrolimus and azathioprine, one on steroids and tacrolimus. They received VEDO induction therapy. No adverse events were reported. Maintenance therapy was started with variable intervals and adjusted to clinical outcome. During maintenance one patient experienced a Norovirus infection and two patients had ITx rejection. The first rejection occurred after the second maintenance infusion, justifying suspension of Vedolizumab and treatment with high dose steroids, thymoglobulin and Infliximab. In the second patient rejection was treated with high dose steroids, thymoglobulin and plasmapheresis, the patient continued Vedolizumab after rejection control. Another patient stopped vedolizumab after the first maintenance infusion because of inefficacy. Two patients completed one year of treatment. Both patients stopped the treatment 15 months after its initiation because of ITx rejection. The histological analysis is ongoing to determine the immunological patterns before, during, and after VEDO treatment.



Discussion: The results of treatment for IBD-like inflammation in ITx with VEDO are disappointing. This drug do not prevent form ITx rejection relapse. Immunological pattern to elucidate possible mechanisms are currently under investigation.

P2.45 - Apraglutide Has an Extended Duration and Induces a Greater Intestinotrophic Effect Compared with Teduglutide, Glepaglutide and Elsiglutide

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Introduction: To assess the impact of the long (30 hour) half-life of apraglutide (FE 203799) on intestinotrophic effect and duration of effect compared with teduglutide, glepaglutide and elsiglutide in a rat model.

Methods: Apraglutide was directly compared to teduglutide, glepaglutide and elsiglutide in Sprague-Dawley rats. The compounds, at equivalent dose levels of 30 or 300 nmol/kg (n=6/group), were tested at intervals of 24 hours (once daily for 5 days) or 48 hours (2 doses at times 0 and 48 hours). Rats were euthanized 96 hours after the first dose. The compounds were also tested after a single injection with the rats euthanized 72 or 96 hours post-dosing. Intestinal wet weight was normalized to body weight and was expressed as % increase over a control group run in the same study.

Results: At 24, 48 and 72 hour dosing intervals, apraglutide induced a greater intestinotrophic effect compared to teduglutide, elsiglutide and glepaglutide at identical doses.

At a 96 hour dosing interval, apraglutide at 300 nmol/kg increased intestine weight over the control group. The effect of apraglutide to increase intestine weight was greater than teduglutide at identical dose.

Elsiglutide and glepaglutide were not tested at a 96 hour dosing interval.

At the 300 nmol/kg dose, 96 hour dosing interval, teduglutide treated rats had a decrease in intestine weight.

Conclusions: This data indicates that apraglutide has the most robust and longest lasting pharmacodynamic effect of the compounds tested. Apraglutide is currently in Phase II development for patients with short bowel syndrome requiring parenteral support.

P2.46 - RESTORE project (improve underSTanding of small bOwel syndRomE in Argentina): First report of a prospective, observational, epidemiological, multicenter study of adult patients with Short Gut Syndrome in Argentina.

Hector Solar [1], Mariana Doeyo [1], Claudia Perez [2], Eduardo Mauriño [3], Florencia Costa [3], Martin Buncuga [4], Adrian Gold [5], Maria Matoso [6], Claudia Kecskes [6], Rodrigo Sanchez Claria [6], Silvia De Barrio [7], Adriana Crivelli [1, 7], Cecilia Igarzabal [8], Alejandra Manzur [9], Patricia Casetta [12], Mariel Calabro [12], Federico Vianno [10], Luciana Donnadio [11], Pablo Calabro [12], Gabriel Gondolesi [1]

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Introduction: There is no centralized registered information regarding patients (pts) suffering from Short Bowel Syndrome (SBS) in Argentina. Estimations based on other countries epidemiology predict an incidence of 8-10 new adult pts/year. In order to compile this information, we started a prospective multicenter observational and epidemiological registry for adults with SBS, independent from the etiology and the treatment proposed. We aim to present the first report of the RESTORE project.

M-M: From 2015 to 2017, design, funding, Institutional Review Board and Ethical approvals were obtained. Since June 2017, 11 centers started activity. Data collection was made using case report forms; a monitor visited and supervised each center initiation and performance. The registered pts are followed at each center at weeks 4, 8, 12, 20 and 24, and yearly thereafter. Dead, intestinal adaptation and transplant have been considered as end-points of the study. The principal investigator developed a prospective database. Statistical analysis was done on SPSS v20.0.

Results: 12 centers were initiated, 10 enrolled 42 pts; 33 pts were actively monitored and analyzed,12 pts completed 1 year of follow up (FU); 19 pts (57.6%) were female; mean age: 52.15 ± 15.4 years. Diagnoses in Figure 1. Mean intestinal length: 51.5 ± 42.4 cm. Anatomy type: T1: 22 pts; T2: 8 pts and T3: 3 pts; ileo-cecal valve was present in 11pts. Colon in 27 pts; Ostomies in 22 pts. Mean ostomy output: 1514 ± 1078 ml/day; Autologous GI tract Reconstruction Surgery (AGIRS) was done in 11 pts before enrollment. Meantime on parenteral nutrition (PN) before enrollment: 27.4 ± 37.18 months; PN and biochemical variables overtime are shown in Table 1; Espen Clinical Classification in Figure 1.

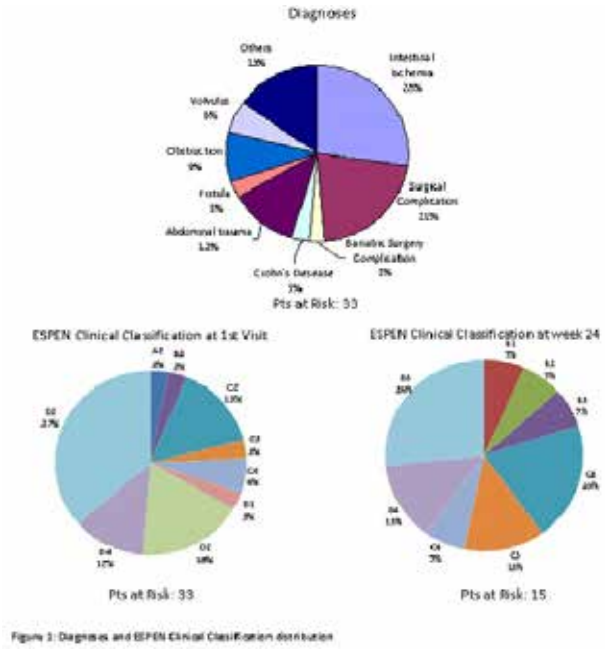

Figure 1: Diagnoses and ESPEN Clinical Classification distribution

Treatments proposed at first visit: PN+ Medical Rehabilitation: 20 pts (60%), AGIRS: 4 pts (12%); post-surgical teduglutide (TED): 8 pts (24%); transplant: 1 pt (3%); at the end of FU: 1pt was lost of FU; 4 pts adapted with AGIRS alone, or in combination with TED. One pt was transplanted and another pt. listed due to liver disease. The overall actuarial survival is 87%; sepsis was the main cause of death (3 / 4 pts).

Conclusions: Although this report still has a limited number of centers, it has registered more SBS adult patients than expected according to theoretical estimations; reinforcing the importance of having registries to understand the behavior of SBS patients overtime and their outcome.

P2.47 - Minimizing intestinal resection strategy for prevention of short bowel syndrome in surgery for chronic radiation enteritis: Shanghai experience

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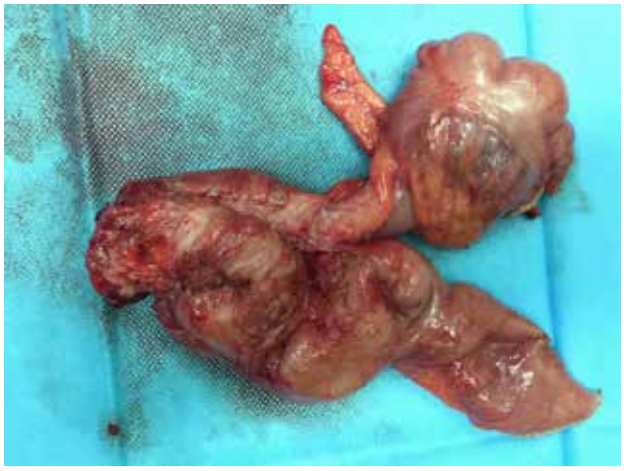
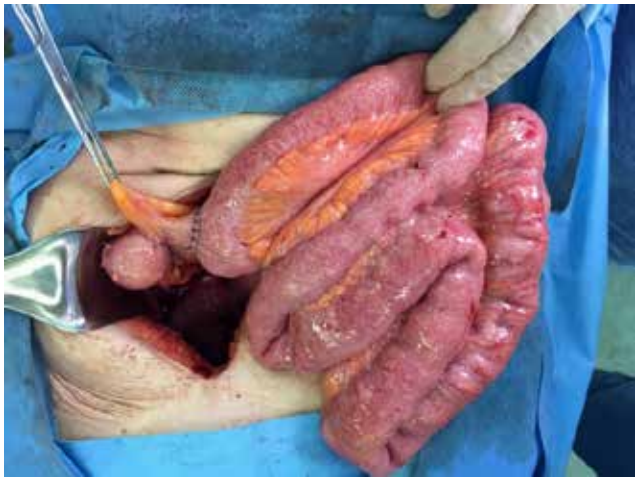
Introduction: Small intestinal fibrosis induced by chronic radiation enteritis (CRE) is a major complication following radiotherapy and an important underlying disease of short bowel syndrome. This study is to investigate the effect of modified surgical strategy on preventing both major small bowel resection followed by late-term short bowel syndrome and short-term postoperative anastomotic leakage. Methods: We divide all CRE patients with pelvic radiation enteritis-induced intestinal stenosis (REIIS) and intestinal obstruction macroscopically into two subtypes:

Type I. Terminal ileum lesion with or without proximal intestine injury (figure 1);



Type II. Isolated intestinal lesion. Records of all 22 type I patients from Apr. 2017 to Dec. 2018 were analyzed. All the patients underwent minimal resection of small intestinal lesion with primary anastomosis between ileum segments and protective proximal loop enterotomy (figure 2).



Postoperatively, stoma effluents were recycled through distal loop where the anastomosis were located. Intraoperative information and postoperative complications were retrospectively analyzed, including patients' general information, intraoperative bleeding volume, length of resected small bowel, adhesion grade, postoperative complication, postoperative hospital stay, postoperative recovery to total enteral nutrition and recycling time of stoma effluents.

Results: All the operations were performed. Length of resected small bowel was 25-100cm. No severe complications like anastomotic leakage were observed postoperatively. All the patients recovered to total enteral nutrition in 5-14 days and began ileostomy recycling in 5-14 days. Postoperative stay was 9-23 days. During a follow-up of 1-21 months, one patient died of cancer recurrence and all the other patients kept well nourished.

Conclusion: Protective proximal loop enterotomy is feasible for the surgery of radiation enteritis presenting with terminal small bowel fibrosis. This strategy can both prevent severe postoperative complications and reduce extensive intestinal resection and thus improve both peri-operative recovery and long-term outcome.

P2.48 - Safety and efficacy of mTOR inhibitors following intestine and multivisceral transplantation

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Purpose: Review the indications, outcomes and frequency of the use of mTOR inhibitors (mTORs) after intestine (IT) and multivisceral transplantation (MVT) assessed across two transplant centers in the United States.

Methods: We evaluated patients receiving everolimus or sirolimus following MVT or IT and compiled retrospective data between 2009-2018 at multiple transplant centers.

Results: 22 patients received immunosuppression including an mTOR. Twenty patients were over 18 years. Twelve patients received isolated IT. The most common reason for transplant was short gut syndrome (45%) followed by dysmotility (22%) and neuroendocrine tumor (18%). Mean age at transplant was 46 years (range 22 - 62) in adults and 2.5 in children. 54% patients were started on mTORs beyond 1 year post transplant. Mean time from transplant to initiation of mTOR was 24 months (range 1 - 78). 63.6% received sirolimus and 36.4% received everolimus. Other medications at the time of mTORs initiation included tacrolimus, prednisone, mycophenolate mofetil (MMF) and azathioprine. 18%, 13.6% and 59% of patients on mTORs were able to discontinue MMF, prednisone or reduce tacrolimus respectively. Only one patient was weaned to mTOR as single immunosuppression agent. Reason for mTOR use was renal dysfunction in 59% of cases; of these, only one patient had chronic kidney disease pre transplant. Mean glomerular filtration rate (GFR) prior to mTORs initiation was 40mL/min/1.73sqm. Of those placed on mTORs for renal insufficiency 69.2% had substantial improvement in GFR (defined as increase of 10 points). Nine patients developed some worsening of proteinuria but none were taken off treatment due to this. 27.3% cases developed acute cellular rejection (ACR), 13.6% had cytomegalovirus and two patients died while being on mTOR therapy. mTORs were discontinued in 11/22 cases due to side effects (54.5%), surgeries (18.1%) or ACR (9%). Sirolimus was discontinued in 8/14 (57%), everolimus was discontinued in 3/8 (37.5%). The mean duration of mTORs use in those stopping therapy was 7 months and 18 months in those remaining on therapy.

Conclusion: Tolerance of therapy remains challenging with almost a third of those started on mTors unable to tolerate long term treatment due to side effects. If well tolerated, mTORs were generally safe and efficacious following IT and MVT. Further studies with a control group are warranted.

P2.49 - Children with paediatric intestinal pseudo-obstruction have higher analgesic requirements post intestinal transplant than those with other diagnoses.

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Introduction: The literature on analgesia post intestinal transplant (IT) is limited though clinical experience suggests that patients with paediatric intestinal pseudo-obstruction (PIPO) may require a different approach to pain management than those with other diagnoses. The aim was to compare the required pain management of children with and without PIPO.

Methods: An electronic case notes review of 20 patients who received IT in a single centre between 2009 and 2018. Patients were divided into two groups according to the underlying diagnosis of PIPO. Pain management from extubation to day 14 post IT was reviewed. Standard analgesia was regular intravenous (IV) paracetamol and morphine, either nurse or patient controlled according to age / ability.

Results: In the PIPO group 7 patients (4 male) underwent isolated IT (2), combined liver- IT (2), multivisceral transplant (3). In the non-PIPO group 13 patients (6 male) underwent isolated IT (6), combined liver-IT (4) or multivisceral IT (3). Diagnoses in the non - PIPO group were Mitchel-Riley syndrome (1), necrotizing enterocolitis (1), TTC7A deficiency (1), gastroschisis (3), long segment Hirschsprung's (1), intestinal lymphangiectasia (1), antenatal volvulus and biliary atresia (1), microvillus inclusion disease (1), progressive familial intrahepatic cholestasis (1), intestinal ischaemia (2).

Median age (range) in the PIPO group was 7 years (1-16) and in the non-PIPO group 5 years (1-13).

71% of patients in the PIPO group had a pre-IT history of chronic pain (compared to 0 in the non- PIPO group) with 29% of patients on regular medications- gabapentin or pregablin and amitriptyline. These patients required increased and prolonged analgesia post-operatively.

43% of patients in the PIPO group and 15% in the non-PIPO group required escalation of pain management from standard medications to a more complex multi-modal approach. Escalation included IV buscopan, clonidine and fentanyl, with the addition of ketamine in the PIPO group. In all cases escalation of analgesia was planned by the specialist paediatric pain team in conjunction with the multi-disciplinary transplant team.

Conclusion: Patients with PIPO and those with a pre-transplant chronic pain management plan are more likely to require escalation of analgesia post IT. Access to a specialist pain management team may be helpful in these patients. A multi -centre study is required to help identify optimal pain management strategies for all IT patients.

P2.50 - Healthcare costs and outcomes in the management of paediatric chronic intestinal failure: early experience of a single-centre intestinal rehabilitation program in Singapore

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Background: Long-term parenteral nutrition(PN) is essential for the survival of children with intestinal failure(IF) but it contributes to morbidity & economic burden. We aimed to characterise the clinical & financial impact of long-term PN burden in the 1st 5 yrs of our intestinal rehabilitation program established in 2014 at a single-centre in Singapore.

Methods: A retrospective cohort review of children with IF who had long-term (>90 days) PN & transitioned to home-PN (HPN) from 2014 – 2018 was done. All complications related to long-term PN & the underlying gastrointestinal / surgical disorder were collected. Financial data was retrieved from the hospital's business office. Costs were categorized into 1)PN-related, 2)underlying disease (UD)-related including investigations, surgery, intensive care, & complications from UD; or 3)unrelated. In Singapore, healthcare cost is borne by the patient, with varying proportion of government subsidy.

Results: 18 children (11 girls) with IF received long-term PN for median duration of 1.36(0.27-7.5) yrs. Aetiologies included necrotizing enterocolitis 50%, paediatric intestinal pseudo-obstruction 27%, congenital mucosal disorders 11%, malrotation 5.6% & inflammatory bowel disease 5.5%. The median age at PN-onset was 0.66(0.03-68) months and at HPN-onset was 2.19(0.63-7.26) years.11 patients received hospital-PN while 7 were transitioned to HPN. 64% achieved enteral autonomy after a median duration of 1.13(0.27-6.95) years of PN support. Central line-associated bloodstream-infections affected 77% of patients with an incidence rate of 4.6 / 1000 catheter-days. Other major complications were recurrent venous thrombosis 50% & intestinal failure-associated liver disease 38%. One patient died from sepsis at 6 months of age, no patient has undergone intestinal or liver transplantation.

The overall median cost of managing children with IF for the 1st year was US$350,232.30 / patient. It dropped to US$59,331.01 in the 2nd yr & US$30,149.91 in the 3rd yr. In the first yr, 95% of costs were UD-related while 5% were PN-related. Subsequently, the proportion spent on PN was 43% while costs due to UD dropped to 45% (Fig).

Conclusion: Long-term PN therapy, whilst an effective life-saving option for paediatric IF, incurs substantial financial burden to families and the healthcare system. These findings should form the basis of a cost-benefit analysis of initiating an intestinal / multi-visceral transplantation program for patients with irreversible IF.

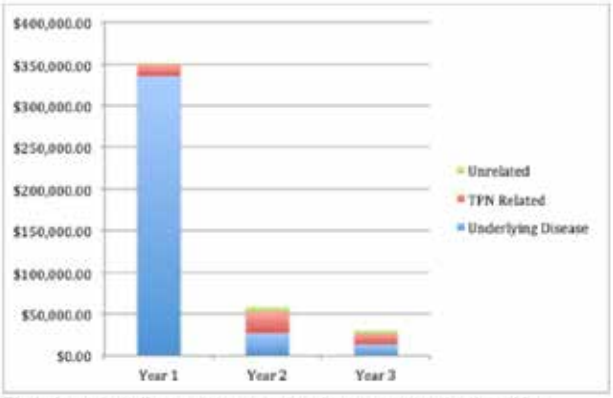

Fig 1. Annual median cost per patient on long term parenteral nutrition.

P2.51 - A training program for SBS patients treated with GLP2 agonist (Teduglutide) elaborate by a multidisciplinary team

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SBS is the main cause leading to chronic intestinal failure. In France, Teduglutide, a GLP2 agonist is available since 2015. A multidisciplinary team (in particularly 5 specialized nurses, physicians, and a “partner” SBS patient) created an educational program for patients who start Teduglutide. The aim of our study is to describe the program and evaluate his feasibility.

Methods: In a reference centre with a cohort of 280 patients with CIF, 42 SBS patients started Teduglutide between last 2015 and December 2018. The multidisciplinary team have conceived a training program dedicated to teach a) to reconstitute and inject the drug b) clinical and biological parameters to monitor at home and c) to recognize the main signs of complications and/or efficacy requiring a call or venue to hospital for HPN or drug adjustment.

Results: The program included a) a written guide (“my patient book”) with information about SBS, drug monitoring, measurement sheets of quantifications, b) an injection training session (hand’on training and video film) d) a smartphone application (Android & iOS) developed together with the patient association "La vie par un Fil" called “Mon Suivi – La Vie par un fil” associated to a training video to monitoring (input - output balance, weight, vital parameters, etc.). Forty five patients had started Teduglutide. At the end of one training session, 28/45 patients were considered as totally autonomous in terms of a) injection of Teduglutide, b) knowledge of SBS, action of drug, clinical parameters requiring a monitoring at home and c) principal actions to do in specific situations such as dehydration, fluid overload, abdominal pain. Ten/45 patients required supplementary training sessions with a community nurse at home. Seven/45 patients were considered as partially autonomous, with the help of a nurse or family member still required. Ten/45 patients were trained to use the Smartphone app for the monitoring and used it regularly.

Conclusion: The arrival of new treatments in SBS is really challenging because rapid changes in digestive parameters may require faster adaptation of parenteral support than usual. A complete training program combining human resources, digital and written tools allows the increase of SBS patient autonomy. The next step should be an impact analyse of the impact of the program on mid and long term terms changes such as hospitalisation rate, global adhesion to SBS treatment and quality of life.

P2.52 - Complete Jejunal Exclusion: A novel method to manage Enterocutaneous Fistulas in the background of short bowel syndrome

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Introduction: Management of enterocutaneous fistulas (ECF) in patients with short bowel syndrome (SBS) is challenging. High output fistulas are unlikely to close spontaneously; however, the success rate of surgical intervention is limited due to poor nutrition, inflammation, limited bowel length and lack of abdominal wall integrity. Here, we describe 8 cases of utilizing complete jejunal exclusion at the ligament of Treitz with a gastrostomy tube drainage to manage the ECF as a temporary measure for subsequent bowel reconstruction or transplant. To our knowledge, this is the first report of this approach.

Methods: Eight patients who underwent jejunal exclusion at our institution were retrospectively reviewed. In all cases, the jejunum was divided 1-2 inches distal to the ligament of Treitz. Both ends were oversewn. A gastrostomy tube was placed for retrograde decompression of proximal enteric secretions without pyloroplasty. In 4 cases of active ECF's, we accessed the ligament of Treitz via a left subcostal incision to avoid the fistula.

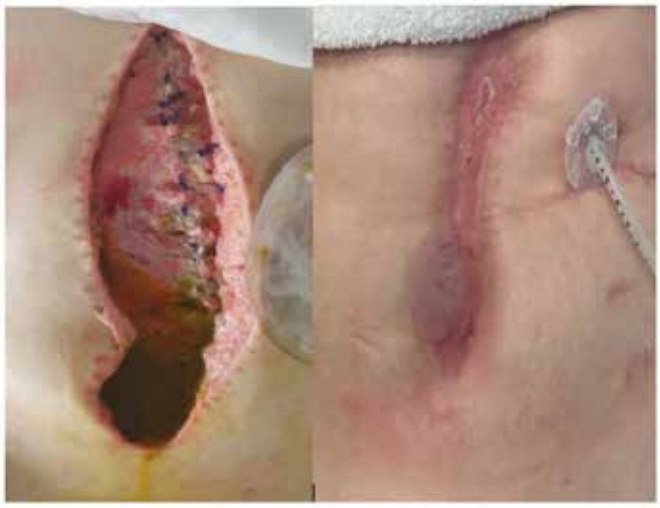
Results: The procedure was done for active ECFs (n=4), impending fistulas (n=1), bridge to transplant following desmoid tumor resection in Gardner's syndrome (n=2), and after graft enterectomy (n=1). Four cases of active ECFs were managed elsewhere without success. All patients were discharged home on TPN. Of the 4 ECF cases, the fistula output decreased substantially in all patients and closed entirely in 2 cases. Two underwent successful reconstruction and 2 are awaiting reconstruction. One who had secondary biliary cirrhosis due to biliary obstruction and TPN induced liver disease died while waiting for multivisceral transplant (MVT). Of the desmoid tumor cases, one underwent MVT, is alive and well 8 years after transplant, while the other refused to undergo MVT and is living with TPN and g-tube decompression 6 years after the procedure. The patient who underwent graft enterectomy is listed for MVT-this patient developed acute pancreatitis after the jejunal exclusion and required G-J tube decompression.

Conclusions: Jejunal exclusion is an effective and generally well tolerated option in the management of intractable ECF in patients with SBS. Associated complications include pancreatitis and liver failure. This procedure should be considered as a bridge to intestinal rehabilitation or transplantation in patients with ECFs that fail to close with medical or traditional surgical management.

Table:

Patient	Etiology	Length of Small Bowel Left	ECF	TPN	TPN status	Length of Stay post procedure (days)	Outcome
Case 1	SMA thrombosis	25cm	Yes	Yes	On	112	Discharged Home
Case 2	Midgut Volvulus	50cm	No	Yes	On	95	Discharged Home
Case 3	Midgut Volvulus	5cm	No	Yes	On	25	Discharged Home
Case 4	Necrotizing Pancreatitis	25cm	Yes	Yes	On	41	Discharged Home
Case 5	Multiple surgical resection following bowel injury at hysterotomy	60cm	Yes	Yes	TPN 4d/week with Teduglutide	13	Discharged Home
Case 8	Transplant graft failure	10cm	No	Yes	On	45	Discharged Home
Case 6	Intraabdominal Desmoid	5cm	No	Yes	Off	31	Discharged Home
Case 7	Intraabdominal Desmoid	6cm	Yes	Yes	On	29	Discharged Home

Picture:



P2.53 - SMOFlipid in pediatric patients with intestinal failure: a single center experience from the United States

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Introduction: The soy-based lipid component of parenteral nutrition (PN) is a known contributing factor to intestinal failure associated liver disease (IFALD). Although effective in reducing hepatotoxicity, lipid minimization (LM) protocols predispose to essential fatty acid deficiency (EFAD). SMOFlipid (soybean oil, medium-chain triglycerides, olive oil, fish oil) was FDA approved for adult patients with intestinal failure (IF) in the United States in 2016 and contains a more favorable ratio of omega-3 to omega-6 fatty acids compared to Intralipid (IL). We reviewed our experience with SMOFlipid in pediatric patients with IF.

Methods: A retrospective chart review was conducted on pediatric patients with IF at our Center who switched from IL to SMOFlipid between 2016-2017. We reviewed data before and 3-6 months after initiation of SMOFlipid (demographics, IF etiology, PN components, liver biochemistry tests, fatty acid profiles, growth parameters, micronutrient labs, abdominal ultrasound and liver histology).

Results: Sixteen eligible patients were included in this analysis (median age: 4 years, range: 4 months-10 years, 50% male). After switching to SMOFlipid, the mean fat component of PN increased (0.4 g/kg/day vs. 1 g/kg/day, P<0.001), glucose infusion rate (GIR) decreased (16.3 mg/kg/min vs. 11.4 mg/kg/min, P=0.01), serum α-tocopherol levels increased (6.8 mg/L vs. 9.2 mg/L, P=0.01), EFAD improved (mean triene:tetraene 0.07 vs. 0.04, P<0.001), and growth improved (mean BMI/Weight:Length Z-score 0.11 vs. 0.95, P=0.03). There was some improvement in liver biochemistry tests, despite increased lipid administration. Two patients had resolution of abnormal sonographic findings, and one patient had histologically-proven resolution of hepatic steatosis and fibrosis. The average cost was $2.70/day for IL and $14.40/day for SMOFlipid (P<0.001). SMOFlipid was not discontinued in any of the patients and no adverse effects were observed.

Conclusion: An increased dose of a balanced lipid emulsion was associated with improved EFAD, improved growth, decreased GIR and increased serum α-tocopherol levels, while not worsening IFALD. Although the daily cost of SMOFlipid is higher than IL, the benefits offered by its better anti-inflammatory profile may prove to outweigh the higher cost. Based on our single-center experience, we recommend the routine use of SMOFlipid in pediatric patients with IF to avoid the potentially harmful effects associated with IL and LM protocols.

P2.54 - Re-analysis of a randomized placebo (PBO) controlled trial of intravenous (IV) choline chloride for IFALD using state-of-the-art analytic and imaging methods and contemporary definition of IFALD

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Introduction: IFALD ,defined as steatosis and cholestasis, is associated with significant morbidity in patients dependent on parenteral nutrition(PN).Choline is an essential nutrient that is a fundamental component of cell membranes, VLDL for triglyceride export from the liver, and normal bile.PN products do not contain sufficient choline.Buchman et al(2001) determined that IFALD may be reversible in choline-deficient patients.The current study wreviewed, transformed and analyzed data from Buchman et al 2001 using state of the art methods to inform a confirmatory phase 3 trial.

Methods: Data were imported from original source documents into an electronic eCTD format. Because MRI-Proton Density Fat Fraction(PDFF)has become the gold standard method for non-invasive quantification of hepatic steatosis, CT data were transformed to MRI-PDFF using an established linear equation (Kramer et al, 2017).The trial was then re-analyzed using MMRM statistical approach, and in two subgroups of patients meeting contemporary definitions of IFALD.Missing data were reasonably assumed to be missing at random.

Results: This was a study of adults dependent on PN for many years(11.8 years(6.47).IV Choline Chloride was safe and well-tolerated. Baseline MRI-PDFF values(mean 19.6%, range [9.8-38.3%])demonstrate moderate to severe fatty liver in the study population.The benefit of IV Choline Chloride vs PBO achieves significance or trend-significance from Weeks 4-24 despite small sample size.Comparing groups on the relative (%) change of MRI-PDFF, drug-PBO differences from Weeks 4-24 are large and clinically meaningful(range 31%-54%).The benefit of IV Choline Chloride vs PBO achieves trend-to or statistical significance from Weeks 4-24 despite small sample size. In the sub-group analyses, improvement in ALP is consistent and substantial, with 20-30% improvement over 12-24 weeks of treatment.

Conclusion: Using MRI-PDFF, a contemporary definition of IFALD, modern analytic approaches, and source-verified data, the original findings from Buchman et al 2001 are replicated and extended. These robust results in a rare, but serious condition affecting PN patients can inform future trials attempting to replicate these promising results in a larger cohort to support the development of a safe, choline PN product.

P2.55 - Decreasing Tacrolimus Time-In-Therapeutic Range is Associated with an Increased Incidence and Severity of Rejection Following Intestinal Transplant

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Introduction: Acute rejection (AR) is a major complication in intestinal transplantation (ITX) that can lead to graft loss. Tacrolimus (TAC) is a mainstay of immunosuppression following ITX to prevent AR. Drug monitoring is routinely employed to ensure adequate exposure to TAC, while limiting adverse effects. Despite established practice, there is limited direct evidence linking therapeutic TAC levels with improved clinical outcomes post-ITX.

Method: This was a single-center review of all adult non-liver containing ITX graft recipients from 2010-2017, who maintained a functioning graft for 1 month. Patients received anti-thymocyte globulin (ATG) induction, with plasmapheresis and IVIG for positive T-cell CDC cross matches (CXM). Maintenance immunosuppression included TAC and prednisone, with mycophenolate or sirolimus added at physician discretion. 12-hour TAC whole blood trough levels were monitored daily in the hospital and every 1-4 weeks following discharge, with target levels of 13-17ng/mL month 1, 12-15ng/mL months 2-3, 10-13ng/mL months 3-6, and 8-12ng/mL months 6-12 post-ITX. Percent time-in-therapeutic range (TTR) for TAC was calculated from the date of transplant until 1 year post-ITX or graft failure using Rosendaal's method (Rosendaal. *Thromb Haemost*.1993;69:236-239.) and patients were divided into TTR quartiles. Multivariable regression was used to identify variables associated with the incidence of AR on biopsy tissue within 1 year of ITX. Additional variables assessed included: graft type, adjunctive immunosuppression, age, sex, ethnicity, indication for ITX, prior transplants, cold ischemia time, DSA > 2,000 MFI, and positive CXM.

Results: A total of 51 patients were included in the analysis, 11 of which had pre-transplant DSA, and 6 patients had a positive CXM at time of ITX (Table 1). Mean TAC-TTR for the cohort was 29.9% ± 11.2, and 19 episodes of AR were observed in the first year post-ITX. Logistic regression demonstrated TAC-TTR<30% was associated with an increasing risk for any rejection episode (Table 2). A similar trend were observed for severe rejection episodes requiring ATG, with TAC-TTR<20% associated with a greater risk for severe rejection (p=0.02;HR:7.7[95% CI:0.9,65.3]).

Conclusion: Our dataset suggests that decreasing TAC-TTR may be a risk factor for both the occurrence and severity of rejection. If confirmed, our results indicate a need for utmost vigilance in TAC trough monitoring within the first-year post-ITX.

Table 1 – Baseline Characteristics

Baseline Characteristics	Final Cohort (n = 51)
Recipient Age, years	46.7 ± 10.1
Donor Age, years	11.6 ± 10.5
Male Recipient Sex	23 (45.1%)
Recipient Ethnicity	
White/European	34 (66.7%)
African-American	6 (11.8%)
Hispanic/Latino	9 (17.6%)
Asian/Pacific Island	2 (3.9%)
Graft Type	
Isolated Intestine	40 (86.3%)
Intestine-Kidney	7 (13.7%)
Intestine-Pancreas	4 (7.8%)
Etiology of Short-Gut-Syndrome	
Crohn's Disease	12 (23.5%)
Vascular Thrombosis	11 (21.6%)
Trauma	2 (3.9%)
Dysmotility Syndrome	8 (15.7%)
Failed Prior Transplant	6 (11.8%)
Other	12 (23.5%)
Adjunctive Immunosuppression	
Mycophenolate	27 (52.9%)
Sirolimus	12 (23.5%)
Mean Cold-Ischemia Time, minutes	435.2 ± 77.8
Pre-Transplant DSA	11 (21.6%)
CDC Cross Match	
B-/T-	45 (88.2%)
B+/T-	2 (3.9%)
B+/T+	4 (7.8%)
Graft Loss Prior to 1 Year	14 (27.4%)
Overall Incidence of Rejection	
Any Rejection	19 (37.2%)
Severe Rejection	11 (21.6%)
Tacrolimus Dosing	
Time-In-Therapeutic Range	29.9% ± 11.2
Time Supratherapeutic	34.2% ± 15.6

Table 2 – Multivariable Logistic Regression Model for Any Acute Rejection

Parameter	P-value	Hazard Ratio	95% Confidence Interval Limits	
TAC-TTR < 30%	0.01	3.7	1.4	10.2
Positive CXM	< 0.01	2.6	1.4	4.8

P2.56 - Outcomes after pediatric intestinal transplantation: A comparative analysis between a single program and the national database

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Introduction: Thirty-seven intestinal transplant (ITx) programs have performed ≥1 pediatric ITx since 1990 according to the 2017 United Network for Organ Sharing (UNOS) database. The median number of ITx per center was 8. Our institution is an aggressive center for pediatric intestinal rehabilitation (IRP), with relatively low volumes for ITx. We hypothesized that outcomes from a medium-size program like ours compared favorably to national data.

Methods: A retrospective review of all ITx done at a main pediatric IRP and ITx program was performed (2004-2019). Demographic, medical, and surgical data were collected. National data was obtained from the UNOS database (n=1500). Mann-Whitney and Chi-Square tests were used for analysis. $p<0.05$ was considered significant. Institutional Review Board approval was obtained (IRB #2019-2474).

Results: Since 2004, 18 ITxp were performed at our institution. The proportion of girls at our center, 8/18 (44%), was identical to UNOS, 598/1346 (p=1.0). Gastroschisis was the main cause of short gut syndrome in both groups (7/18, 39% locally, vs. UNOS 341/1500, 23%, p=0.13). Mean age at transplant was similar (3.94±3.72 vs. UNOS 3.61±4.35 years, p=0.33). Mean waitlist time was longer for our patients, although not significantly (394.11±480.37 vs. UNOS 220.23±336.92 days, p=0.062). There was a trend in shorter mean distance between donor and recipient hospitals in our program (466.47±335.93 vs. UNOS 547.39±436.09 days, p=0.65) while the mean cold ischemia time was significantly shorter in our group (6.98±1.73 vs. UNOS 7.88±2.58 hours, p=0.049). There was a significant difference between groups regarding intestinal venous drainage through the portal vein for isolated small bowel ITx (3/15, 27%, vs. UNOS 247/440, 57%, p=0.005). The incidence of multivisceral transplants was significantly higher nationally (UNOS 1034/1500, 69%, vs. 3/18, 17%, p<0.001). There was no statistical difference in overall graft survival (11/18, 61%, vs. UNOS 46%, p=0.19) although it was higher in our group. There was a trend in improved overall patient survival in our patients (15/18, 83%, vs UNOS 832/1347, 62%, p=0.062).

Conclusion: Timelier listing for isolated ITx is associated with a lower incidence and need for multivisceral transplantation in aggressive intestinal rehabilitation program. Shorter cold ischemia times associated with shorter travel distance between donor and recipient hospitals may contribute to higher patient and graft survival.

P2.57 - Do children with short bowel syndrome secondary to complex gastroschisis have a worse prognosis?

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Introduction: Short bowel syndrome (SBS) is the main cause of intestinal failure (IF) and complex gastroschisis (CG) is the most frequent underlying cause in our population. It has been reported that children with SBS related to CG have a worse prognosis. The present work aims to analyze our results in the treatment of SBS secondary to CG and compare them with those obtained in cases of SBS related to other underlying diseases.

Methods: A descriptive, retrospective study was carried out, using data collected from institutional electronic records and the specific IF database. Inclusion criteria: patients under 18 years of age, with IF defined as parenteral nutrition (PN) dependency greater than 2 months and diagnosis of SBS. Patients were divided into 2 groups: G1 included cases of SBS associated with CG and G2 patients with SBS related to other diagnosis. Intestinal rehabilitation (sustained suspension of PN), need for intestinal transplantation and mortality were analyzed for both groups. Additionally, the influence of different exposure variables such as anatomical features of the digestive tract and adverse events related to prolonged PN, was analyzed for the group of patients with CG.

Results: We obtained a final number of 86 patients with 24 in G1 and 62 in G2. Both groups were comparable. No statistical difference in intestinal rehabilitation (G1 78.9% vs G2 57,14%) and mortality rate (G1 20.8% vs G2 20,9%) was found, although a trend to better outcome in achieving intestinal rehabilitation was observed for patients with CG. Additionally, all the patients in G1 with complete colon are currently off-TPN with a significant statistical association of this variable to intestinal rehabilitation. Regarding need for transplantation, taking into account all the patients that were transplanted as well as those that are candidates in the waiting list, both groups exhibited similar results with no statistical difference (G1 20,8% vs G2 14,5%).

Conclusions: CG is the main individual cause of IF in our population. In the context of specialized multidisciplinary treatment, our results show that the majority of patients with SBS secondary to CG survive and succeed in suspending PN, with similar results as those observed in patients with SBS secondary to other entities. The preservation of the colon whenever possible, as well as the prevention of adverse events related to PN, can improve the outcome in these patients.

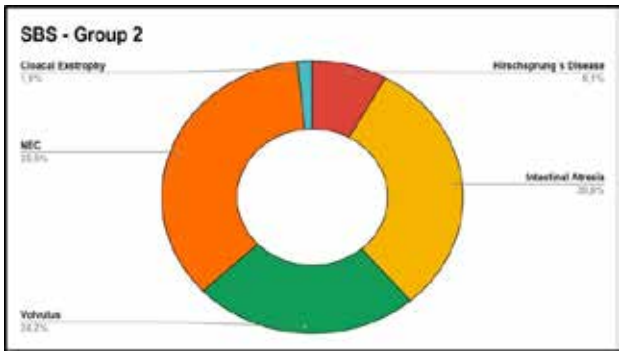

Figure 2 – Comparative variable analysis for both groups

VARIABLES		Group 1 SBS secondary to CG n=14		Group 2 SBS non related to CG n=62		p value
Sample distribution by gender	% of female pt	9	37,50%	24	38,71%	1.000 (ns)
Type of case	% of referred pt from other institutions	10	79,17%	53	80,60%	1.000 (ns)
Age at the 1st evaluation	Mean age in months	11,42	DS 20,52	16,16	DS 36,53	0.5438 (ns)
Weight at the 1st evaluation	Mean weight in kg	6,72	DS 5,12	7,85	DS 9,82	0.0287 (ns)
Length of residual small bowel (RSB)	Mean lenght of RSB in cm	52,27	DS 37,006	47,41	DS 46,52	0.0704 (ns)
Presence of ileocecal valve (ICV)	% of pt with ICV	6	25,00%	24	38,71%	0.3139 (ns)
Presence of complete colon (CC)	% of pt with CC	14	58,33%	32	51,62%	0.8091 (ns)
Catheter - Associated Infections (CAI)	% of pt with at leastone episode of CAI	18	75,00%	53	80,64%	0.5663 (ns)
Venous Thrombosis (VT)	% of pt with presence of VT	10	41,67%	30	50,00%	0.2200 (ns)

References - Pt: patients, ICV: ileocecal valve, CC: complete colon, CAI: catheter associated infections, VT: venous thrombosis

P2.58 - Chronic hyperammonemia an important cause of morbidity in isolated intestine transplant patients with venous outflow to the vena cava

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Background: There are limited options for superior mesenteric vein (SMV) outflow in isolated intestine transplant (ITx), the two most common being anastomosis to the recipient superior mesenteric vein or to the vena cava. Previous research comparing these two options demonstrated no difference in early clinical outcomes. This paper reports four cases of symptomatic late hyperammonemia occurring in ITx patients more than 1-year from transplant. Each affected patient experienced marked encephalopathy. In each case, a very low protein diet was effective in lowering ammonia levels and ameliorating symptoms. Each affected ITx patient had direct SMV-vena cava drainage of their graft. This study reports an analysis of all living ITx patient at this single center to determine if hyperammonia is associated with vena cava drainage alone or if it occurs generally in this population.

Methods: ITx recipients at a single center were identified. Random serum ammonia levels were obtained with routine blood draws. Ammonia levels were analyzed in relation to both (1) SMV drainage technique and to (2) time from transplant. Liver function was also assessed using standard lab values.

Results: There were 71 ITx patients between 2003 and 2018, 26 patients with SMV-SMV anastomosis (37%) and 45 with SMV-vena cava anastomosis (63%). Of these patients, 37 are currently living (52%). For SMV-vena cava patients, the available ammonia levels were consistently greater than 50mcg / dL. Among affected patients, the peak levels would reach as high as 150-200mcg / dL. For SMV-SMV patients, the levels were always less than 50mcg / dL. There was one SMV-SMV patient with intermittent encephalopathy, but she had peak ammonia levels of 60mcg / dL. She was ultimately diagnosed with a rare neurocognitive disorder.

Conclusions: This study demonstrates that hyperammonemia is not uncommon among late survivors of ITx, but only in those patients with SMV to vena cava anastomosis. This hyperammonia may result in marked encephalopathy as seen in four patients in this cohort. A very low protein diet is effective in minimizing this process. In ITx patients with SMV-vena cava anastomosis, routine monitoring of serum ammonia levels is indicated.

P2.59 - Simultaneous Serial Transverse Enteroplasty (STEP) in Size Mismatch Small Bowel Transplantations

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Background: Small bowel transplantation (SBTX) in children receiving larger grafts from adults can be challenging because of size mismatch. The aim of the present study was to assess whether a simultaneous serial transverse enteroplasty (STEP) can address the problem of size mismatch.

Methods: Three different size ratio groups between donors and recipients were compared in a porcine model with a 14-day follow-up. The groups were size matched, size mismatched (1:3.8 weight ratio), and size mismatched+STEP (each n =8).

Results: It was technically feasible to simultaneously perform a STEP and SBTX of a mismatched intestinal segment. The postoperative clinical course was uneventful. No signs of bleeding, leakage, stenosis, or ileus were observed and the intestinal segment was well perfused at relaparotomy. Body weight decreased in all groups, but the percentage decrease was lowest in the mismatched+STEP group. Vital enterocyte masses were similar in all the groups (citrulline levels) and the nutritional status was best in the STEP group (transferrin levels, p =0.04).

Conclusions: We have demonstrated that a simultaneous STEP and SBTX procedure is technically feasible and clinically useful in overcoming the challenges associated with size mismatched SBTX. Our short-term findings justify further investigation in a larger series to elucidate the long-term outcomes of this procedure.

POSTERS PRESENTED ON FRIDAY JULY 5, 2019

P3.21 - Fibrinolytic Shutdown Is Associated With Intraoperative Thrombosis and Hemorrhage During Visceral Transplant

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Introduction: End stage liver disease (ESLD) is characterized by a precarious imbalance of hemostasis. Detrimental consequences of hypofibrinolysis, also known as fibrinolytic shutdown, have been recently demonstrated, and its significance in visceral transplant remains unknown.

Method: To fill this gap, following IRB approval, this retrospective study included 49 adult recipients of visceral allografts (14 without the liver, 35 multivisceral (MVT) with the liver) transplanted between 2010-2018 in a single university hospital, and for whom pre-incisional thromboelastography was available. Based on % clot lysis 30 min after maximal amplitude, patients were stratified into 3 fibrinolysis phenotypes: fibrinolytic shutdown, physiologic fibrinolysis, and hyperfibrinolysis.

Results: Fibrinolytic shutdown occurred in 57% of patients, with higher incidence in recipients of multivisceral (69%), compared to visceral (29%) allografts (P=.04). Of the 35 MVT, 26% had normal liver function, 46% had parenteral nutrition-associated liver disease and 28% had severe ESLD with extensive portal vein thrombosis. Fibrinolytic shutdown was statistically associated with ESLD, as incidence of fibrinolytic shutdown in the presence or absence of ESLD was 73% versus 39% (P=0.02). Intraoperative thrombosis (18%) occurred only with MVT, and accounted for 36% of in-hospital mortality. Intraoperative thrombosis occurred solely in recipients with an abnormal fibrinolytic phenotype (fibrinolysis shutdown- 8/9 and hyperfibrinolysis- 1/9). A clinically meaningful reduction in incidence of intraoperative thrombosis was noted in recipients who received iv heparin thromboprophylaxis. Logistic regression identified pretransplant platelet count as a risk factor for fibrinolytic shutdown [OR 0.992, 95%CI (0.984-0.998); χ2=7.8, P=0.005).

Conclusions: This study highlights fibrinolytic shutdown as a dominant and clinically important feature of the hemostatic imbalance in recipients undergoing visceral transplantation.

P3.22 - Current picture of intestinal transplantation for intestinal failure in Japan

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Introduction

The prognosis of intestinal failure has improved dramatically in the past few decades with the development of parenteral nutrition. However, PN-dependent patients still have numerous complications. Intestinal transplantation (ITx) is able to significantly improve their prognosis and quality of life. As the ITx has become covered by national health insurance in 2018 in Japan, the number of ITx is expected to increase in the near future. Therefore, we report on the current picture of the ITx for intestinal failure in Japan.

Methods

The ITx have been performed in Japan since 1996. Standardized form were sent to all known ITx programs, asking for information on ITx performed between 1996 and 2017. All programs responded. Patient and graft survival estimates were obtained using Kaplan-Meier method and analyzed with Wilcoxon statistics.

Results

Five institutes provided data on 26 isolated ITx and one simultaneous liver and intestinal transplant in 23 Patients. There were 14 cadaveric and 13 living related donor transplants (Figure 1). Causes of intestinal failure included short bowel syndrome (n=9), motility disorders (n=14), re-transplantation (n= 3), and other (n=1). The median age at ITx was 15.2 years (ranged 0.7 to 35 years). The overall 1- , 5- and 10- year patient survival rates were 88%, 70% and 51%, respectively. (Figure 2). The overall 1- , 5 and 10 -year graft survival rates were 81%, 58% and 39%, respectively. More than 80% of all current survivors discontinued PN with satisfactory performance status.

Figure1

Figure2

Conclusions

ITx has become an effective therapy for patients with intestinal failure who cannot tolerate PN in Japan. Further improvements are expected with early referral due to suitable donor organ and pre-transplant management.

P3.23 - Copper deficiency in infants with intestinal failure: hematological manifestations

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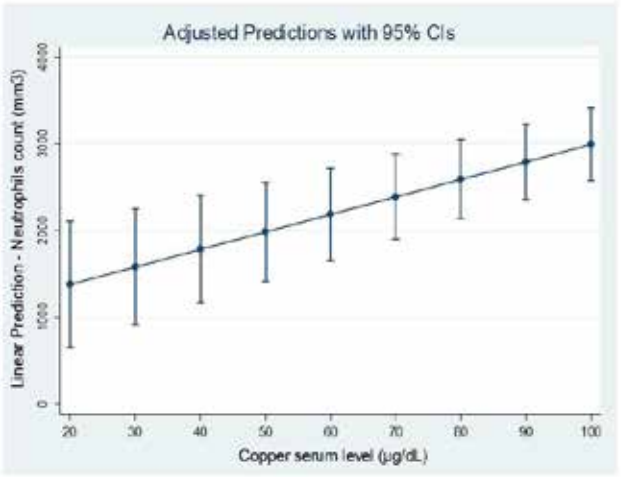
Introduction: Hematological cytopenias have been reported in copper-deficient children with intestinal failure (IF) and receiving parenteral nutrition (PN). However, no cohort study has investigated a possible association between copper deficiency and low blood cell count in patients who had their copper plasma levels monitored according to a standard protocol. We investigated how much copper plasma levels influence anemia, neutropenia and thrombocytopenia in children receiving long-term home PN.
Methods: Children with IF admitted to a pediatric intestinal rehabilitation program and who were receiving home PN were followed-up prospectively from July 2015 to November 2018. Outcome variables were hemoglobin (Hb, g/dL), neutrophils and platelet counts (mm3); plasma copper levels during the follow-up were considered as the main explanatory variable. Patient's micronutrient status was routinely monitored at 3-month intervals or once a month when deficiency was detected. All patients were receiving a fixed dose of vitamins, and multi-trace element solution including copper (at a standard dose of 20mcg/kg). Complete blood counts were performed bi-weekly. Generalized estimating equations models were adjusted for vitamin B12, iron and folate plasma levels.
Results: Thirteen patients aged 34.2 months (IQR: 25.3; 41.1) were included; median time on PN was months 26.4 (15.2 to 32.9). An average of 7 (range 2 to 15) copper measurements/patient were performed; 53.8% of patients had at least 1 copper measurement below normal. Eight patients who had cholestasis had trace elements of PN discontinued. All but one patient had anemia; neutropenia was seen in 11 patients (among them 8 had < 1000 neutrophils/mm3), and 8 patients had thrombocytopenia.
Copper deficiency (plasma level <72µg/dL) was associated with lower Hb and lower neutrophils and platelet counts. The decrease of 10 µg/dL in plasma copper resulted in decreases in Hb level (β coeff.: -0.08 (95% CI: -0.02;-0.14, p=0.009), in neutrophil (β coeff. -201.6, 95% CI:-134.8;-268, p<0.001) and in platelet counts (β coeff. -6278, 95% CI: -2026;-10529, p=0.004). The figure shows predictions and marginal effects of copper serum levels on neutrophils count.



Predictions and marginal effects of copper serum levels on neutrophils count

Conclusion: Copper deficiency is associated with lower blood cell counts and higher risk of anemia, neutropenia and thrombocytopenia. This effect was more pronounced for neutropenia. Copper status should be routinely monitored in children with IF receiving long term PN.

P3.24 - First clinical multi-center experience of IGL-1 for intestinal graft preservation

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Introduction: The gold standard for intestinal allograft preservation is University of Wisconsin solution (UW). In animal models, Institute Georges Lopez solution (IGL-1) improved intestinal graft viability and epithelial repair compared to UW. It is an extra-cellular preservation solution with high sodium and low potassium content in contrast to UW and presence of polyethylene glycol, resulting in lower viscosity. The aim of this study is to evaluate IGL-1, for the first time, as a preservation solution for clinical intestinal transplantation (ITx).

Methods: We performed a retrospective analysis (January 2014 to April 2018) of all ITx where the graft was preserved using IGL-1 in 4 European centers.

Results: Thirteen ITx were performed in 13 patients (1 child / 12 adults, 7 females / 6 males) for short bowel syndrome (n=7), motility disorder (=4) and diffuse portomesenteric thrombosis (n=2). Seven multivisceral and 6 isolated grafts were transplanted. Vascular perfusion with 4-6 liters of IGL-1 was used without luminal preservation. Median cold ischemia time was 485 minutes (range: 192-840 minutes).

In all cases, the bowel appeared macroscopically well vascularized after reperfusion with minimal signs of reperfusion edema. Histology after reperfusion was available in 3/13 cases, with a maximal Park/Chiu score of 2.

One-year graft survival was 76%. Three patients required a transplantectomy (1 for CMV reactivation, 2 for refractory cellular rejection). Two patients died after transplantectomy: 1 from intestinal failure associated liver disease and 1 from bacterial sepsis, resulting in a 1-year patient survival of 83%. Ten patients are alive with a functioning graft and one requires parenteral nutrition following transplantectomy.

Conclusion:This multicenter experience suggests that IGL-1 can safely be used for preservation of intestinal grafts with good short-term results, comparable to the results from the International Intestinal Transplant Registry. Further histological data is being collected from all centers to evaluate preservation capacity of IGL-1.

P3.25 - Intestinal Cholesterol Absorption Is Preserved After Isolated Intestinal Transplantation Despite Increased Cholesterol Synthesis

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Introduction. We aimed to investigate cholesterol metabolism in relation to nutritional status and serum lipids after isolated intestinal transplantation (ITX).

Methods. Seven patients who had undergone isolated ITX including ascending colon at median age of 17.3 (range, 5.9-52) years due to intestinal failure caused by chronic intestinal pseudo obstruction (n=5) and total intestinal aganglionosis (n=2) were included median 3.5 (IQR, 2.9-7.4) years after ITX. Blood samples were analyzed for fat-soluble vitamins (A, E, D-25-OH), prealbumin, and cholesterol (total, LDL, HDL) and triglyceride levels. In six patients and 14 heathy age- and gender-matched controls, cholesterol metabolism was assessed with serum non-cholesterol sterols. The ratios to cholesterol (102 x µmol/mmol of cholesterol) of the serum cholesterol precursors (cholestenol, desmosterol and lathosterol) reflect cholesterol synthesis, while those of plant sterols (campesterol, sitosterol, and avenasterol) and cholestanol reflect cholesterol absorption efficiency. Lathosterol/cholestanol ratio reflects the balance between cholesterol absorption and synthesis and campesterol/cholestanol ratio reflects the plant sterol intake.

Results. Patients were on tacrolimus-based maintenance immunosuppression without current signs of acute or chronic transplant rejection. All patients had weaned off PN median 39 days (IQR 21-215) after ITX and had a median body mass-index of 18.2 (IQR, 16.6-19.1) kg/m2. The levels of fat-soluble vitamins and prealbumin were mostly in normal range while plasma HDL cholesterol was low and triglyceride levels were increased in most patients (Table 1). Cholesterol precursor levels were significantly increased while plant sterols and cholestanol were not significantly different between patients and controls (Table 2). Increased lathosterol/cholestanol-ratio suggest that cholesterol synthesis markedly predominated absorption in patients' whole body cholesterol homeostasis while the campesterol/cholestanol ratio suggest that the plant sterol intake was decreased in patients compared to controls (Table 2).

Conclusion. Following isolated ITX, intestinal cholesterol absorption efficiency is preserved, while cholesterol synthesis increases likely to compensate malabsorption of bile acids. Satisfactory nutritional status, normal fat-soluble vitamin levels and preserved cholesterol absorption suggest that the compensatory increase was sufficient to maintain adequate lipid absorption.

Table 1. Plasma cholesterol, triglycerides, prealbumin and fat-soluble vitamins after intestinal transplantation.

Variable		Patients N=7	Reference range	Off reference range N, (%)
Plasma Cholesterol	mmol/L	3.5 (3.0-4.0)	1.2-4.3	0 (0)
Plasma HDL	mmol/L	1.2 (0.8-1.3)	>1.2	low, 4 (57)
Plasma LDL	mmol/L	1.8 (1.3-2.3)	1.2-4.3	0 (0)
Plasma Triglycerides	mmol/L	1.9 (1.3-2.3)	<1.7	high, 5 (71)
Prealbumin	mg/L	289 (250-330)	170-350	low, 1 (14)
Vitamin A	umol/L	2.2 (1.6-2.8)	0.7-4.2	0 (0)
Vitamin D-25	nmol/L	70 (19-72)	>50	low, 2 (29)
Vitamin E	umol/L	22 (17-29)	12-37	0 (0)

Data are median (IQR).

Table 2. Serum non-cholesterols sterols after intestinal transplantation.

Variable	Patients N=6	Matched controls N=14	P-value
Cholesterol synthesis			
Cholesterol	55 (33-83)	14 (13-15)	**<0.005**
Desmosterol	128 (114-155)	77 (68-85)	**0.001**
Lathosterol	335 (240-473)	102 (77-108)	**0.001**
Cholesterol absorption efficiency			
Campesterol	205 (149-289)	320 (204-372)	0.076
Sitosterol	139 (92-412)	177 (116-194)	0.680
Avenasterol	45 (30-73)	44 (34-54)	0.934
Cholestanol	205 (149-237)	166 (150-192)	0.216
Ratios			
Lathosterol/Cholestanol-ratio	2.44 (1.30-3.31)	1.18 (0.95-1.12)	**0.026**
Campesterol/cholestanol-ratio	0.97 (0.73-1.40)	1.72 (1.23-2.28)	**0.017**

Data are median (IQR), values are 10^2 x µmol/mmol of cholesterol. P-values are Mann Whitney U test.

P3.26 - Complications of the aortic conduit after intestinal transplantation with liver containing grafts - A single center experience

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Introduction

Complications originating from the aortic conduit after intestinal transplantation (ITx) are currently not well described in the literature. The aim of this study was therefore to report a single center experience with diagnosis and management of complications affecting the donor aortic conduit after ITx with liver containing grafts.

Methods

From 1998 to 2018, 35 ITx were performed in Gothenburg, Sweden. 29 of 35 grafts were liver containing intestinal allografts supplied by an aortic conduit (figure 1). The recipients were 24 adults (median age 38 years, range 16 – 66 years) and 5 children (median age 8 years, range 3– 10 years). The aortic conduit was anastomosed to either the aorta (n=20) or the iliac artery (n=9). The most common underlying conditions were intestinal failure (n=18) and non-resectable neuroendocrine pancreatic malignancies with liver metastases (n=6). Immunosuppression consisted primarily of ATG induction, tacrolimus and steroid bolus and tapering. Median donor age was 23 years (range 2-56 years) and median cold ischemic time was 443 min (range 90 - 873 min).

Results

Four patients (4 / 29, 14%) presented with some type of complication originating from the aortic conduit requiring intervention (figure 2). The complications were: stenosis at the origin of the superior mesenteric artery (SMA) branch (n=1), acute bleeding caused by bacterial and fungal arteritis of the conduit (n=1), stenosis of the conduit caused by kinking of the conduit close to the aortic anastomosis (n=1), inflammatory aneurysm of the donor conduit, affecting the origins of the coeliac trunk and the SMA (n=1). The complications were diagnosed from months up to several years after ITx.

Discussion

In our experience, complications affecting the donor aortic conduit after ITx may present in the early or late post-transplantation period. The insidious clinical presentation and the relatively high prevalence (14%) may warrant specific post-transplantation surveillance of the donor aortic conduit. A timely multidisciplinary therapeutic approach involving interventional radiology was crucial.

Figure 1. Donor aortic conduit anastomosed to the recipient aorta

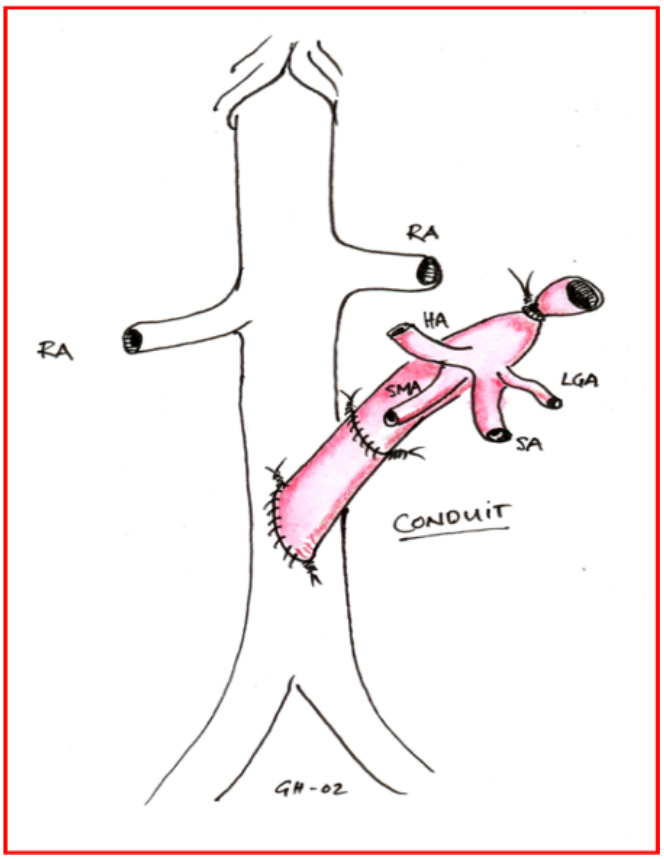

Figure 2. Complications affecting the donor conduit of 29 ITx with liver containing grafts

Age at Tx	Indication for ITx	Time to presentation	Main symptom	Type	Management	Outcome
5	IF	16 years	Postprandial abdominal pain	Stenosis SMA	IRx	Resolved but persistent pain
38	NEPT	2 months	Fever, hemorrhage	Bleeding due to arteritis in conduit	SR	Died
57	IF	3 months	Abdominal pain	Kinking of conduit	SR/IRx	Resolved
43	NEPT	5 years	Abdominal pain, fever	Inflammatory aneurysm conduit	SR/IRx	Resolved but persistent pain

Tx: transplantation, ITx: intestinal transplantation, SMA: superior mesenteric artery, IF: intestinal failure, NEPT: neuroendocrine pancreatic tumor, SR: surgical revision, IRx: interventional radiology

P3.27 - Gastric Acid Suppression May Lead to an Increased Risk of Vancomycin-Resistant Enterococcus Colonization

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Introduction: Gastric acid suppression therapy has been reported to change the gastrointestinal microbiome, resulting in increased gastrointestinal infections. This may be of increased importance in intestinal transplantation subjects as immunosuppressive agents are associated with peptic ulcers, leading to increased gastric acid suppression therapy. Also, immunosuppressive therapy leads to a higher risk of vancomycin-resistant enterococcus (VRE) colonization. However, the effect of gastric acid suppression therapy on vancomycin-resistant enterococcus (VRE) colonization has not been investigated.

Methods: Subjects who had surveillance rectal swabs for VRE at a university hospital were investigated. Surveillance was performed on subjects with prior hospitalization within 3months, history of VRE colonization / infection, or positive VRE findings from an adjacent patient. Gastric acid suppression therapy was defined as use of proton pump inhibitor or histamine-receptor-2 antagonists.

Results: Of 886 subjects who underwent VRE screening, 452 were included with 69 VRE positive and 383 VRE negative subjects. In univariable analysis, gastric acid suppression therapy, antibiotics use, male gender and prior hospitalization were significant risk factors for VRE colonization. Multivariable analysis showed that gastric acid suppression therapy (OR 2.873, 95% CI 1.473-5.605, P=0.002) and antibiotics use (OR 3.896, 95% CI 2.019-7.520, P<0.001) significantly increased VRE risk. Of antibiotics, carbapenems (OR 3.836, 95% CI 1.603-9.182, P=0.003) glycopeptides (OR 2.784, 95% CI 1.155-6.712, P=0.023), and cephalosporins (OR 2.210, 95% CI 1.213-4.025, P=0.010) were most significantly associated with VRE colonization. The unfavorable effect of gastric acid suppression therapy on VRE colonization was consistent, regardless of antibiotics type.

Conclusion: Gastric acid suppression therapy significantly increased VRE colonization risk. Gastric acid suppression should be administered according to strict guidelines. Physicians should be made aware of the increased VRE risk, and should consider VRE surveillance in those under long-term gastric suppression therapy.

P3.28 - The effect of a novel immunosuppressive drug, PQA-18, in rat small intestinal transplantation

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Introduction: PQA-18 (Prenylated quinolinecarboxylic acid compound 18) has been reported as a novel immunosuppressant that attenuates various cytokine productions, such as IL-2 & TNF-a, and differentiation of macrophages by inhibiting PAK2 inhibitor. In this study, we investigated this drug function mainly on macrophages using the rat small intestinal transplant model.

Methods: Male Dark Agouti (DA) (RT-1a) and Lewis (RT-1l) rats, 7 to 9 weeks old, were used as donor and recipient, respectively. An approximately 15 cm ileal grafts from the donor was heterotopically transplanted to the recipient rats. A Thirty-Vella loop was placed in the right abdominal flank. The recipient rat was treated with PQA-18 (4 mg / kg / per day) by intraperitoneal injection (ip) from postoperative day 1 (POD1) to two weeks. The control group, without PQA-18, was treated with just the same amount of Dimethyl sulfoxide (DMSO), the solvent for PQA-18. We firstly compared with graft survival of both groups. The rejection was manifested by progressive stoma coloring from ischemia and necrosis and the development of an abdominal mass, based on our previous study. Next, total cells from intestinal mesenteric lymph nodes (MLN) and graft Payer's patch (PP) were collected on POD6 and the number of macrophages was investigated using FACS cell analyzer.

Results: The graft survival was significantly prolonged by PQA-18 injection. While the survival time was 7.0 ± 0.77 days in the control group (n=9), the PQA group showed 10.7 ± 1.26 days' survival (n=10) (p<0.001).

The number of macrophages was also significantly reduced to 9.62 ± 1.22 % in MLN of the PQA group, while the number was 22.05 ± 2.00 % (p=0.004) in the control group. In addition, the number of infiltrated macrophages in PP was18.72 ± 2.33% in the control group, whereas the PQA-18 group indicated 6.55 ± 1.26% (p=0.007). The infiltration of macrophage was significantly suppressed in the PQA group.

Conclusion: PQA-18 significantly provided the prolongation of the graft survival in the rat small intestine transplantation model, together with the inhibited number of macrophages in the graft MLN & PP. It was suggested that PQA-18 has the suppressive effect not only on the differentiation but infiltration of macrophages. Further studies of the effect of this drug on macrophages are undergoing.

P3.29 - Ten years (or more) later, with or without the intestinal graft: present and future?

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Introduction: Intestinal transplantation (IT) remains a challenging procedure. The long term outcome, especially if the graft has been removed, is not well known. We report on clinical and pathological features with and without graft at 10 years or more after IT to discuss possible improvements.

Methods: Of 71 children transplanted between 1989 and 2007, 38 survived more than 10 years after IT: 26 with a functional graft, 9 on home parenteral nutrition (PN), 3 lost to follow-up. The median follow-up was 14.6 years, in our pediatric center, then in Beaujon Hospital for 21 patients. Long term biopsies were available for 21 patients. Data are medians.

Results: Indications of IT were: short bowel syndrome (34%), congenital enteropathy (34%), motility disorder (32%). Age at IT was 4.1 years and at last follow-up 20.1 years. Patient and graft survivals were 53% and 34%. The graft was removed in 12 (34%) for rejection; 5/12 patients were re-transplanted, 3 are well after 9.8-17.4 years follow-up. Five (14%) patients died, 2 transplanted (lymphoma, sepsis), 2 after re-transplantation, one on home PN (sepsis).

The 26 patients with graft were free of PN, 65% had liver-small bowel transplantation. Overall and fat absorptions were 91% and 89%. The height percentile (-0.5 SD) was higher than at IT. The measured renal clearance was 88 ml/min/1.73 m^2. Five patients (19%) had a lymphoproliferative syndrome, 42% a graft rejection more than one year post-IT, 42% had DSA (donor specific antibodies) without rejection. On biopsies they had a mild to moderate increase of mononuclear cells in the lamina propria, and of eosinophils for half of them. There was no sign of vascular rejection. 3/7 children had a school delay, 2/19 adults were unemployed, 8 (31%) had psychiatric disorders.

The graft had been removed in 9 patients: all were stable on home PN. On liver biopsy, 2/8 patients had fibrosis ≥ F3, 6 steatosis. Two received GLP-2 with decreased PN needs. 3/4 children had a school delay, 1/5 adults were unemployed, 5 patients (56%) had psychiatric disorders.

Conclusion: IT remains difficult but leads to digestive autonomy and catch-up growth without major complications of immunosuppression. The long-term pathology is reassuring despite the presence of DSA. The prognosis in case of graft removal is acceptable. Re-transplantation carries a significant mortality. Multidisciplinary care with early psychosocial follow-up is essential.

P3.30 - Clinical implications of mucosal eosinophilia in the long term intestinal transplant patient

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Introduction: A child, 6 years following isolated small bowel transplant (SBTx) for intestinal failure secondary to gastroschisis with impaired venous access, developed faltering growth associated with increased stool output. The gastrointestinal biopsies (GI) showed severe eosinophilia throughout the GI tract, affecting native as well as graft bowel. It is unclear whether mucosal eosinophilia is causative of gastrointestinal symptoms, a novel pattern of rejection, a feature of infection, or inconsequential.

Aim: Review the histology of patients who are greater than 5 years post SBTx to identify mucosal eosinophilia and correlate this with patient clinical course.

Population: 32 patients (18 boys) underwent annual GI biopsies. Indications for SBTx were short gut =20; motility disorder 10; microvillus inclusion disease =2. Ten had isolated bowel or modified multivisceral, whilst 22 had liver containing grafts.

Results: In total 327 biopsy reports were analysed ranging from 5 to 17 years following transplant. 153 /327 (47%) reported to have normal amounts of mucosal eosinophils; 121/327 (37%) moderate; 53/327 (16%) severe eosinophilia.

12 patients had no increase in eosinophils at any time; 10 had a moderate increase; 10 had a severe increase, of which 7 had severe eosinophilia confined to the oesophagus only which was diagnostic of eosinophilic oesophagitis (EO). Of the 3 with severe eosinophilia in other areas of the GI tract, 2 were at the time of late onset severe acute rejection and the other is the index case as described above.

As a proxy for graft function, 4/12 (33%) required enteral supplements in those with normal mucosal eosinophils; 60% with moderate; 60% with severe, of which 3 require PN.

Discussion: Eosinophils are increased in over 50% of biopsies. EO was an isolated finding in 22% of patients indicating a need for long term upper GI endoscopic surveillance. In those confined to EO, there is little impact on graft function. A moderate increase in eosinopils is associated with increased need for enteral supplementation. Eosinophilia is an important finding in late onset acute rejection.

Conclusion: Increased mucosal eosinophils may be associated with reduced graft function and the inflammatory reaction of late onset acute cellular rejection. Whether this is causative or secondary is unclear.

Longitudinal studies from the time of SBTx will ascertain whether early eosinophilic infiltrates have a bearing on subsequent transplant pathology.

P3.31 - Curcumin shifts the differentiation potential of intestinal stem cells toward the enterocyte lineage

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Introduction: Intestinal stem cell (ISC) is the fundamental unit for the regeneration of intestinal epithelium. Curcumin is a natural polyphenol extracted from the plant Curcuma longa. Curcumin has been found to have anti-inflammatory, anti-oxidation, as well as anti-cancer effects. In recent years, curcumin also was reported to regulate the activity of embryonic and mesenchymal stem cells. In this research we aimed to investigate the effects of curcumin on ISCs.

Methods: Purified curcumin was purchased from Sigma-Aldrich. Mice ISCs were isolated from B6 mice and subjected to organoid culture under the treatment of curcumin at different concentrations for 10 days. At the end of treatment, the images of organoids under each treatment group were photographed by microscopic cameras, and the organoid morphology, number, and area were further analyzed by ImageJ software. The ISC markers of proliferation and differentiation were analyzes by real-time PCR, and immuno-fluorescence staining.

Results: The average number of the organoids was 33, 47, 43, and 20 per well after the treatment of 0, 1, 5, and 25 μM of curcumin, respectively. The average size of organoid was significantly larger in the curcumin-treated groups (Figure 1). The ISC proliferation markers Lgr5 showed modest decrease after curcumin treatment: 0. 66- (1 μM), 0. 74- (5 μM), and 0. 56- (25 μM) fold compared with the control. Of the four differentiation markers, curcumin treatment resulted in significant increase of villin with 1. 87- (1 μM), 2. 19- (5 μM), and 12. 21- (25 μM) fold increase. Confocal imaging of anti-villin-stained organoids also demonstrated more abundant villin expression in the organoids under curcumin treatment (Figure 2).

Conclusion: ISCs treated by curcumin showed significant upregulation of villin, which represents the differentiation potential toward "enterocyte", which makes up the absorptive function of intestinal epithelium. The molecular mechanism of this effect and its clinical application is under investigation in the in vivo mice model.

Figure 1. Effect of curcumin on the formation of intestinal organoids.

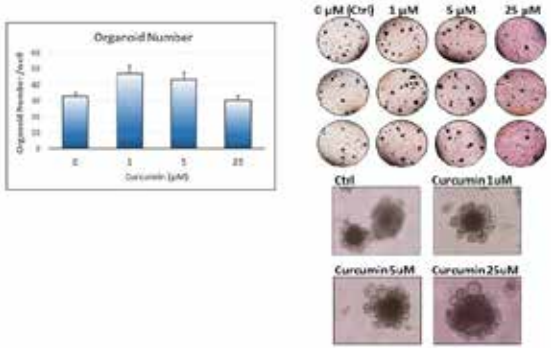
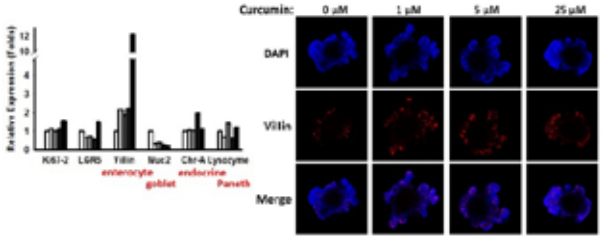


Figure 2. Effect of curcumin on the expression of ISC markers.



P3.32 - Safety and efficacy of standardized versus individualized parenteral nutrition mixtures in a pediatric home parenteral nutrition population

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Introduction: Current guidelines on pediatric Parenteral Nutrition (PN) conclude that standardized PN mixtures are not suitable for children with chronic Intestinal Failure (IF) on home PN. However, studies evaluating efficacy or safety of standardized PN are lacking. Possible advantages of standardized PN could be a reduction in costs and a longer shelf life of PN. Therefore, this study was designed to assess the effects on growth and safety of standardized PN compared to individualized PN.

Methods: Retrospective cohort study in Dutch children on home PN between June 2017 and July 2018, in which Individualized PN was compared to standardized PN. Growth was assessed by calculating the difference of Weight-for-age (WFA), Height-for-age (HFA) and weight for height (WFH) SD scores between date of inclusion and 6, 12 and 24 months prior to inclusion. Primary outcome was growth over 2 years, secondary outcomes were electrolyte disturbances and biochemical abnormalities such as liver function. Non parametric tests were used to explore differences between groups.

Results: 50 patients (50% female, median age 6.5 years) were included, of whom 16 (32%) received standardized PN mixtures. Age (11 vs 5 years), gestational age (GA) (39.2 vs 36.2 weeks) and PN duration (97 vs 39 months) were significantly higher in the group receiving standardized PN (p: ≤.001; .027; .013 respectively). Type of underlying disease did not differ between groups. For children receiving standardized PN mixtures, median weight gain in 2 years was significantly higher compared to the individualized PN mixtures group of children where a mean SD score decrease was seen (+0.38 SD score vs -0.55 SD score, p: .003). No significant differences were demonstrated in HFA SD score change, WFH SD score change (Table 1), or electrolyte disturbances (Table 2) between groups. Median total bilirubin was 6.0 μmol / L (5.0 – 13.0) in the standardized PN group and 5.0 μmol / L (4.0 – 9.0) in the individualized PN group (p: .473).

		Standardized	n	Individualized	n	p-value
Weight	6 months	.07 (-.01 – .30)	15	-.02 (-.28 – .63)	32	.592
	12 months	.16 (-.04 – .46)	15	-.19 (-.59 – .30)	25	.047
	24 months	.38 (-.34 – .80)	12	-.55 (-1.11 – -.07)	20	.003
Height	6 months	-.04 (-.09 – .22)	15	-.07 (-.33 – .23)	30	.700
	12 months	-.11 (-.28 – .53)	15	-.23 (-.39 – .14)	25	.410
	24 months	-.15 (-.65 – .39)	12	-.30 (-.86 – .35)	20	.580
Weight for Height	6 months	.12 (-.19 – .58)	15	.16 (-.34 – .73)	30	.819
	12 months	.10 (-.49 – 1.12)	15	-.19 (-.50 – .28)	25	.288
	24 months	.54 (-.50 – 1.52)	12	-.18 (-.99 – .50)	20	.071

Table 1. Median Change in SD Score over 6, 12 and 24 Months

All data are presented as median (interquartile range)
Mann-Whitney U test was used to determine p-value

	Standardized	Individualized	p-value
Sodium	0	0	-
Potassium	1 (6.3%)	3 (9.4%)	1.000
Calcium	0	3 (9.1%)	.542
Magnesium	1 (6.7%)	3 (10%)	1.000
Phosphorus	4 (25%)	9 (28.1%)	1.000
Chloride	2 (14.3%)	5 (16.7%)	1.000

Table 2. Number of Electrolyte Disturbances

Normal Laboratory Range: Sodium 135-145 mmol/L, Potassium 3.5-5 mmol/L, Calcium 2.15-2.75 mmol/L, Magnesium 0.68-0.88 mmol/L, Phosphorus 1.00-2.05 mmol/L, Chloride 98-107mmol/L
Fisher's exact test was used to determine p-value

Conclusion: In children receiving standardized PN mixtures, change in WFA SD score was significantly higher compared to children receiving individualized PN. Standardized PN mixtures are at least non-inferior to individualized PN mixtures in terms of electrolyte disturbances and biochemical abnormalities in a home PN cohort. Therefore, standardized PN mixtures can safely be administered to patients with chronic IF if the composition of this mixture meets the nutritional need of the patient.

P3.33 - Clinical outcomes of children weaned from parenteral nutrition after neonatal gastrointestinal surgery

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Introduction: The majority of children with intestinal failure due to short bowel syndrome (SBS) [dependence on parenteral nutrition (PN) for at least 90 days] are nowadays capable to be weaned from PN. Scarce evidences are available regarding the follow-up setting after intestinal adaptation. The aim of the study was to investigate the occurrence of morbidities after intestinal adaptation in children who underwent neonatal gastrointestinal (GI) surgery.

Methods: In our Home PN Centre we develop a multidisciplinary and long term follow-up to obtain a primary and secondary prevention of the unsuspected and life threatening complications after intestinal resection. Specifically, patients after intestinal adaptation enter in a follow-up program that includes dedicated staff in gastroenterology, nutrition, paediatrics, surgery, nephrology and radiology. Each patient underwent to a serial exams/clinical evaluations including stools assessment for steatorrhea and haematochezia, endoscopy, nutritional intake, urinary analysis, ultrasound and X-ray follow through of GI tract and Breath H2 test.

Results: We included in the analysis 47 children (27 males) with intestinal failure after neonatal GI surgery. The mean gestational age at birth was 32.8±5.1 weeks and the age at the last follow-up visit was: 7.8±5.8 years (0.6-24 years). Among all children 33 were weaned from PN dependence. Causes leading to SBS were: necrotizing enterocolitis (9/33), multiple bowel perforations (6/33), volvulus (5/33), intestinal aganglionosis (4/33), gastroschisis (2/33), intestinal atresia (7/33). The duration of PN of these children was 1.1±1.8 years (3 months-9 years). The length of small bowel residual was 51±39 cm (14-160 cm), 13/33 children had totally preserved the colon, whereas 16/33 had a partial residual colon. Among 33 infants weaned from PN, 42.4% developed morbidities during the follow-up period. Specifically, 3 children were identified as having anastomotic ulcers with clinical anemia, 3 children developed gallstones, 3 children developed kidney stones, 2 children had symptomatic D-lactic acidosis and 1 child developed acute pancreatitis and cholecystitis and 2 child developed venous trombosis. The occurrence of morbidities was found after 4.5±3.3 years (range 0.1-10.7 years) the weaning from PN.

Conclusions: This study suggest that the occurrence of morbidities after PN weaning is not a rare event. Therefore a multidisciplinary and long term follow-up is mandatory.

P3.34 - Inclusion of the pancreas as a part of the multivisceral allografts: A single center experience.

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Introduction: Intestinal transplantation provides a therapeutic option for patients with irreversible intestinal failure and complications of total parenteral nutrition. For technical reasons, the pancreas has been transplanted en bloc with the multivisceral allografts. Here, we report the advantages and complications related to the pancreas inclusion in the multivisceral (MV) and modified multivisceral (MMV) allografts.

Methods: Retrospective analysis of 64 recipients of MV and MMV allografts transplanted between 2013-2018 was performed at the Miami Transplant Institute. Pancreas was included in all of the 64 recipients. We recorded the pre-transplant history of diabetes, its type and treatment, and the development of new-onset diabetes post-transplant. Pre- and post-transplant acute pancreatitis was documented and recorded. Graft and patient survival due to pancreatitis was also recorded.

Results: The five recipients with pre-transplant history of diabetes (type 2 in four recipients, and type 1 in one recipient) demonstrated clinical cure from diabetes with no need for insulin or oral hypoglycemic drugs at 3, 6 and 12 post-transplant months. The incidence rate of post-transplant acute necrotizing pancreatitis in recipients with no prior history of acute pancreatitis was 3% (2 / 60) while none of the recipients with pre-transplant history of acute pancreatitis developed it post-transplant (0 / 4). Acute pancreatitis progressed to fatal necrotizing pancreatitis in 50% (1 / 2) of the recipients who developed post-transplant acute pancreatitis. No technical problems related to the pancreas were encountered.

Conclusion: Pancreas inclusion in MV and MMV allografts brought the cure for recipients with pre-transplant history of diabetes and those with a past history of acute pancreatitis, as well.

P3.35 - Quantitative dynamics of parenteral support in intestinal failure – importance of sodium for the recovery of body mass index

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Introduction: Intestinal failure (IF) is the inability to maintain protein-, energy- and / or fluid- and electrolyte balance because of reduced absorption with the necessity of parenteral support (PS). The ability to adapt is mainly determined by the functional anatomy (type-I: jejunostoma, type-II: jejunocolic anastomosis, type-III: jejuno-ileo-colonic anastomosis). We determined the dynamical changes of PS over time and as a result of reconstructive surgery or medication with Teduglutide.

Methods: Monocentric analysis of 56 patients with IF. Analysis of the relation of the PS-composition, anatomic type, surgery and Teduglutide to BMI over time (initially, time of max. support, last contact).

Results: 50 / 56 patients were followed for 869 ± 750 days (range 41 - 4011) with 8 ± 6 observation time points (mean interval 92 days) per patient. At the initial contact 27 patients had type-I-, 16 type-II-, 2 type-III-anatomy and 5 functional IF. During the observation period 4 type-I-patients were converted to type-II-anatomy and 7 to type-III-anatomy. At the initial contact type-I-patients received 2926 ml volume, 244 mmol Na and 24 kcal / kg per day and type-II-patients received 1515 ml volume, 107 mmol Na and 19 kcal / kg per day. At this time they were on PS for 1157 ± 1756 days (range 0 – 6202). Based on urinary Na and volume we increased PS volume, Na and energy: type-I patients: +277 ml / d, +2 kcal / kg / d, +65 mmol / d; type-II-patients: +284 ml / d, +3 kcal / kg / d, +45 mmol / d. Due to intestinal adaptation and / or surgery is was possible to reduce all three parameters significantly (type-I: -1982 ml / d, -17 kcal / kg / d, -192 mmol / d; type-II: -635 ml / d, -7 kcal / kg / d, -69 mmol / d). The BMI increased over time (type-I: +2,4; type-II: +1,9). In the exploratory analysis, increased sodium support was more strongly associated with increasing BMI than increased volume or energy support.

Conclusion: Significant dynamic adjustments were required during the course of IF. Initially often intensification of volume, Na and energy support was necessary even if these were already provided at high doses. Sufficient sodium support appears to have the strongest impact on the recovery of BMI. Spontaneous (or medically enhanced) adaptation as well as reconstructive surgery allow reductions and in some cases weaning of PS over time.

P3.36 - Burden of care for children after establishment of enteral autonomy following intestinal failure: a 12 month follow up study

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Introduction: The importance of a multidisciplinary team for intestinal rehabilitation in children with intestinal failure (IF) is accepted internationally and is a standard of care for patients managed by the New Zealand National Intestinal Failure Service (NZ NIFS). The aim of this study was to understand the ongoing burden of care for children with IF in NZ who achieved enteral autonomy as their primary outcome.

Methods: The NZ NIFS patient registry collected data for patients with IF as defined by the requirement for intravenous nutrition (IVN) for ≥ 21 days for paediatric patients up to 18 years of age and ≥ 30 days for preterm neonates (< 34 weeks gestation). Data were collected from October 2015 to October 2018.

Primary clinicians of patients with IF reported data in conjunction with NZ NIFS and information was obtained from patient records. Data collected included ethnicity, social deprivation index, cause of IF and clinical outcome. For patients that achieved enteral autonomy as their primary outcome and had at least 12 months follow up, further information was collected regarding feeding outcomes and multidisciplinary professionals involved in their care at 12 months after ceasing IVN. The number and indications for readmissions for this patient group over this 12 month period were also collected.

Results: Of 208 children with IF over a 3 year period, 128 (62%) patients achieved enteral autonomy and had 12 months follow up after ceasing IVN. Of this group, most common causes of IF were mechanical obstruction and short bowel syndrome.

At 12 months follow up, 117 (92%) children were having an age appropriate oral diet, including 27 (21%) also needing supplementary drinks, and/or enteral feeding in combination with their oral diet. One hundred and seven (84%) children required review by a paediatrician and 56 (44%) still required a surgeon. Community nurse input had continued for 61 (48%) of children and allied health services including dietitians 56 (44%) and speech and language therapists 42 (33%) were also required.

Twenty nine (23%) of the children were readmitted to hospital for reasons related to IF during this period.

Conclusion: The burden of care for children with IF does not end with enteral autonomy and this group of patients often require ongoing interventions and multidisciplinary input.

Table 1: Multidisciplinary professional input for NZ children with IF 12 months after they achieved enteral autonomy

Multidisciplinary professional	Number of patients (n = 128)
Paediatrician	107
Neonatologist	47
Surgeon	56
Gastroenterologist	19
Community nurse	61
Dietitian	56
Occupational therapist	31
Pharmacist	11
Physiotherapist	35
Psychologist	22
Speech and language therapist	42
Social worker	16
Unknown input	2

P3.37 - Luminal preservation of the intestinal graft: an update on the international multicentre study LUMINTRAL

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Introduction: Graft survival rates in intestinal transplantation (ITx) are the lowest among solid organ transplantation. Unique for ITx is the presence of metabolically-active luminal content consisting of microbes, dietary and waste products. Ischemic damage during cold storage decreases mucosal integrity, which contributes to graft rejection and infections. Cold storage of the bowel is limited to 10 hours, after which it is deemed unsuitable for transplantation. Luminal preservation (LP) with polyethylene glycol (PEG) has shown promising effects in improving graft-viability in experimental animal models. The ITx centres in The Netherlands and Belgium joined forces with the aim to analyse the effect of LP on graft viability.

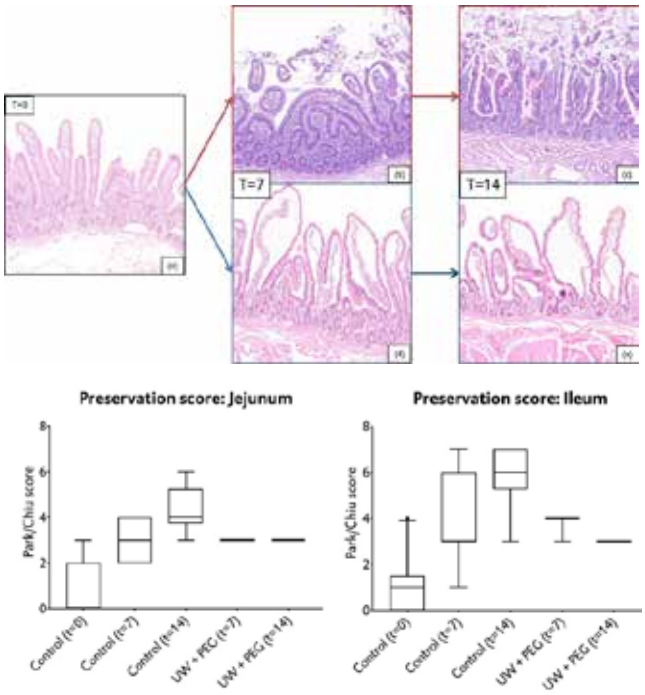
Methods: A prospective study was set up with 4 study groups:

1. Control: University of Wisconsin solution (UW) for vascular perfusion (VP) only
2. VP + LP: UW+PEG
3. Institut Georges Lopez-1 solution (IGL-1) for VP only
4. VP + LP: IGL-1+PEG

Inclusion criteria follows recommendations from the Organ Procurement and Transplantation Network for ITx, with extended age to 70 years (due to donor shortage) and no anthropomorphic features taken into account. Donors underwent standard dissection for organ procurement. If LP was included, the intestine was perfused with PEG (6.4% w/v) through the nasogastric tube. Samples were taken at 0, 7 and 14 hours after start of preservation. Analyses include histology (Park/Chiu preservation score), and further studies on gene and protein expression, and bacterial localisation and composition.

Results: So far, 9 bowels were included. In Dutch cases (N=7), 4 grafts received VP-only and 3 grafts received LP. In Belgium, 2 VP-only experiments were performed so far.

VP-only samples show decay of the intestinal microscopic structure over time with necrosis of villi tips and mucosal disintegration (Figure 1 a, b, c). LP samples show a conserved epithelial lining up to 14 hours of cold storage, with increasing signs of subepithelial oedema (Figure 1 a, d, e). Preservation scores reflect these findings (Figure 2).



Conclusion: These preliminary data suggest that LP with PEG reduces preservation injury in intestinal grafts. LP might thus improve graft viability and increase its preservation time-window. Different LP solutions are being tested and further analyses are underway to address barrier function and the cause of the subepithelial oedema.

P3.38 - Two decades of intestinal transplantation (ITx) in Leuven.

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Introduction: ITx was initiated at the University Hospitals Leuven in 2000 after preclinical animal studies. We report our long-term experience.

Methods: In 2000-2019 19 ITx were performed in 19 patients. Data were extracted from a prospectively maintained database. Kaplan-Meier was used for survival estimation.

Results: Median follow-up is 6yr 11mth (1yr-16yr). Median age was 40yr 5mth (2yr 9mth-56yr 8mth); male / female ratio was 9 / 10; peds / adult ratio was 4 / 15. Indications were complicated intestinal failure / disease not treatable by any other means and due to: ischemia (4), volvulus (4), splanchnic thrombosis (4), Crohn (2), chronic intestinal pseudo-obstruction (3), microvillus inclusion disease (1), Churg-Strauss (1). 9 were isolated ITx, 6 combined liver-ITx, and 4 MVTx. 4 received a kidney and 2 a colonic segment. 1 was a live-donor Tx. MVTx was done after visceral artery embolisation, dramatically reducing blood loss. The Leuven immunomodulatory protocol {Donor-specific blood transfusion, low Immunosuppression (IS), reduced periTx inflammation} promoting T-regs was used in 17 recipients. In total 2 severe grade 3 early Acute Rejections (AR) in 2 patients (10,5%) and 4 severe grade 3 late AR in 3 patients (15%) were seen. There was no graft loss to rejection except in the live-donor recipient in whom a transplantectomy was done 7 mths postTx. Renal failure was not seen except in 1 combined kidney Tx recipient. No patients developed PTLD. 4 died (2 aspergillus, 1 NSAID-induced graft ischemia, 1 sepsis). Of the 15 survivors, 13 are nutritionally independent. In 2, a transplantectomy was done (1 graft ischemia > protocol biopsy; 1 multiresistent CMV enteritis). The latter is listed for reTx. So far no proven chronic rejection / late immunological graft loss was seen. 1 / 10yr patient & graft survival are 90% / 84% & 84% / 77%. Costs of ITx (albeit >other organ Tx) become lower than TPN >2yrs. Launch of a comprehensive / multidisciplinary intestinal failure center has increased patient referral. 3 are awaiting ITx, 1 combined liver-ITx, and 4 MVTx.

Conclusion: Long-term outcome of ITx under low IS compares favorably with global data and other organ Tx. PreTx embolisation dramatically changed the nature of MVTx. Survival equal or superior to TPN, better quality-of-life, and cost-effectiveness support application of ITx earlier in the course of intestinal failure. With growing waiting list at our center, referral of suitable intestinal donors is critical.

P3.39 - Risk of post-transplant lymphoproliferative disorder (PTLD) with Epstein-Barr virus (EBV) serostatus in donor and recipient in intestinal and multivisceral transplant

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Introduction: Post-transplant lymphoproliferative disorder (PTLD) is one of the most serious complications that can develop after a transplant and rates are reported to be highest in intestinal and multivisceral transplants. This study looks at the risk of developing PTLD with different Epstein-Barr virus (EBV) serostatus in donor and recipient.

Methods: This is a retrospective observation study of case notes. Key data collected includes EBV status in the donor and recipient prior to transplant, time to development of PTLD, histology specimen reports and mortality outcomes.

Results: The intestinal and multivisceral transplant service at Addenbrooke's Hospital, Cambridge, UK transplanted 80 patients from 2000-2018. There were 12 cases which developed PTLD giving a rate of developing PTLD of 15% in our cohort and mortality of 16.7%. Histology was obtained in 11 cases with one case having an inaccessible lymph node but characteristic features of PTLD. The histology specimens showed 100% stained positive for EBV, whilst 66.7% were lymphomas and 33.3% were pre-lymphomas. The development of PTLD occurred within 3 months in 66% of cases, 3-6 months in 17% of cases, and 12-18 months in 17% of cases.

Information on donor and recipient EBV serostatus was available in 44 consecutive patients, which included 10 of the 12 cases of PTLD. 20 patients developed persistent EBV viraemia, and 10 of these patients developed PTLD, taking approximately 2 weeks to progress.

The risk of persistent EBV viraemia developing with different donor and recipient EBV serostatus and subsequent risk of developing PTLD is shown below in table 1.

Donor EBV serostatus	Recipient EBV serostatus	Rate of EBV viraemia	Risk of EBV viraemia developing into PTLD
Positive	Positive	14/34= 14.7%	5/14= 36%
Negative	Positive	2/4= 50%	1/2= 50%
Positive	Negative	4/6= 67%	4/4= 100%
Negative	Negative	0	0

Table 1

The risk of PTLD developing in groups with different donor and recipient EBV serostatus is shown below in table 2.

Donor EBV serostatus	Recipient EBV serostatus	Rate of PTLD	OR of developing PTLD
Positive	Positive	5/34= 14.7%	1.32
Negative	Positive	1/4= 25%	1.38
Positive	Negative	4/6=67%	5.55
Negative	Negative	0/1= 0%	0

Table 2

Conclusion: The key finding of this study is that when an EBV seronegative recipient receives and intestinal graft from an EBV seropositive donor, there is 67% risk of developing EBV viraemia and in this group 100% will develop PTLD. Furthermore, the two deaths directly attributable to PTLD occurred in this group, suggesting that primary infection has a more serious disease course. Taken together, this gives a strong argument for matching EBV serostatus, particularly for recipients who are EBV negative. In circumstances where this is not possible, for example a super-urgent listing due to graft failure or a highly sensitised recipient, a persistent EBV viraemia should be treated early and effectively to stop progression to PTLD.

P3.40 - Improving the care of pediatric intestinal failure in the public health care system through a public-private partnership: the Brazilian experience

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Introduction: In Brazil, the majority of the population relies on the public health care system (PHCS). Due to funding restrictions, PHCS has some limitations, as a large part of the budget must be designated to basic health needs, a priority condition in a developing country. In the last years, some initiatives were developed in order to mitigate this condition and improve public access to specialized health care, including the treatment of intestinal failure (IF).

Methods: A model of public-private partnership (PPP) was developed, involving the Federal Government (FG) and Hospital Sirio-Libanes (HSL), a private hospital considered a center of excellence. By this model, HSL is responsible for the development and management of specialized medical programs not available in the PHCS, in exchange for fiscal incentives.

Results: In 2009, a project named PROADI-SUS was initiated between the FG and HSL. This partnership was responsible for the development of a pediatric liver transplant program, which performed more than 1000 pediatric liver transplants, promoted research activity and diffusion of medical education to other centers. Due to the scarce of intestinal rehabilitation centers in Brazil, and the absence of a pediatric multivisceral transplant team, by the end of 2016 the same strategy was utilized to develop a program specialized in the treatment of IF in the PHCS. The program was instituted in a pediatric public hospital (Hospital Menino Jesus), and due to the complexity of IF patients, improvements were performed in several areas of the hospital, benefiting not only the IF patients, but the general population. Medical resources not available in the public hospital are obtained in the private hospital; transplants are performed in the private hospital and as soon as the patient is stable, the post-operative is followed by the same team in the public hospital. The intestinal rehabilitation center is now receiving patients from all over Brazil, and has started to teach and support other public hospitals in order to disseminate the treatment of intestinal failure through the country.

Conclusion: The association of a private center of excellence with the public system, through a PPP, promoted a significant improvement in the treatment of IF in the Brazilian PHCS. In the next years, the dissemination of the knowledge acquired with this PPP will permit the creation of new public intestinal rehabilitation centers, benefiting more patients of the public system.

P3.41 - Pharmacokinetics and Pharmacodynamics of Glucagon-like Peptide (GLP-2) Analogue Apraglutide (FE 203799) in Adult Healthy Volunteers: Results of a Phase I Trial

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Introduction: To investigate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of the novel synthetic peptide analog of glucagon-like peptide-2 (GLP-2) apraglutide (FE 203799) in male and female healthy volunteers following subcutaneous (SC) and intravenous (IV) injection.

Methods: A total of 40 subjects were randomized to receive a single ascending dose of either apraglutide or placebo (3:1 ratio) at doses of 2.8, 5.7, 11.4, 28.4, and 56 mg. The first cohort received the lowest dose level of apraglutide by SC injection. Subjects were enrolled into the next dose level cohort sequentially and received the next higher dose level after all subjects in the preceding dose level cohort had been assessed.

Results: Apraglutide was considered safe and well tolerated at all doses with no Serious Adverse Events (SAEs). No immunogenicity was observed. The dose comparisons performed indicated that peak concentrations and exposure were similar for most dose levels when both genders were pooled (Tukey-Kramer p-values >0.05). Dose proportionality analyses demonstrated C_{max} was less than dose proportional with a single ascending dose of apraglutide, whereas AUC0 t/Dose and AUC0-∞ showed no significant difference between dose levels. No gender effects were observed. The rate and exposure to apraglutide was proportional over the dose range when administered via SC injection. Following SC administration, dose-adjusted PK parameters showed dose-proportional kinetics and no accumulation. The half-life was approximately 30 hours. The single-dose administration of SC apraglutide was generally well tolerated. The AEs reported at 2.8 mg SC, 5.7 mg, and 56 mg dose levels were only mild in severity. Four (4) moderate AEs were reported for 11.4 mg and 28.4 mg dose levels and no severe AEs were reported. Increasing single doses of apraglutide did not affect heart rate or cardiac conduction and in the studied range of plasma concentration, up to approximately 1500 ng/mL, apraglutide did not have a clinically relevant effect on ECG parameters.

Conclusions: This study in healthy volunteers exposed to single ascending doses of apraglutide confirm a favorable safety profile. The long pharmacokinetic half-life of approximately 30 hours for apraglutide supports a dosing interval of one week or longer in clinical trials. Apraglutide is currently in Phase II development for patients with short bowel syndrome requiring parenteral support.

P3.42 - Acute dehydration and hypercalcemia in patients with total intestinal aganglionosis on long term parenteral nutrition

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Objectives and Study: Total intestinal aganglionosis (TIA) is the rarest and the most severe form of Hirschsprung´s disease. Patients are dependent on long term parenteral nutrition (LTPN) and at risk of dehydration episodes, acute renal failure and hypercalcemia. The objective of this study was to identify the risk factors for hypercalcemia in children with TIA on LTPN.

Methods: We retrospectively analysed the medical records of 16 patients with TIA divided into 2 groups, group A who presented at least one episode of acute dehydration and hypercalcemia and group B (no history of hypercalcemia). Calcium & phosphorus status were analysed in blood and urine, PTH, 25-OHD3 plasma levels, kidney function, PN intake of calcium, phosphorus and bone mineral density (BMD) using X-ray absorptiometry. Values were reported as mean +/- SD or median [IQR].

Results: Both groups were composed of 8 children. No difference were found on steady state between the 2 groups in terms of blood calcium, phosphorus, urea, creatinine and glomerular filtration rate. Urinary calcium divided by creatininuria of group A was lower than group B (0,64 ± 0,60 vs 1,80 ± 1,28; p=0,03). Group A patients received higher PN calcium intake (0,49 ± 0,05 vs 0,40 ± 0,07 mmol/kg/day; p=0,02). On steady state PTH in group A was lower than in group B (20,8 ± 15,3 vs 32,5 ± 41,5 ng/l; p= 0,03) within the normal ranges (normal: 10-50 ng/l). In group A average PTH (ng/l) before and after hypercalcemia was within the normal range while reduced during the dehydration episode (pre-hypercalcemia 24.2 ± 7.4 vs per-hypercalcemia 8.2 ± 4.7 vs post-hypercalcemia 23.9 ± 6.7). Median BMD lumbar spine z-score was -0,2 [0,7] in both group.

Conclusion: Patients who presented at least one episode of acute dehydration associated with hypercalcemia received higher PN calcium intake, although they were in line with ESPGHAN guidelines. On steady state the hypercalcemia group had a lower urinary calcium excretion rate than group B. Patients with TIA presents high stool output and are at risk of acute and chronic dehydration. These data underline the importance to assess carefully the calcium metabolism during the follow-up of patients on LTPN for TIA with high stoma output. To prevent hypercalcemia it's important to correct rapidly acute dehydration episodes and on long term to provide high water-electrolytes supplementation, to limit calcium intake and to monitor plasma and urinary calcium, 25-OHD3 and PTH.

P3.43 - Bloodstream infections in children following intestinal transplantation

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Background: Infection is the leading cause of death in small bowel and multivisceral organ transplantation. It has been reported that the incidence of blood stream infection (BSI) is higher in children compared to adults, reaching almost 80% in some centers. In the UK there is limited data describing the incidence, aetiology and outcome of BSI in children receiving small bowel and multivisceral organ transplant.

Methods: Retrospective review of patients undergoing small bowel and multivisceral transplants at a tertiary centre from 1993 until 2015.

Results: A total of 92 patients received isolated small bowel (n=30), liver-small bowel (n=49), liver, small bowel and pancreas (n=8), multivisceral (n=1) and modified multivisceral (n=4) transplants. Mean age at transplant was 4.3 years (range 7 months to 16 years). Bacteremia was observed in 58% (53/92) of patients (total of 103 episodes); eight patients had ≥3 episodes of BSI. Gram positive organisms were the most frequently isolated (73/103 episodes), with coagulase negative Staphylococci accounting for 63% of these cultures. Gram negatives and Candida were identified in 12% (12/103) and 5% (5/103) of episodes respectively. All Gram negative BSI occurred ≥150 days post-transplant, while 60% of infection caused by Staphylococcus aureus and Enterococcus was observed <150 days post-transplant. Overall survival was higher in those without culture confirmed bacteremia (54% vs.40%). Thirty day mortality post bacteremia was 6.8% in this cohort.

Discussion: In this retrospective case series 58% of patients suffered from at least one episode of bacteraemia, an incidence lower than that previously reported. Timing of BSI differed by aetiology, with Gram negative infections observed later than Gram positive infections. Overall survival was lower in those with BSI, compared to those without BSI.

Conclusion: Blood stream infections are common following intestinal transplantation and vigilance and prompt treatment may prevent mortality in children following intestinal transplantation

P3.44 - Sublingual tacrolimus use in intestinal transplant recipients

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Introduction: Therapeutic tacrolimus concentrations are essential to prevent rejection in intestinal transplant patients. Traditional administration of liquid tacrolimus via jejunal tube (JT) immediately post-transplant may require high doses and result in delays in achieving therapeutic concentrations, likely due to decreased enteral bioavailability. Tacrolimus may be administered via the sublingual (SL) route, with passive diffusion of drug across oral mucosa. Administration via the sublingual route avoids enteral metabolism and bypasses the liver first-pass effect, and may result in faster onset of action. There is a paucity of data regarding SL tacrolimus use in intestinal transplant patients.

Methods: This was a retrospective, single center review of adult intestinal or multivisceral transplant patients transplanted between 06/2017 and 12/2018 who were converted from JT to SL tacrolimus within the first 30 days after transplant due to subtherapeutic tacrolimus troughs (less than 20 ng/mL). Daily tacrolimus doses, routes, drug levels, and incidence of rejection were recorded.

Results: Sixteen patients met inclusion criteria: 12 intestine, 2 multivisceral, 1 intestine+ liver, and 1 intestine+ kidney. Subjects were initiated on JT tacrolimus immediately postoperatively, and were transitioned to SL tacrolimus at an average of 6 ± 3.4 days postoperatively. The mean daily JT dose was 12.2 ± 3.9 mg and the mean JT tacrolimus trough was 9.6 ± 5 .4 ng/mL prior to transition. After changing to SL, the mean daily SL dose was 10.4 mg ± 3.8 and the mean tacrolimus trough was 21.8 ± 3.8 ng/mL. Subjects reached therapeutic levels (greater than 20 ng/mL) 1.9 ± 0.8 days after transition and stayed on SL dosing 13.7 ± 8.1 days during the first month. The conversion ratio of JT to SL tacrolimus was 0.4 ± 0.3. No adverse effects as a result of administering the drug via the sublingual route were noted, and 2 patients were treated for rejection during the first month.

Conclusion: The use of sublingual tacrolimus allowed for rapid achievement of target tacrolimus troughs in intestinal transplant patients with the use of lower doses than jejunal tube tacrolimus administration, and may provide a viable option for immunosuppression immediately post-transplant. Limitations include the retrospective nature of the study, as well as conversion of doses prior to reaching steady state. Further prospective dose conversion studies in intestinal transplant patients are warranted.

P3.45 – Intestinal failure-associated liver disease (IFALD) in the SMOF era: what has changed?

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Introduction: IFALD is the most severe complication of intestinal failure (IF). Since 2009, we have used a composite lipid emulsion containing fish oil, medium chain triglycerides, olive oil and soybean oil (SMOF lipid) in our cohort of IF children. The aim of this study was to assess the hepatic profile of children with IF receiving this lipid emulsion.

Methods: This study was a retrospective review of the children followed in our center for intestinal failure from 2009 to 2019 who received at least two years of parenteral nutrition (PN) and SMOF lipid and who were still on home PN on January 2019. The data was collected from charts review, using the latest clinical, biological and radiological data available.

Results: One hundred and nine children were included. Of these, 60 (55%) were born after 2009 and received SMOF lipid exclusively. Most children (66%) were followed for short bowel syndrome (whom 17 had extensive Hirschsprung's disease), 25 (23%) for congenital enteropathy, and 13 (12%) for chronic intestinal pseudo-obstruction. They received PN a mean of 5.4 days/week with SMOF lipid 1.5 g/kg/day.

Sixty-six percent of patients had abnormal liver tests, 53% elevated ALT, 48% elevated GGT, 22% elevated bilirubin with 9 of them having elevated conjugated bilirubin; 29 patients had low PT and 20 had low platelets rate.

Ultrasound showed splenomegaly in 35 patients (32%). Only 8 patients (7%) had signs of cirrhosis or portal hypertension.

Forty-five children underwent liver biopsy, fibrosis was seen in 33, 5 had F4 or cirrhosis, 16 had steatosis. Thirteen patients had both fibrosis and steatosis.

In the meantime (2009-2019), 43 other children were followed in our HPN center for more than two years but left the program: 19 were weaned from PN, 5 died from non-digestive complications (sepsis, cancer), 15 were transferred to adult centers, 4 underwent liver- small bowel transplantation. Only one child – born in 2011 - showed a rapid progression to cholestasis and severe portal hypertension and received liver-intestine transplantation for life threatening IFALD.

Conclusion: After ten years of using SMOF, children with IF on long term parenteral nutrition rarely evolve to severe and life threatening IFALD. However, most patients still present with abnormal biologic profiles and steatosis/fibrosis on biopsies. Identifying predictive factors for IFALD should help in the prevention of IFALD and the management of these patients.

P3.46 - A Novel Pump Device for Recycling Gastrointestinal Fistula Losses: Design and Feasibility Study

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Introduction: Enterocutaneous fistulae are a common cause of intestinal failure, and may necessitate parenteral nutrition (PN) and prolonged hospitalisation. Refeeding of fistula losses back into the distal gut is known to be beneficial, however implementation has been limited because devices are not commonly available, and manual recycling is unpleasant and labour-intensive. We present a novel device designed to enable easy and efficient chyme recycling, and report data from a first-in-human feasibility study.

Methods: The novel device comprises a compact centrifugal pump that can be placed inside a standard stoma bag. The pump is connected to an intestinal feeding tube which is inserted into the distal fistula limb. The pump is activated across the stoma bag by magnetic coupling to a custom-designed hand-held driver unit, effecting intermittent bolus refeeding while avoiding contact with the stoma effluent. Five speed settings were included to handle different chyme viscosities. Nutritional, medical, psychological and human-use factors were evaluated in an initial feasibility study.

Results: Following benchtop validation, the device was tested in 10 patients (1 drop-out due to unrelated obstruction; median 31d; IQR 22-50d). Indications for inclusion were remediation of high-output fistula / stoma losses (n=7), dependency on PN (n=5), and gut rehabilitation prior to restoration of continuity (n=10). A range of chyme viscosities were successfully recycled with increasing efficiency over the course of the trial, due to iterative device improvements. Patients consumed low residue diets. Once established, chyme recycling was well-tolerated in all patients, using regular boluses of up to 200 ml per episode, performed as many times as needed per day. Patients experienced a variety of benefits including reduced net losses (>65% average volumes), PN cessaton (4/5 patients, including all patients employing the final device iteration), liver function improvement, electrolyte normalisation, and improved quality of life. Of 6 patients with continuity restored at the time of reporting, none experienced post-operative ileus.

Conclusions: A novel chyme recycling device was developed and feasibility confirmed in an initial study. The device is easy to use and demonstrates multiple potential benefits including weaning of PN, gut rehabilitation, improved surgical outcomes, and reduced costs of care in these complex patients. A larger efficacy trial is currently planned.

P3.47 - Multimodality Surgical Management of Patients with Global Gut Dysmotility: Techniques and Long-Term Outcome

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Introduction: Global gut dysmotility (GGD) is a severely disabling disorder with the potential to develop gut failure with impaired quality of life. With the lack of effective medical therapy and pacing technology, surgical management with different modalities including gut transplantation (GTx) has recently evolved as part of the multidisciplinary treatment approach for this orphan population.

Methods: Between August 2012 and January 2019, a total of 172 patients with the diagnosis of GGD were referred to Cleveland Clinic, Center of Gut Rehabilitation and Transplantation (CGRT). TPN dependence was documented in 116 (76%). Of those, 82 (71%) underwent rehabilitative surgery (RS) and/or GTx. The diagnosis was confirmed by exclusion of gastrointestinal mechanical obstruction with radiologic evidence of global dysmotility including capsule endoscopy and sitz marker methodology. Most patients were adult female (88%) with extensive psychiatric history in more than 50% of the cases. Previous management included pharmacologic therapy, gastric pacing, partial colon resection, and external venting.

Results: With the intent to treat or as a bridge to GTx, 62 (76%) underwent RS with completion colectomy and ileorectal anastomosis (n=47), pyloroplasty (n=27) and chimney ileostomy (n=40). GTx with liver-free (n=19) and liver-contained (n=1) allograft was performed in a total of 20 (24%). Of these transplant recipients, 7 (35%) failed RS at our institution. With a mean follow up of 32 + 15 months, 160 patients are currently alive with an overall survival rate of (93%). In those with TPN dependency, the survival rate was better after RS (94%) compared to GTx (80%). Restoration of oral tolerance with achievement of full nutritional autonomy was accomplished in 20 (32%) and 10 (63%) of the current survivors, respectively.

Conclusion: Gut Rehabilitative surgery and transplantation are effective treatment modalities for GGD patients. RS can be utilized as a long-term therapy or bridge for gut transplantation.

P3.48 - Body composition of pediatric patients with intestinal failure

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Introduction: Infants and children with intestinal failure (IF) are at risk of growth failure and altered body composition with increased fat and decreased lean mass compared to healthy children. Data from our cohort of patients with IF show normal growth on growth charts. However, body composition has not yet been assessed. The goal of the current study was to compare body composition of patients with IF treated by our program to healthy children using the United States National Health statistic database.

Methods: We conducted a retrospective cohort study of patients referred to our program between January 1st 2013 and July 15th 2018. For routine clinical monitoring, all patients with IF have annual Dual-energy x-ray absorptiometry (DXA) to assess bone mass. All patients with a DXA within the timeframe of the study and aged 8-18 years were included. Data related to demographics, residual bowel anatomy, nutritional support and growth anthropometrics were collected. Statistical analysis included means with SD for continuous variables and frequencies with percentages for categorical variables. Height, weight, fat, lean and bone mass were converted to their respective z-scores; regression analysis assessed predictors of body composition.

Results: Thirty-seven patients met inclusion criteria and a total of 68 DXA results were collected. The mean age at the time of the DXA was 10.7±2.2 years. Subjects demonstrated normal growth with weight and height z-scores of -0.67±0.99 and -0.7 ±1.3, respectively. Lean and fat mass z-scores were -1.61 ±1.09 and 0.24± 0.74. Z-score for total body less head (TBLH), bone mineral density (BMD) and bone mineral content (BMC) were -1.19 ±1.37, -0.9 ±1.08 and -0.86 ±1.29 in the lumbar spine (LS). Small bowel length predicted 38% of the change in BMD in the LS. Linear growth was the most important predictor of BMC in the TBLH. There was a positive relationship between weight z-scored and fat mass z-scores (p=0.01) and a trend towards increased fat mass with longer time on parenteral nutrition (PN) (p = 0.09).

Conclusions: The results suggest normal growth and body composition in our patients with IF. This suggests that patients with IF have potential to accomplish normal body composition during growth. Further research is needed in the younger age group as well as separating those on and off PN. It is also important to determine positive contributors to body composition to increase efficiency of care in this population.

P3.49 - GLP-2 therapy for patients with short gut syndrome and intestinal insufficiency: A single center experience with future considerations

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Introduction: The field of gut rehabilitation has recently evolved to restore nutritional autonomy without the need for home parenteral nutrition (PN) and subsequent transplantation.

Methods: A total of 35 short gut syndrome (SGS) patients received glucagon-like peptide-2 (GLP-2) and were followed from April 2013 through February 2019 in the Cleveland Clinic-Center for Gut Rehabilitation and Transplantation. Of these, 34 were adults with a mean age of 53.4 ± 12.6 years (range: 14-72) and a female to male ratio of 2.5:1. Thirty-two (91%) of the 35 patients, were PN-dependent and 3 required IV fluid with micronutrient replacement. Leading causes of SGS were vascular occlusion (n=11), inflammatory bowel disease (n=10) and secondary motility disorders (n=5). Autologous gut reconstruction was performed in 32 of the patients (20 at our center and 12 at other institutions) with a mean small bowel length of 88.8 ± 56cm (range 10-220cm). Intestinal lengthening utilizing serial transverse enteroplasty (STEP) was performed in 11 patients. The retained colon was partial in 31 (88.6%) patients and full with intact ileocecal valve in the remaining 4 (11.4%). The duration of GLP-2 therapy ranged from 2 to 63 months with an average dose of 0.32mL / d.

Results: With a mean follow up of 34 ± 19 months, 33 patients (94.3%) are currently alive and 2 died of PN-related liver failure and advanced systemic arteriosclerosis. Full nutritional autonomy was achievable in 18 (54.5%) of the 33 current survivors with an overall success rate of 54.5%. Of these 18 patients, 14 (78%) continued to sustain the restored nutritional autonomy for 1 to 48 months after discontinuation of GLP-2 therapy. Meanwhile, a reduction in PN and IV fluid requirements was observed in 19 patients who failed to restore (n=15) or sustain (n=4) nutritional autonomy. None of the patients developed significant complications that warranted permanent discontinuation of GLP-2 therapy. There were no documentation of recurrent or de novo malignancy except in one adult patient who developed prostate cancer.

Conclusion: GLP-2 is an effective therapy for patients with SGS-associated intestinal insufficiency. This novel treatment should be more frequently utilized as a primary therapy or as an adjunct to autologous reconstruction and bowel lengthening. In addition, such a biologic agent should considered as an innovative approach to enhance the recovery and function of rejected intestinal allografts.

P3.50 - Portal hypertensive surgery for management of diffuse portomesenteric venous thrombosis - Surgical technique and long-term outcome

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Introduction: Patients with diffuse portomesenteric venous thrombosis (PMVT) are often referred to the abdominal organ transplant centers particularly those with experience in gut transplantation. Despite the proven therapeutic efficacy of multivisceral transplantation (MVTx) for these complex patients, the forgotten different modalities of portal hypertensive surgery could be a better alternative particularly for those with compensated liver disease and gut varices in the milieu of a thrombophilic state.

Methods: Between Aug2012 and Jan2019, a total of 28 patients referred to our center with diffuse PMVT underwent surgical intervention. Indication was history of variceal bleeding and occult varices in the setting of thrombophilia. All except 1 were adults with a mean age of 42±15 yrs. Precipitating causes of PMVT were thrombophilia (78%) and pancreatitis (18%). All patients had clinical, endoscopic and radiologic evidence of PMVT with stigmata of extra-hepatic portal hypertension. Variceal bleeding was reported in 36% patients. Type of shunt was determined intra-operative suitable visceral vascular anatomy and transplantation dictated by co-existence of advanced liver disease.

Results: Portal hypertensive surgery was performed in 27 patients (96%) while MVTx was performed in one. The surgical modality was atypical non-selective portosystemic shunt in 14 patients (52%) and gastro-esophageal devascularization in the remaining 13 (48%). Partial gastric devascularization was commonly performed in patients with atypical shunt that may not completely decompress the left portal hypertensive compartment. Splenectomy was unavoidable in 4 patients. The utilization of autologous and synthetic vascular grafts are shown in Table 1.

Table 1: Use of native veins and prosthetic grafts as portosystemic surgical shunts

Type of shunt used	Native vein	PTFE graft
No. of patients	11 (78.5%)	3 (21.5%)
Type of vein used (n)	1. Coronary vein (1) 2. Cadaveric vein graft (1) 3. Gastroepiploic vein (1) 4. Jejunal branch (2) 5. Adrenal vein (2) 6. Perisplenic collateral (1) 7. Gonadal vein (2) 8. Portal hilar collateral (1)	1. Corono-caval (1) 2. Mesocaval (1) 3. Portal hilar collateral to cava (1)
Complications (Clavien): Minor (grade 1 - 2) Major (grade 3 - 4)	 7 (63%) 2 (18%)	 1 (33%) 2 (67%)
Mean follow up (months)	26	40
Recurrence of GI bleed	1/11 (9%)	0%
Shunt patency	9 (82%)	2 (67%)

With a mean follow up of 40±26 months, overall shunt patency was radiologically documented in 78% patients. Recurrence of bleed occurred in only 1 patient (7%) despite shunt patency. Throughout the follow up period, surgical complications were minor (grade I & II) in 64% patients and major (grade III & IV) in 21% [Clavien grade]. With one mortality due to acute leukemia, all patients are currently alive with an overall survival rate of 96%.

Conclusion: Portal hypertensive surgery is a viable alternative to MVTx for the management of diffuse PMVT and preserved hepatic function. Portal decompressive surgery should always be considered for thrombophilic patients with silent gut varices who are in need of life-long anticoagulation therapy.

P3.51 - Sensitivity of differential time to positivity compared to pour plates for diagnosing catheter-related bloodstream infection: an evaluation in patients with chronic intestinal failure

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Background: Clinical findings are unreliable for establishing the diagnosis of central venous catheter-related bloodstream infection (CRBSI) because of their poor sensitivity and specificity. Therefore, in order to establish a diagnosis of CRBSI, when this is clinically suspected and the central venous catheter (CVC) is to be preserved, ESPEN recommend that paired quantitative blood cultures (pour plates) or paired qualitative blood cultures from a peripheral vein and from the catheter are recommended, with continuous monitoring of the differential time to positivity (DTP). However, it is unclear whether quantitative or qualitative cultures provide the optimal method for diagnosing CRBSI in patients with intestinal failure (IF). A retrospective evaluation was undertaken in intestinal failure patients with long term CVCs to evaluate DTP against pour plates for the diagnosis of CRBSI.

Methods: A list of patients with a diagnosis of CRBSI was obtained from the intestinal failure (IF) unit database for a five year period, 2013 to 2017. Microbiology records were reviewed to obtain further information about blood culture and pour plate examinations. Organisms and times of collection, loading and positivity were recorded. Patients with a contemporaneous set of central and peripheral pour plates and blood cultures were included in an analysis of the sensitivity of DTP compared to pour plates.

Results: There were 61 (45.5%) episodes in 56 patients where complete sets of central and peripheral blood cultures and pour plates were received. All 61 episodes had positive central blood cultures, 59 (96.7%) had positive central line pour plates and 17 (27.9%) had positive peripheral pour plates. Using pour plates as the gold standard, DTP sensitivity was 96.0% for 50 episodes where pour plates were consistent with CRBSI. The sensitivity increased to 100% for 17 episodes where there were no delays in either collection or loading of blood cultures.

Conclusions: This is the first evaluation to support the use of DTP as a sensitive test in diagnosing CRBSI in IF patients and provides confidence to IF centres where pour plate cultures are not available. DTP can be used as a primary diagnostic test for CRBSI in patients with IF; however, in order for this to be of maximum value to clinicians, time to positivity needs to be routinely reported with blood culture results.

P3.52 - The Use Of Alemtuzumab As Immunosuppressive Induction In Intestinal Transplantation Among Pediatric Population

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Purpose: Many different pre-conditioning immunosuppression protocols have been reported to improve outcomes of patient and graft survival in intestinal transplantation(IT). The use of Alemtuzumab as an immunosuppressant inducer is not well studied in pediatric IT. Our aim is to analyze its impact on immunological complications among this population, comparing different protocols used in our center.

M&M: A retrospective study of immunosuppresion protocols in pediatric(<18yrs) IT was conducted. 103 IT (55multivisceral, 25intestinal, 22hepatointestinal, 3modified multivisceral) were performed in 84patients (male predominance-60%-,mean age 5.3yrs) between Oct1999-Oct2018.

Mean time on the waiting list was 272days and waiting list mortality was25%. Main indications for the transplant on the first instance were short bowel sd.(69%), motility disorders(12%) and epithelial diseases(9.5%). The colon was included routinely from2012. Native spleen was preserved in 22/55(40%) of multivisceral grafts.

Immunossupression evolved over time in different stages, so we divided patients in 4 groups according to pre-conditioning regime (I-Basiliximab(n=13), II-Thymoglobulin(n=17), III-Basiliximab(n=56) and IV-Alemtuzumab(n=17)). Manteinance was performed in all cases with FK and steroids and also with Azathioprine in group I. Nowadays we use Alemtuzumab for patients >4yrs and retransplantation of any age and Basiliximab for the rest.

Results: Groups with highest and lowest acute rejection rates were group II(65%) and IV(12%) respectively($p<0.05$). The latter presented the highest rates of PTLD(29%) and haematological disorders(35%). Despite this, it is the group with the lowest loss of grafts(45%).

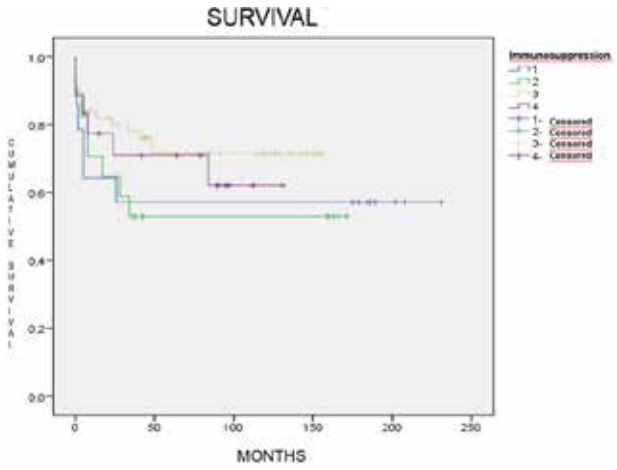
Only 2cases of humoral rejection were observed in the whole series in group I and group IV, respectively. Regarding chronic rejection, 3cases in group I(23%) and 3cases in group III(5%) were observed. There were no cases of GVHD among patients in group I but 1case in group II(6%), 10in group III(18%) and 3in IV(18%) were registered.

Finally, 35/84(42%) patients died during follow-up and survival percentages between 53%(group II) and 73%(group III) were recorded.

Conclusions: Alemtuzumab appears to be effective in pediatric IT patients with high immunological risk or retransplanted due to its low rates of acute and chronic rejection; however, further studies are needed to conclude its safety in pediatrics and the impact on PTLD, GVHD and hematological disorders compared to other therapies.

COMPARATIVE ANALYSIS ACCORDING TO IMMUNOSUPPRESSIVE PROTOCOL

n=103	Protocol I (n=13)	Protocol II (n=17)	Protocol III (n=56)	Protocol IV (n=17)	p
Acute rejection	3 (23,1%)	11 (64,7%)	17 (30,4%)	2 (11,8%)	0,005
Chronic rejection	2 (15,4%)	0 (0%)	3 (5,4%)	0 (0%)	0,180
Humoral rejection	0 (0%)	0 (0%)	0 (0%)	1 (5,9%)	0,164
GVHD	0 (0%)	1 (5,9%)	10 (17,9%)	3 (17,6%)	0,260
PTLD	3 (23,1%)	3 (17,6%)	7 (12,5%)	5 (29,4%)	0,41
Haematological disorders	1 (7,7%)	1 (5,9%)	9 (16,1%)	6 (35,3%)	0,09



P3.53 - Do patients with gastroschisis have worst outcomes after pediatric intestinal transplantation?

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Introduction: Gastroschisis (Gx) is the leading cause of short gut syndrome in our intestinal rehabilitation population and the principal reason for intestinal transplantation (ITx). We investigated the results after ITx in this group of children and compared them to those with other etiologies.

Methods: A retrospective review of all ITx performed at our center was done. Eighteen ITx were done in 18 children between 2004-2018. Outcome data was collected for both surgical and non-surgical factors, and analyzed. Chi-square and independent t-test were used for statistical analysis. $p<0.05$ was considered significant. The study was approved by our Institutional Review Board (IRB #2019-2474).

Results: Eighteen patients underwent ITx. The most common diagnosis leading to ITx was Gx (7/18, 39%). Other causes included midgut volvulus (3), necrotizing enterocolitis (2), Hirschsprung's disease (2), motility disorders (2) and other causes (2). Boys predominated in both groups (4/7 Gx vs. 6/11 in all others, p=0.91). Mean age at listing was similar (3.4±5.1 in Gx vs. 3.1±2.7 years in all others, p=0.70). The mean time on the waitlist prior to ITx was also similar in both groups (1.4±1.5 vs. 0.9±1.2 years, p=0.41). Both groups were transplanted at a similar age (5.3±4.7 vs. 4.0±3.2 years, p=0.5). One of 7 patients in the Gx group underwent multivisceral transplant compared to 2/11 in the all others group (p=0.83). Initial feeds were started later after the transplant in the Gx group (48.9 ±72.9 vs. 18.6±13.4 days, p=0.24) and mean post-operative hospital stay was also longer in the Gx group (112.9±165.5 vs. 78.7±53.9 days, p=0.53). However, a significantly greater proportion of Gx patients (6/7, 86%) were discharged on full enteral feeds compared to the patients in the all other group (4/11, 36%), p=0.04. Overall patient and graft survival in the entire cohort at 1 year was 89% and 83% respectively. 1-year patient survival was similar in either group: Gx 6/7 (86%) vs 10/11 (91%) in all others (p=0.73). 1-year graft survival was also equal in both groups: 5/7 (71%) in the Gx group vs 10/11 (91%) in all others (p=0.28).

Conclusions: Outcomes after pediatric ITx appear satisfactory and similar regardless of the underlying diagnosis and represents a viable alternative to long-term parenteral nutrition. Gastroschisis patients appear to have longer lengths of stay after ITx, but also appear to achieve a more complete recovery in terms of independence from parenteral nutrition.

P3.54 - Grafted colon in intestinal transplantation: does it make a difference in the outcome of the patients?

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Introduction: To include the colon as part of an intestinal or multivisceral graft is still a matter of debate. While some groups consider that it might be important for water absorption and residue breakdown without posing risks to patients, others state that its inclusion could result in an increase in infectious complications. Our aim was to analyze if the presence of the grafted colon in our patients has meant differences in their outcome.

Methods: Retrospective review of our historical series of intestinal and multivisceral transplants comparing patients that received a colon as part of the graft to those that didn't. A total of 107 patients received an intestinal or multivisceral graft between 1999-2018. Main indications were short gut syndromes (60 patients, 56.1%), motility disorders (16 patients, 15%) and untreatable diarrheas (14 patients, 13.1%). It was used a graft without colon in 61 [group no colon (33 M, 28 F)] and with colon in 46 [group colon (27 M, 19 F)]. We compared the appearance of complications (such as rejection or infections) and survival curves adjusted by treatment protocol. A p-value below 0.05 was considered statistically significant.

Results: Average ages and weights at transplant were similar in both groups, with 67.5 months (6-361) and 17.2 Kg (4-52.7) in patients without a grafted colon and 64 months (6-216) and 16 Kg (3-59.2) in patients with colon. One hundred and two patients had a small bowel stoma. Timing of stoma take-down was similar in no colon group compared to colon group, with a median of 9.5 (1-125) months and 8 (1-50) months respectively. Rates of acute and chronic rejection were similar in both groups (39% / 10% no colon vs 35% / 4% colon). Rates of GVHD (15% no colon vs 15% colon) and PTLD (20% no colon vs 13% colon) were also similar. Median of septic episodes was 2 in both [no colon (0-8), colon (0-6)]. Among the multiple infectious agents analyzed, only clostridium showed a statistically significant higher rate of infection in colon group (2% no colon vs 15% colon). Patient and graft survival, adjusted by immunosuppression protocols, did not show differences.

Conclusion: Colon inclusion as part of the intestinal graft does not produce a higher rejection, GVHD or PTLD rates, nor a survival decrease. Even though the infection rate is also similar, there are differences in the infectious agents between the groups.

P3.55 - Allointestine colon conduit urinary diversion in combined intestine and kidney transplant : A case report

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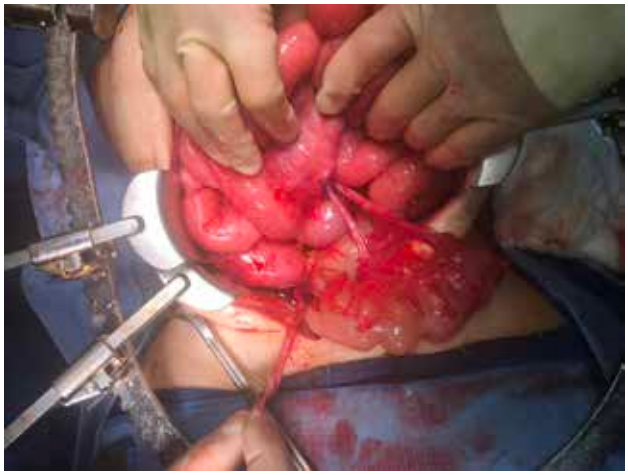
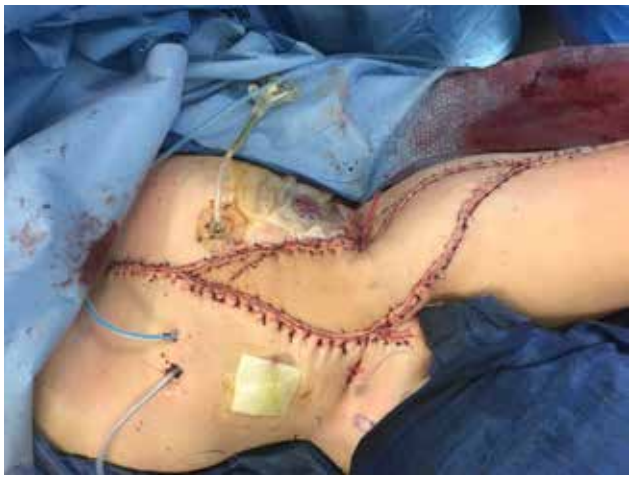
Introduction: In intestinal transplant candidates, the incidence of renal failure is high and is associated with increased mortality. Additionally previous surgeries and loss of abdominal domain may make standard kidney transplant with ureterocystostomy impossible. .

Methods: We present an extreme case of combined small intestine, colon, and kidney transplant in a patient with short gut syndrome due to radiation enteritis, severe loss of abdominal domain, failed previous kidney transplant, and absence of native urinary system.

Results: Our patient is a forty years old female with a past history of bladder Rabdomyosarcoma as an infant, who underwent bladder resection and post resection radiation. She developed radiation enteritis, renal failure, and eventually received a living related kidney transplant. Her renal allograft subsequently failed due to multiple urinary obstructions despite multiple revision surgeries, as well as chronic immunosuppression toxicity. As a result, she had short gut syndrome and renal failure with no feasible route of urinary drainage. In addition, she had severe loss of abdominal domain due to abnormal abdominal development from the radiation she received as an infant. She had multiple complications of her short gut syndrome and she underwent a simultaneous small intestine, colon, and kidney transplant. Donor was an eight years old female (132 cm, 23.4 kg), who became brain dead after severe exacerbation of asthma attack. Since there were no viable routes for urinary drainage, as there were no viable native intestines, and native and previous transplanted kidney ureter had been obstructed, a 10 cm allograft colon segment was used as a urinary conduit. The patient also underwent a complex abdominal closure with pedicled left anterior lateral thigh perforator flap by the plastic surgery team. One hundred days post transplant the patient is parenteral nutritional independent with normal renal function and her transplant colon conduit is healthy and functional.





Conclusion: In extreme cases of kidney transplant in intestinal transplant recipient patients with no feasible urinary drainage path, transplant intestine can successfully be used as a conduit. In review of literature, and to the best of our knowledge, this is the first description of utilization of allograft intestine as a urinary conduit.

P3.56 - Lower incidence of catheter related bloodstream infections (CRBSI) in children with short bowel syndrome(SBS) on parenteral nutrition(PN) treatment at home when compared to other aetiologies of IF

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Great Ormond Street Hospital for Children NHS Foundation Trust

Introduction: Currently the best outcome for chronic intestinal failure (IF) is achieved by discharging children home after parent / carer(s) have undergone a formal training programme to connect and disconnect PN infusions from the child's central venous catheter (CVC). Catheter related bloodstream infections (CRBSI) are the most common potentially life-threatening complication. The aim of this study was to prospectively compare the incidence of CRBSI in short bowel syndrome (SBS) with IF related to other aetiologies in children at home with care by parent(s).

Methods: A prospective record was kept of blood culture results from all children managed by our IF rehabilitation service over a 4-year period from January 2015-January 2019. CRBSI was diagnosed when a child presented with significant fever and/or other symptoms suggestive of septicaemia and blood culture from the central venous catheter (CVC) was positive (in the absence of other focus of infection). The total number of children on long-term PN at home, the number with short bowel syndrome (SBS) and the number of CRBSI in each group were calculated.

Results: A total of 67 children(31 male, 36 female) aged from 6 months to 18 years were treated with PN at home. Eighteen cases had SBS (aetiology: volvulus in 7, necrotising enterocolitis in 6, gastroschisis in 2, long segment Hirschprungs in 2 and congenital in 1) . Ten were male and 8 female and aged from 6 months – 18 years. Other children were diagnosed with motility disorder in 27, primary mucosal disease in 14 and IF secondary to a haematological/immunology disorders in 8 cases. There were a total of 38,606 line days with 16,197 line days in SBS and 22409 with other conditions. There were a total of 112 CRBSIs giving an overall infection rate of 2.95/1000 line days. Sixteen infections were in children with SBS, giving an infection rate of 0.98 infections/1000 line days. Non-SBS children had 96 infections in 22409 line days, an infection rate of 4.2/1000 line days. There was a significant difference in infection rate between those with and without SBS $p<0.00001$.

Conclusion: Children with SBS had a significantly lower incidence of CRBSI than those with IF due to other aetiologies. Factors related to the underlying disease may contribute to the rate of CRBSI. Further studies are needed comparing disease groups in children.

P3.57 - Evidence of liver tolerance to severe hyperacute rejection in a pioneer model of multivisceral xenotransplantation.

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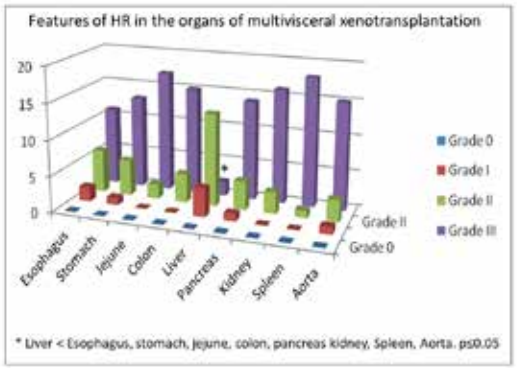
Xenotransplantation would be a solution for organs scarcity for transplantation however hyperacute rejection (HR) impair the this therapeutic method. We have described a model of discordant multivisceral xenotransplantation to assess the features of HR in various organs (1-3). Here we compare HR in the liver with the other organs of multivisceral xenograft. Method– After general anesthesia, multivisceral grafts containing esophagus, stomach, small intestine, colon, liver, pancreas, spleen and kidneys were recovery with a vascular pedicle containing the aorta with celiac axis and superior mesenteric artery and vena cava containing the hepatic veins were recovery from rabbits and implanted heterotopically in swine by aorta-aorta and cava-cava anastomosis (n=19). Multivisceral allotransplantation using rabbit-to-rabbit (n=5) composed the negative control group for HR. Three hours after graft reperfusion we sacrificed the animals and collected organs samples for histological study and IgG assessment by immunofluorescence. Features of HR were semi-quantitative graded in (0=normal, I=mild (edema, vascular congestion, and clumping of platelets in the microcirculation), II=moderate (diffuse edema, presence of some fibrin thrombi, intense vascular congestion, epithelial dysplasia, and foci of hemorrhage) and III=severe (presence of fibrin thrombi in all vessels, extensive interstitial edema, diffuse interstitial hemorrhage and confluent necrosis). T Student was used to compare HR in all organs from xenografts. Results – All animals were alive and well at the experimental end. The occurrence of HR was macroscopically noted in xenograft in 15 minutes. The autopsy revealed HR in all organs from multivisceral xenograft; however, we observed less severe HR in liver compared with esophagus, stomach, small intestine, colon, pancreas, spleen and kidneys (figure 1). IgG fixation was strong in in xenografts and absent in allografts. The occurrence of HR was absent in all allografts. Conclusion –Heterotopic discordant multivisceral xenotransplantation is a relevant tool to study HR. IgG fixation by immunofluorescence was strong in the sites of HR. Therefore, we show for the first time that the liver is more tolerant to HR after multivisceral xenotransplantation than the other abdominal organs.



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P3.58 - Modified Spiral Intestinal Lengthening and Tailoring for Short Bowel Syndrome

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Background: The spiral intestinal lengthening and tailoring (SILT) procedure is a new surgical technique for autologous intestinal reconstruction in patients with short bowel syndrome. The aim of this work is to present a first description of a modified SILT technique by which the mucosal layer is left intact to possibly reduce the severe postoperative complications of intestinal leakage and abdominal abscess formation.

Materials and methods: The modified SILT technique was performed on a 10-cm-long intestinal segment in 2 pigs to determine the technical feasibility. Thereafter, the short-term clinical feasibility was monitored clinically in 2 dogs by gastrointestinal X-ray series at postoperative day 4 and by relaparotomy postoperative day 10.

Results: It was technically feasible to lengthen the intestinal segment from 10 cm to 20 cm and tailoring it from 3 cm to 1.7 cm in diameter, while leaving the intestinal mucosal layer intact. The postoperative course was uneventful for both dogs. The gastrointestinal X-ray series showed an inconspicuous intestinal transit time without any signs of stricture, perforation, or leakage. In the relaparotomy, the initially achieved lengthening and tailoring extents were preserved and the operated intestinal segment was well perfused with no early signs of necrosis, stenosis, or leakage.

Conclusions: Leaving the mucosal layer intact during SILT is technically and clinically feasible in the short term in a large animal model. Further studies are needed to fully assess the impact of this technical modification on the long-term outcome of larger series.

P3.59 - Surgical rehabilitation of pediatric chronic intestinal failure, long term results and change of paradigms at a single center

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Introduction: Autologous gastrointestinal tract reconstruction surgery (AGIRS) and serial transverse enteroplasty (STEPS) are worldwide accepted strategies for children and adults aiming to achieve intestinal rehabilitation. The aim of this study is to show a series of children with intestinal failure (IF) that underwent surgical rehabilitation at a single center and their outcomes.

Material and methods: This is a retrospective review of a prospectively filled database, from March 2006 to December 2018, including every patient <18 years of age with chronic IF that was referred to this program and underwent abdominal surgery with the aim of intestinal rehabilitation. Demographic data, diagnosis, type of surgery, intestinal anatomy (type 1 -terminal jejunostomy-; type 2 -jejuno colonic anastomosis-; type 3 -jejuno ileo colonic anastomosis-; subtypes A < 40 cm and B > 40 cm) and PN independence are analyzed.

Results: From a total number of 102 Pediatric patients (pts) referred with IF, 18 underwent rehabilitation surgery; 17 of them are followed at our center and were included in the analysis. Type of surgery performed was: STEP (6); AGIRS (11). The mean time of follow up after surgery is 65 months (sd ± 49.6). A total of 8 pts gained enteral autonomy after surgery, in a mean time of 12.3 months (sd ± 7), additionally 2 pts reached enteral autonomy on hormonal therapy (teduglutide), initiated 63 and 129 months respectively after surgery (table 1).

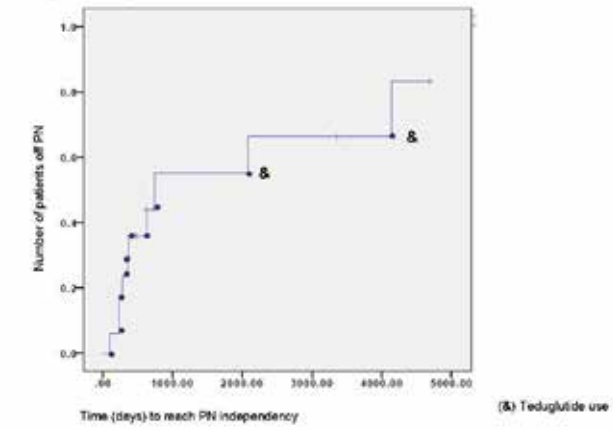
Table 1. Patients grouped according to PN dependency after surgery

	INTESTINAL SUFFICIENCY (N=10)	PN DEPENDENCY (N=7)
Diagnosis	IA 4; NEC 1; GASTROS 2; HIRSCH1; THROMBOSIS 1; VOLV 1	NEC 2; IA 2; GASTROS 2; VOLV 1
Neonatal IF ¶	8	6
Premature ¶	4 (mean GE* 34 weeks)	3 (mean GE* 35 weeks)
Length of remnant SB** #	35.5 cm (± 21.3)	23.7 cm (± 17.9)
ICV*** present ¶	3	2
Total Colon present ¶	3	3
Anatomy type 1	4	3
2A /2B	3/0	2/1
3A /3B	3/0	1/0
Teduglutide use (&)¶	2	0
AGIRS/STEP ¶	7(1&)/3(1&)	4/3

*GE gestational age; **SB small bowel; ***ICV ileo-cecal valve.
IA intestinal atresia; GASTROS gastroschisis; HIRSCH hirschprung; VOLV volvulus; NEC nectrotizing enterocolitis.
¶ ns
 # p 0.01

Seven pts continued on PN; from those, 2 pts underwent intestinal transplant due to loss of venous accesses, 1 pt died on the intestinal transplant waiting list due to liver failure and 4 pts remain PN dependent with no indication of transplantation (2 are in the process of starting teduglutide treatment). At the end of the studied period, the Kaplan Meier freedom from PN survival is 83.2% (graphic 1).

Graphic 1: Kaplan Meier freedom from PN survival



Conclusions: Surgical rehabilitation should be considered as the first strategy to achieve intestinal autonomy; the indication for STEP or AGIRS should be done in the context of a multidisciplinary team. The only variable analyzed that showed statistical significance for surgical rehabilitation was residual small bowel length. The introduction of hormonal therapy provides an additional benefit, limiting the need for transplantation.

P3.60 - Native spleen preservation attenuate graft versus host disease in an experimental model of modified multivisceral transplantation.

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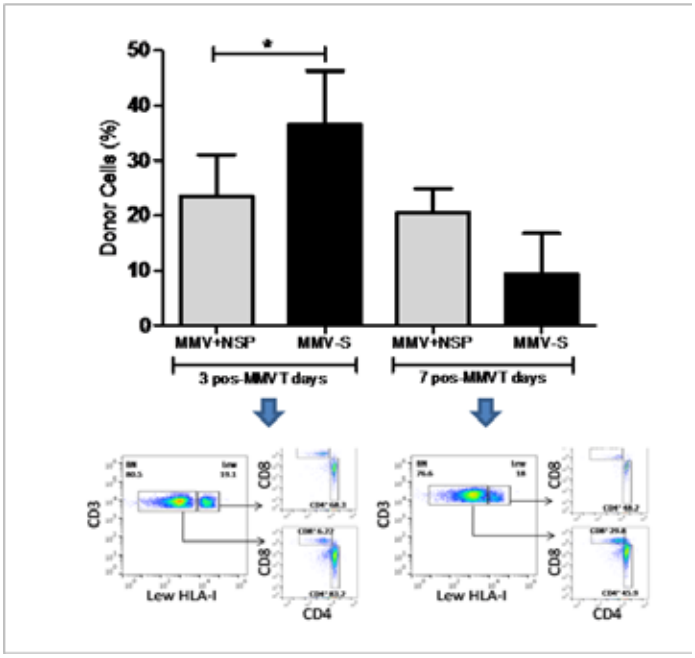

Introduction: Native spleen used to be removed in patients undergoing modified multivisceral transplantation (MMVT) increasing the risk of sepsis and graft-versus-host disease (GVHD). The mechanistic basis of these effects including mixed chimerism level is poorly understood. Based on a novel experimental procedure of MMVT that triggers GVHD, we aimed to evaluate the effects of native spleen preservation in this model in order to gain insight into the mechanisms that may mediate this phenomenon.

Material and Methods: Heterotopic MMVT from Lewis to Brown Norway rats was performed. MMVT graft consisted of stomach, duodenum, pancreas, spleen and the small bowel of the donor. The native spleen was removed (MMVT-S) in half of the MMVT recipients J(N=5), while the remaining preserved their own spleen (MMVT+NSP) (N=5). After MMVT mixed hematopoietic chimerism was determined in native spleen and peripheral blood samples by flow cytometry using strain-specific HLA antibodies. Also, histopathological (using Pintar score) and clinical signs of GVHD such as skin rash were evaluated.

Results: all animals in the group MMVT-S presented clinical signs of GVHD such as skin rash, weight loss, and diarrhea, among others, between 7-10 days after transplantation. Skin rash was particularly remarkable in the ears and periocular area. Clinical signs of GVHD were less frequent in MMVT+NSP recipients (40%; $p<0.05$). Also, significant differences between groups were observed in the histopathological study and mixed chimerism in peripheral blood 3 days after MMVT (36.6 and 23.62 % in MMVT-S and MMVT+NSP respectively) (Figure 1). Also, native spleen showed an 18±5 % of chimerism (CD3+ donor cells) 1 week after transplantation. After day 10 post-MMVT, when the signs of transient GVHD disappeared, both groups presented graft rejection.

Conclusions: Native spleen preservation in MMVT recipients attenuated the occurrence of GVHD and reduced the level of chimerism compared to recipients that underwent spleen removal during MMVT. Despite more studies are necessary, our preliminary results suggest that native spleen preservation increase the efficacy in removal of anti-recipient reactive clones that would explain the protective effect of native spleen preservation against GVHD.

POSTERS PRESENTED ON SATURDAY JULY 6, 2019

P4.01 - Reduction of central line associated bloodstream infections and line occlusions in pediatric intestinal failure patients on long-term parenteral nutrition using an alternate locking solution, Kitelock

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Background: Patients with intestinal failure (IF) are dependent on parenteral nutrition (PN) for growth and survival, however are at high risk of central line associated bloodstream infections (CLABSI) and line complications, resulting in significant morbidity and mortality. 70% ethanol locks have been used for the treatment and prevention of CLABSI with success but reported issues relate to product availability and catheter patency. KiteLock 4%, an EDTA solution, is an effective non-antibiotic antimicrobial, anti-biofilm and anticoagulant agent shown to significantly eradicate clinically relevant microorganisms by 87% within central venous access devices. Adult studies have demonstrated efficacy of EDTA in CLABSI reduction, however there remains a deficit of pediatric data. Our objective was to determine Kitelock efficacy in the prevention of CLABSIs and reduction in line occlusions in pediatric IF patients on long-term PN.

Methods: We conducted a retrospective cohort study of patients managed by IF programs at 2 tertiary Canadian pediatric centres between April 1, 2016 to December 31, 2018 who received Kitelock. Data was collected for 12 months prior to and following initiation of Kitelock. CLABSIs, line replacements and use of alteplase (per 1000 catheter days) before and after initiation of KiteLock were compared using a Wilcoxon matched-pairs signed-ranks test. Data was reported as medians (interquartile ranges) and frequencies (proportions).

Results: Twenty patients (10 girls; median age 83 months [range, 8-232 months]) began KiteLockâ for recurrent infections or sluggish / occluded line. The rate of CLABSI prior to starting KiteLock was 2.7(0-4.0) per 1000 catheter days. Patients received KiteLock for a median of 365 (278-365) days with no infections in the 12 months following commencement of KiteLockâ (p=0.002). Median rates of occlusive episodes for the entire cohort prior to starting KiteLock were 0 (0-5.0) in the 12 months prior to starting KiteLock and 0 (0-2.0) after starting therapy (p=0.018). In patients with occlusions (n=9), the median rate of alteplase use prior to starting Kitelock was 5.5 episodes (2.7-19.2) compared to 2.7 episodes (0-2.7) (p=0.018)

Conclusions: Results demonstrate a significant decrease in CLABSI with KiteLock and a reduction in catheter occlusions. Our preliminary findings suggest KiteLock is effective in reducing CLABSI and catheter occlusions in pediatric patients with long-term central access requirements.

P4.02 - Micronutrient levels in intestinal failure patients dependent on parenteral nutrition at home over a 5-year period

Sunita Amar Rajani, Raquel Núñez-Ramos, Sarah Macdonald, Venetia Simchowitz, Jutta Koeglmeier, Susan Hill

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Introduction: To analyse longitudinal changes in micronutrient blood levels in all patients already established for >12 months on parenteral nutrition (PN) treatment in our home intestinal failure (IF) rehabilitation service.

Methods: Laboratory reports of blood micronutrient levels and concurrent CRP levels in children with IF established on PN >12 months prior to 2013 were reviewed in 2013, 2015 and 2017. Peditrace ® or additrace® supplement was routinely included in PN and doses adjusted according to blood levels with additional enteral supplements if appropriate. Results were categorised as deficient (> 10% below normal range) or normal, based on mean of 2 values (one value only for vitamin D) obtained over 6-months in each time period, 2013, 2015 and 2017. The study was approved as an audit. Two tailed Fisher's exact test was used to calculate p values.

Results: 30 patients(16 male) diagnosed with motility disorders in 12(40%), short bowel syndrome (SBS) in 7(23%), mucosal disorders in 11(37%). Five children weaned off PN, 2 transitioned to adult care and 1 died(due to underlying disease). IV lipids including vitlipid ® were added to PN 2 or 3 nights / week in 27, four nights in 2 and not given to one child. Please see results table for levels obtained in each time period (samples not obtained if patient no longer on PN or blood sample insufficient for analysis). There was a similar incidence of each micronutrient deficiency in the different diagnoses.

Micronutrient	Number(%) normal values /total patient number measured 2013	Number(%) normal values /total patient number measured 2015	Number(%) normal values /total patient number measured 2017	P value comparing 2013 with 2017
Copper	16/30 (53.3)	23/30 (76.6)	19/22*(86.3)	**0.017 significant**
Zinc	27/30 (90)	28/30 (93.3)	21/22*(95.4)	0.6
Selenium	24/30 (80)	27/30 (90)	19/22*(86.3)	0.7
Vitamin A	17/30 (56.6)	22/26*(84.6)	20/23*(86.9)	**0.033 significant**
Vitamin E	30/30 (100)	25/26*(96.1)	22/23*(95.6)	0.444
Vitamin D	26/30 (86.6)	23/28*(82.1)	16/22*(72.72)	0.29
Iron	11 /14*(78.5)	9 /15*(60)	8/13*(61.53)	0.41
Ferritin	26/30 (86.6)	20/26*(76.9)	19/23*(82.6)	1.0
Number of patients with no deficiency	5/30 (16.6)	7/30 (23.3)	7/22* (31.8)	0.31

*<30 patients as patients no longer on PN or results not available due to insufficient sample

Table showing prevalence of micronutrient deficiencies in long term home PN patients

Conclusions: The majority of children with chronic IF on home PN had some micronutrient deficiencies with increasing incidence of normal levels with time. Two or 3 nights / week appeared sufficient for maintaining fat soluble vitamin levels. There were significantly less cases of low copper and vitamin A levels with time. Our results emphasise the importance of routine monitoring of micronutrients and the need to prescribe home PN according to individual requirements.

peditrace® commercially available preparation of micronutrients

additrace® commercially available preparation of micronutrients

vitlipid® commercially available preparation of lipids

P4.03 - The role of parenteral nutrition in children after bone marrow transplantation

Sunita Amar Rajani, James Evans, Dominika Gayda-Pimlott, Duncan Cartner, Paul Veys, Jutta Köglmeier

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Background:

The first successful bone marrow transplant (BMT) in a child was carried out in 1968. Since then it has become an established therapy for a variety of childhood conditions including malignancies not responding to chemotherapy or radiation, congenital immunodeficiencies and haemoglobinopathies. Complications are common and include graft versus host disease (GVHD), graft failure or rejection, veno occlusive disease and malnutrition. Parenteral nutrition (PN) is used for gut sterilisation in the conditioning phase and offered to children with severe mucositis and GVHD of the gut following transplant and as part of the standard protocol for cord transplant.

Methods:

Patients undergoing BMT in a large nationally commissioned referral centre were identified from the patient data base between January 2014 and May 2018. Underlying pathology, date and type of BMT, number, age, sex and outcome of children requiring PN for less or more than 28 days and those referred for home PN were recorded.

Results:

254 (152 males and 102 females) children underwent a BMT during the study period, 64 patients received PN for less than 28 days of which 9 died. PN was required for more than 28 days in 125 of which 41 died. 15 children were discharged on home PN. The indications were chronic GVHD in 9 and colitis or enteropathy in 6.Four children passed away during this period; one from line sepsis and one each due to pulmonary hypertension, lung GVHD and intracranial relapse of leukaemia. 5 children were successfully weaned off intravenous nutrition and 6 remain on home PN.

Conclusion:

The majority of children undergoing BMT requires PN. Long term PN > 28 days is common and a small percentage of patients will need home PN. Although home PN improves the overall outcome the mortality rate amongst those patients is high.

P4.04 - The Surgical Management Of Acute Bowel Ischemia In Elderly Patients In Order To Avoid Short Bowel Syndrome : A Multicenter Study

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INTRODUCTION: This is a multicenter study performed in two Italian tertiary care centers: Emergency General Surgery Unit at St. Orsola University Teaching Hospital-Bologna and Department of Surgical Sciences at Umberto I University Teaching Hospital-Rome. The aim was to compare the results of different approaches among patients with acute bowel ischemia over 65 years of age.

METHODS: Sixty-three patients were divided in two groups: 1) VSgroup- 28 patients treated at Department of Surgical Sciences and 2) GEgroup- 35 patients treated in Emergency General Surgery Unit. Mean age was 80 years, significantly higher for the GEgroup ($p<0.001$). Gender was predominantly female in both groups, without statistical difference. Pre-operatively, laboratory tests didn't show any difference in white blood cell count, serum lactate levels or serum creatinine among patients, while increase of c-reactive protein was observed in VSgroup with significant difference ($p<0.001$). The main cause of acute bowel ischemia was embolism in VSgroup ($p=0.03$) and vascular spasm in GEgroup ($p<0.001$). On CT scan, bowel loop dilation was present in 58.7 % of patients without statistical difference in both groups.

RESULTS: The time lapse from diagnosis to operation didn't show significant differences between two groups (mean 349.4 min). Pre-operative heparin therapy was administered in VSgroup more frequently ($p< 0.001$). In VSgroup, thrombectomy was the most frequent procedure (19 patients) associated with bowel resection in 9 cases. In GEgroup, 22 patients had an explorative laparotomy ($p<0.001$) , 8 had a bowel resection with anastomosis and 5 a bowel resection plus stoma. A second look was required more significantly in VSgroup ($p<0.001$). Post-operative morbidity affected significantly GEgroup ($p=0.02$). The 3-day survival was significantly higher in the VSgroup ($p< 0.001$). At discharge 32 patients (50.8%) were alive, 21 in VSgroup ($p< 0.001$). Only one patient among both groups (1.6%) had a short bowel syndrome.

CONCLUSIONS: In elderly patients with acute bowel ischemia, surgery should be always pursued whenever the interventional radiology is not assessed as a viable option. Both groups of patients showed an excellent outcome in terms of avoiding a short bowel syndrome. A multidisciplinary management by a dedicated team could offer the best results to prevent large intestinal resections.

P4.05 - Rice based post-operative diet (Japanese diet) after intestinal transplant

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Introduction: Nutritional management after intestinal transplant is very important part of transplant, but post-operative diets vary depending on countries because they are based on cultural background. Rice based diet (so called Japanese food) is usually used after post-operative treatment in Japan. We introduced rice based post-operative diet and assess its safety and efficiency.

Methods: Patients who received isolated intestinal transplant in our institution were reviewed. All patients received rice based post-operative diet after intestinal transplant. Tacrolimus based immunosuppressions were administrated intravenously then orally. Diet starting date, advancing, parental nutrition off and outcome were assessed.

Results: Three patients were received rice based diet after intestinal transplant. Age at transplant was median 17 year olds. (Ranged 14 year olds to 32 year olds) Original diseases were congenital microvillous atrophy, Hirschsprung's allied disease and short gut syndrome. Types of donor were living donor (n=1) and cadaveric donor (n=2). Induction therapies were Daclizumab (n=1) and rabbit anti thymus globulin (n=2). Everolimus was added at one month after intestinal transplant for two patients. Intestinal graft length was median 160cm (150-260cm). Two patients had enteral feeding tube. All patients started rice based post-operative diet as rice gruel (Omoyu) at post-operative day (POD) 26 (ranged POD 7 to POD49) orally. Diet was advanced to rice gruel in three degree (rice: water=1:20), five degree (rice: water=1:10) and regular (rice: water=1:5). Diet reached regular gruel at mean POD 45 (ranged POD18 to POD87). Side dish started later avoiding protein oral intake. Patients are free from parental nutrition at median POD119 (ranged POD 22 to 209). Longer graft tend to leave parental nutrition early. Parental nutrition could be terminate with regular diet for patient with long graft. All patients survived longer than 3 months. There was no complication according to race based post-operative diet.

Conclusion: Rice based post-operative diet after intestinal transplant was safe after intestinal transplant. Rice based post-operative diet had great advantages its form and less protein. Softness of gruel were easily controlled with rice water ratio. Polished rice has less protein. The contents of side dish were need to be further evaluation.

P4.06 - Combined multivisceral and renal transplant in a patient with JAK-2 mutation

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Duke University Hospital

43 y.o. male with JAK-2 mutation developed cirrhosis due to Budd-Chiari syndrome and had extensive portal and mesenteric vein thrombosis that precluded a liver transplant alone. His liver disease was complicated by refractory ascites, encephalopathy, severe muscle wasting and MELD-Na of 36. In addition, he developed hepatorenal syndrome and hemodialysis was initiated. Despite lack of intestinal failure, the patient required a multivisceral graft for anatomical reasons of lack of ability to restore portal inflow to the liver graft.

Multivisceral transplant (MVT) including liver, pancreas, stomach, intestine and partial colon was performed followed by kidney transplant the following day. Despite preoperative partial arterial embolization of the native superior mesenteric and splenic arteries, he required massive transfusion of 47 units PRBC's due to incomplete embolization and severe portal hypertension. The patient received Thymoglobulin induction and has been on triple drug immunosuppression (tacrolimus, mycophenolate mofetil, prednisone).

Thrombophilia was managed with IV heparin perioperatively and enoxaparin was started postoperatiely. This was associated with gastrointestinal bleed from the gastrojejunal anastomosis during the first postoperative week. The heparin dose reduction during the period of GI bleed was associated with the development of non-occlusive thrombi in both internal jugular veins. In addition, he was treated with hydroxyurea for thrombocytosis, subsequently plateletpheresis and anagralide when platelet count reached >1.4 million. By the time of discharge, the patient was on full enteral nutrition and had normal renal function.

This case highlights the indication of MVT for patients with hypercoaguable states and extensive portomesenteric thrombosis. In this patient, his hypercoaguable state was more extensive than many due to involvement of his hepatic veins leading to Budd Chiari syndrome. The cause of his hypercoaguable state was known to be a JAK-2 mutation, although the cause is not always identifiable. Perioperative anticoagulation with standard medications prevented thrombotic complications, however thrombocytosis developed (likely from splenectomy) and was not controlled by hydroxyurea and required the use of plateletpheresis and anagralide. Our plan will be for life-long anticoagulation and we anticipate switching from enoxaparin to apixaban after discontinuation of protocol monthly bowel biopsies and ostomy closure.

P4.07 - Does our current dietetic input meet the long term needs of our post transplant patient population?

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Introduction

As a super-regional centre with patients from all over the UK frequent face to face contact is not feasible, therefore telephone or email dietetic consultations are necessary. Current dietetic review practice is to personally see patients at their annual review and outpatient appointments to provide assessment of nutritional parameters, intake and matching this to need. Telephone consultations are more ad hoc but are amenable to be standardised so to provide a robust dietetic follow up. We therefore report on current practise and recommendations for future standards of care.

Aim

To review our current practise of dietetic input and provide recommendations for future standards of care.

Methods

Dietetic notes of all patients who have a small bowel containing graft throughout 2018 who are cared for at Birmingham Children's Hospital, were retrospectively reviewed to identify all patient contact during the study year. We then looked at the intensity of nutritional support and dietetic needs. Of note, some patients will also have local dietetic intervention.

Results

32 patients were under review throughout 2018. Table 1 shows the dietetic input required and table 2 the median number of reviews each group received. As expected the patients requiring the most intense dietetic intervention have received the most input. It is vital however to consider individual patient need as some patients on less intense intervention required more frequent review demonstrated in the range of patient contacts. 6 patients also had local dietetic input.

Table 1. Baseline characteristics of all children receiving follow up at Birmingham Children's Hospital post isolated small bowel or combined small bowel transplant

Demographics	
Patients	32
Age [1]	12.7 (5.2-19.9)
Years since transplant [1]	8.5 (0.8-16.7)
Boys/girls	19/13
Isolated bowel Tx/liver and bowel Tx	9/23
Type of nutritional support required	
Combined parenteral and enteral	3 (13%) 2 had short term episodes
Enteral via a feeding tube	15 (45%)
Oral nutritional supplements	3 (9%)
Diet	11 (33%)

[1] Information at 31st December 2018

Table 2. Frequency (contacts/year) of dietetic review for all patients under follow up at Birmingham Children's hospital in 2018 post isolated small bowel or combined small bowel transplant.

Combined parenteral and enteral	4.5 (2-8)
Enteral via a feeding tube	3 (0-11)
Oral nutritional supplements	2 (1-3)
Diet	1 (0-5)

Conclusion

Dietetic input into small bowel graft patients in imperative. Rationalisation of resources means that those at high risk or high supplemental needs should be prioritised and a standard of care developed.

We propose the following standard:-

- Develop care pathway for each group highlighting frequency of follow up and method to escalate concerns to consultant.
- Written information for families regarding review process to ensure early reporting of concerns.
- Referral to local Dietitian where appropriate.
- Telephone proforma to ensure consistency.

P4.08 - Clinical And Histologic Characteristics Of Intestinal Failure Associated Liver Disease In Pediatric Patient Population

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Introduction: Our aim was to assess clinical and histologic characteristics of intestinal failure associated liver disease (IFALD) in children.

Methods: This was a retrospective single center study. In total, 89 consecutive children with intestinal failure (IF) and liver biopsy obtained between years 2006-2018 were included. Liver biopsies were analyzed for histology with simultaneous measurements of serum liver biochemistry, citrulline, spleen size and cholelithiasis (ultrasound, n=86). Presence of esophageal varices was based on gastroscopy (n=70). Fisher's exact and Mann Whitney U test were used for comparisons.

Results: Median patient age was 3.1 years (IQR 0.6-9.3), age-adjusted small bowel length was 26% (17-48%) and 49 patients were currently receiving PN at the time of liver biopsy. The causes of IF included short bowel syndrome (SBS, n=67), primary motility disorders (n=20) and enteropathies (n=2). Significant histologic liver fibrosis (Metavir stage ≥2), cholestasis, portal inflammation and steatosis was observed in 36%, 29%, 26% and 31% of patients. Any degree of cholestasis (49% vs 5%), portal inflammation (43% vs 5%) and fibrosis (65% vs 38%) were more frequent during PN (P<0.05 for all), whereas steatosis (30% vs 29%, P=NS) and significant fibrosis were equally common after weaning off PN (Table). Splenomegaly was observed in seven (8%) and esophageal varices in one (1.4%) patient, mostly during PN delivery. Cholelithiasis was observed in six (7%) patients. Presence of significant liver fibrosis associated with short remaining small intestine, prolonged PN, missing ileocecal region and elevated ALT (Table). One patient died of IFALD and one with associated extrahepatic portal vein occlusion underwent liver transplantation after weaning off PN.

Conclusion: Cholestasis and portal inflammation are nearly exclusively associated with PN delivery, whereas significant fibrosis and steatosis frequently persist after weaning off PN. Splenomegaly and esophageal varices were infrequent complications of pediatric IFALD. Although IFALD was uncommon cause of death or liver replacement therapy, long-term significance of persisting fibrosis and steatosis needs to be resolved.

Table. Comparison according to the presence of significant liver fibrosis

Variable	Metavir <2 (n=57)	Metavir ≥2 (n=32)	P-value
Currently on PN, n (%)	28 (49)	21 (66)	0.183
Duration of PN (mo)	7.0 (2.9-15)	15 (5.4-45)	**0.012**
SBS as cause of IF, n (%)	41 (72)	26 (81)	0.311
Age adjusted small bowel length (%)	29 (21-50)	23 (16-34)	**0.016**
Ileocecal valve (ICV) preserved, n (%)	32 (56)	10 (31)	**0.029**
Colon in continuity, n (%)	47 (84)	25 (78)	0.570
Citrulline (umol/L)	18 (12-27)	20 (11-29)	0.930
Bilirubin >20 umol/L, n (%)	8 (14)	9 (28)	0.159
ALT >40 U/l, n (%)	13 (23)	18 (56)	**0.002**
GT >50 U/l, n (%)	15 (26)	11 (34)	0.474
Splenomegaly, n (%)	3 (5)	4 (13)	0.232
Cholelithiasis, n (%)	4 (7)	2 (6)	1.000

Data are median (IQR) or frequencies. P-values are Fisher's exact or Mann Whitney U test.

P4.09 – Anastomosis Less Than 10 Cm From The Ileocecal Valve In Intestinal Failure Associated With Short Bowel Syndrome Is Safe. Experience Of 9 Years In The Unit Of Intestinal Failure. National Hospital Guillermo Almenara Irigoyen. Lima Peru.

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Introduction: The short bowel syndrome (SBS) associated with intestinal failure (IF) is defined as a state of transient intestinal insufficiency characterized by abundant losses by enterostomy that lead to nutritional, hydroelectrolytic and metabolic alterations. In Peru, it is mainly produced by intestinal ischemia and postoperative complications.

In surgical management it has been tried to recover the largest amount of intestine, however, anastomosis has been avoided very close to the ileocecal valve (ICV) adducing greater risk of dehiscence due to high intraluminal pressure and little vascularity.

A series of patients with anastomosis less than 10 cm from the ICV are analyzed in the present study.

Patient materials and methods: Series of cases of patients older than 18 years with a diagnosis of SBS associated with IF; with ileal jejunal anastomosis less than 10 cm from the ICV. Where a standard protocol was implemented.

Between 2011 and 2018, 120 patients with a diagnosis of SBS associated with IF were treated. We performed 52 surgeries of autologous gastrointestinal restitution (AGIR). In 11 of them, an ileal jejunal anastomosis was performed less than 10 cm from the ICV and 5 of them were made to the same ICV.

We did not find anastomosis dehiscence and 2 complications occurred: a hemoperitoneum reoperated at PO1 for hemostasis and an inadvertent lesion reoperated at PO2 to perform raffia. After the AGIR there were 7 patients with more than 1 meter of residual intestinal length (170 cm average) and 4 patients with less than 1 meter of residual intestinal length (69 cm average); the Nutrition Parenteral was administered 21 and 35 days on average respectively; and the autonomy for the oral diet was given at 3 to 5 weeks.

Conclusion: The AGIR in IF associated with SBS with anastomosis very close to the ICV are safe if they are performed with regulated techniques.

P4.10 - Chronic Intestinal Failure: When Children Become Adults

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Rationale: Major advances in recent years have resulted in improved survival for patients with chronic intestinal failure (CIF). There is very little data on the future of children that became adult with CIF. The aim of our work was to describe this population since the existence of our center.

Methods: In an approved HPN centre for adult with a dedicated activity for CIF since 1984, we collected retrospectively all data related to patients treated with home parenteral nutrition during infancy (at least 4 years before transition to our centre) and transferred in our centre since 1984. We evaluated demographic data, the social evolution and the main complications at the adulthood. The final time of data collected was the 1th December 2017. Results were expressed as median[±SD].

Results: Among a total of 870 HPN patients since 1984 and 2017, 44 young adults (17F/27M) were transferred from 3 paediatric hospitals. Age of transition was 19±2 years. The principal etiologies of CIF were short bowel syndrome (n=18), CIPO (n=21), mucosal disease (n=5). At the end of follow up defined as the latest news (december 2017) or death, 7/44 patients were deceased (2 after intestinal transplantation, 3 after a sepsis, 2 due to liver failure), 3/44 were weaned off PN (2 due to growth factors, 1 after intestinal transplantation), 33/44 were alive requiring HPN (6±1,7 infusions/week; 2,2±1,3l/day; 29±13kcal/kg/day). Oral intake was 2000±1085kcal/day but 9/44 presented remaining oral disorders. Seventeen/44 had a regular work (35±6,5hours/week). 23 lived with their parents; 17 lived in partnership and 7 had at least one child.

Conclusions: Despite progress in survival and quality of life in HPN, many children who become adults stay with their parents and do not work. The transition requires probably a better social, educational and psychological preparation if we want to improve the future of these patients.

P4.11 - Intestinal failure management in the middle-income countries without home parenteral nutrition

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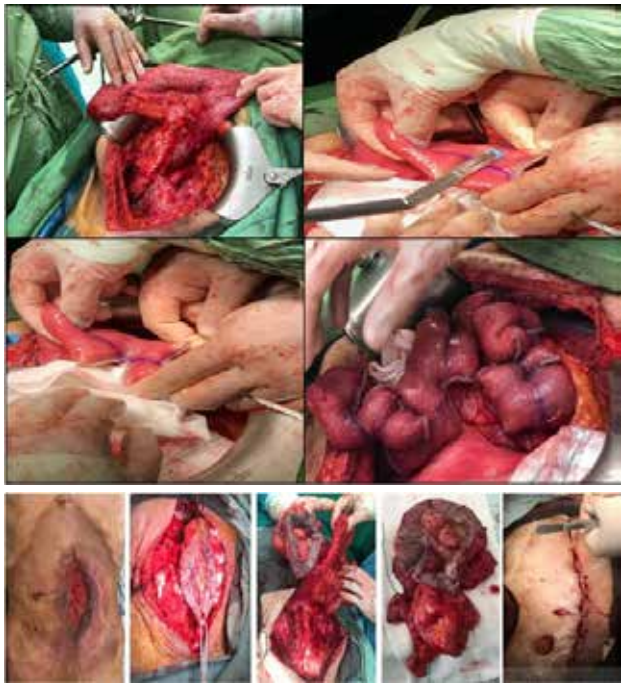
Introduction: Intestinal failure (IF) - a life-threatening medical status- is a rare disease still remains orphan in most countries. However, the management of this condition is still unclear in the middle-income countries (MIC) not benefiting from HPN. The current study aimed at investigating the current management of IF utilized in our center.

Methods: In the current cross-sectional study, data were retrospectively collected from 30 patients (25 males, 5 females) who had IF between January till October 2018, at Intestinal Rehabilitation Unit of BOOALI SINA hospital affiliated to Shiraz University of Medical Sciences, Iran.

Results: This cross-sectional survey included 30 patients (mean age: 44.13±10.32 years). The study participants consisted of 5 females (16.7%) and 25 (83.3%) males. Short bowel syndrome and Entero-cutaneous fistula were reported in 60 % and 26.7 % of patients, respectively. In the present study, the most common Shaffer functional classification type of IF was type 3 (66.67 %). Mesenteric Ischemia was the main cause of IF in the present study (46.7 %). The most common complication was CI (46.7%). The overall mortality rate for 1 year was 16.7 %. STEP procedure was performed on 2 patients (6.7%). Nine patients were uneventful at home without the need for home parenteral nutrition.

Conclusion: For the first time, this study presents a guideline on the development patterns and management exigence of IF in patients from MIC not benefitting from home parenteral nutrition. It is recommended to pursue the development of registries and reproduction of health policies in terms of the promotion of long-term care for patients with IF in MIC not benefitting from HPN in further studies.



P4.12 - Immune response in an experimental model of pig to rabbit abdominal fascia transplantation.

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Introduction: Lack of enough space for safe closure after transplantation leads to the use of fascia and abdominal wall grafts to overcome this problem. Little is known about the immunogenicity of fascial transplants. We have been using an experimental model of fascia transplants in rabbits for the last 4 years. Here we show the results of a subset of 9 pig to rabbit xenotransplants.

Methods: Fascia procurement: a midline abdominal incision in the pig served for a 3 x1 cm fascial graft procurement. The graft was kept at 4ºC in serum (7) or glutaraldehyde (G) (2) and transplanted 24 h later in the rabbits, removing a similar size fascial tissue. Macroscopic examination was also done.

Blood from pigs and rabbits was drawn, and fascial biopsies at 0,14,28 and 90 days, and rabbit spleen after sacrifice.

Donor specific antibodies (DSA) determination was performed by flow cytometry crossmatch (FCM-XM), using F(ab ')2 Donkey Anti-Rabbit IgG PE as secondary antibody. The mean fluorescence intensity ratio (△MFI) was calculated as the difference of the test serum MFI with respect to the negative serum (unimmunized rabbit) MFI. △MFI> 100 was considered positive. Additionally, a functional assay of cytotoxic capacity was performed in the positive sera by complement-dependent cytotoxicity (CDC-XM).

Results: There were not appropriate blood samples from 2 rabbits. One rabbit died of diarrhea on POD 16. All the transplants had an important reaction at 1 month, with seroma or graft detachment. At 3 months, the G grafts maintained an important reaction, but the other were integrated except one that had a big ventral hernia.

Flow cytometry results were positive in all the surviving rabbits at 30 days, except in those with G treated grafts. At 60 days, 4/4 had negative results (2 of them G treated). The antibodies showed cytotoxic activity by CDC-XM test in all serum tested (3 rabbits).

Conclusions: All the xenografts showed important immune reactivity at 1 month, but this decreased after 3 months, and tissue integration was observed at 3 months except in those treated with G. In this model, the immune reaction seem to decrease after the first month, with good integration of the graft in the majority of animals after 3 months. The G solution used had some other components that could explain the tissue reaction.

P4.13 - Central line-associated blood stream infection (CLABSI) complications seen in total paranteral nutrition (TPN) in patients admitted to intensive care unit (ICU)

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Introduction: Total parenteral nutrition (TPN) is used when gut fails to provide complete nutrition. Central line sssociated blood Stream infection (CLABSI) is a major complication of this therapy. It is defined as a laboratory-confirmed blood-stream infection not related to an infection at another site that develops within 48 hours of a central line placement. Of all the healthcare-associated infections, CLABSIs are known as the most costly, and most cases are preventable with proper aseptic techniques, surveillance, and management strategies.The objective of this study was to report the incidence of CLABSI and associated mortality in patients admitted to our intensive care unit (ICU) whom started on TPN.

Methods: The study was approved by our institution's Ethics Committee (no: 23/01/2019, B.10.1.TKH.4.34.H.GP.0.01/8). All patients who received TPN in our adult ICUs from the period between January 01, 2018 till December 31, 2018 were included. Data were retrieved from the hospital electronic data base. Total number of patients receiving TPN and catheter-related complications were recorded. Demographics and CLABSI rates were documented. In the case of tunneled catheters, the definition was changed as follows; signs of inflammation confined to an area (typically < 2 cm) surrounding the catheter exit site and the presence of exudate that proves to be culture positive.

Results: A total of 186 patients were determined to receive TPN in adult ICUs for a one-year period. There were 92 males (49.4 %) and 94 females (50.5 %). The incidence of CLABSI was 4.8 % (n=9) during this period. The average duration of TPN was 16 days (range 2-430 days). The great majority of catheters was transient (n=184, 98.9 %). Empiric antibiotherapy till the results of blood cultures obtained were started, and all catheters were removed and cultured. Acinetobacter baumanni and pseudomonas aeruginosa were the most commonly isolated bacterial infectious agents (66.6 %). Staphylococcus aureus (SA), methicillin resistant SA (MRSA), coagulase-negative staphylococci, enterococci, klebsiella and the other gram-negative bacilli and fungal infections constituted the smallest group (33.3 %) in our CLABSI series.

Conclusion: CLABSI is a very common problem in the intensive care unit. These infections can cause mortality, and costly. Only through best practices, protocols, checklists, and establishing a culture of patient safety in healthcare institutions can one reduce CLABSI to zero.

P4.14 - Financial burden of critically-ill patients receiving parenteral nutrition (PN) in a reference intensive care unit (ICU) in Istanbul: An additional cost from Syrian refugees

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Introduction: The number of critically-ill patients has increased over the years due to progress in intensive care medicine and parenteral nutrition (PN) techniques. Long-term survival is possible and does not depend only primarily on the disease etiology (head trauma and pulmonary complications etc.) but on accompanying morbidities and complications such as central venous catheter infections. Prolonged ICU admissions are costly as well. Therefore, covering the cost of these critical patients (primary disease treatment including interventional and surgical issues, all consultations and treatment protocols) is an important issue, and having health insurance coverage for their treatment and all of the needed follow-up care (including almost 4 millions Syrian refugees, as well) is critical.

Methods: A computer-based analysis was done retrospectively to search the covering health insurance programmes of our patients treated in our adult ICUs during January to December 2018. Syrian refuees were also included in the study, as state insurance coverage was supplied to all. Other then known government-issued general health insurance, private health insurance options and the payments done by the patients' own resources were also interrogated.

Results: A total of 186 patients were included in the study. Mean age was 51 years (range, 18–91). The average period of ICU stay was 45 days (range, 1–204), including longer hospitalization time due to surgical complications or existing comorbidities. The postoperative stay in intensive care unit (ICU) was also included in this period. In our data, the only health insurance coverage was seen to be supplied by the state (n=186, 100 %). There was no private insurance coverage. No patients used their own financial resources for treatment, as well (including Syrian refugees).

Conclusion: It is well-known that state insurance in Turkey covers all policlinic applications and postdischarge home care (including all refugees), and patients pay only a small amount of fee as employee contribution for the medications at pharmacies. The new information in the present study is the governmental coverage of all Syrian refugees in ICUs, as well. Taking the great amount of bill that an ICU patient should encounter, the importance of state insurance is obvious for the comfort of patient and the ease of financial portion of their treatment.

P4.15 - IF associated liver disease – a single centre cohort study of adult patients referred for consideration of intestinal transplantation

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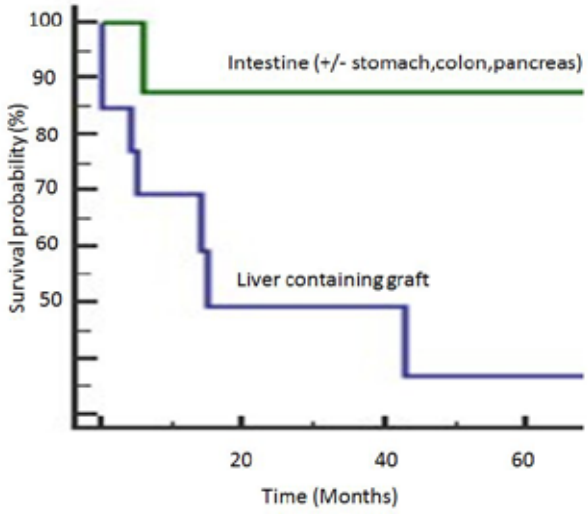
Introduction: Patients requiring long term parenteral nutrition for intestinal failure are at risk of developing associated liver disease (IFALD) which can progress to cirrhosis that requires liver transplantation along with the intestine. There is evidence to suggest that pre-emptive intestinal transplantation in this setting can prevent progression of liver disease and may improve fibrosis.

Methods: A retrospective review of liver biopsies, liver blood tests (at the time of biopsy) intestinal anatomy and outcomes in patients referred to Addenbrooke's Hospital Cambridge UK between 2008 and 2018 for consideration of transplantation for IFALD. Fibrosis was scored subjectively by pathologists as mild, moderate, severe or cirrhosis.

Results: 21 patients (out of a total of 82) underwent transplantation for IFALD. In 13 cases, liver fibrosis was considered too advanced for intestine alone and they required liver containing grafts, the others received intestine without liver. Post transplant survival is shown in fig 1. In addition, 13 patients have been referred and / or listed and 9 died on the waiting list, 5 of which from advanced liver disease. Liver biopsies which showed at least moderate fibrosis (in the absence of additional pathology) from patients with >20cms intestine to stoma were performed at a mean of 11.6 years (SD7yrs) after starting PN (n=15), those with <20cms to stoma were performed at a mean of 2.2 years (SD 0.6yrs) (n=10). LFTs in patients (excluding end stage disease and severe cholestasis) were calculated . Mean bilirubin and ALT in patients with cirrhosis or severe fibrosis were 30 umols / l (+ / -11) and 52 U / l (+ / - 34). Only 10 out of 24 patients with at least moderate fibrosis on biopsy showed bilirubin and / or ALT >1.5x ULN.



Conclusions:

Patients with ultrashort intestine are at risk of early progression to significant degrees of IFALD.

Liver blood tests are not predictive of underlying IFALD.

Post-transplant survival in patients with IFALD requiring liver transplantation is inferior to that of those receiving intestine alone

Earlier detection of IFALD and referral for pre-emptive intestinal transplantation is indicated

P4.16 - Clinical presentation and outcomes of Chronic Intestinal Pseudoobstruction in pediatric patients

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Introduction: Chronic intestinal pseudoobstruction (CIPO) presents symptoms of intestinal obstruction without any lesions occluding the intestine. It is a rare and difficult disease entity not diagnosis but also treatment. The standard diagnosis and management has not yet be established enough. In this study, we are aim to report clinical outcomes of pediatric intestinal pseudoobstruction and predictive factor for the poor outcomes.

Methods: We retrospectively reviewed the 76 patients who were diagnosed as a primary pediatric CIPO between January 1985 and December 2017 in one institute. Age at diagnosis ranged between 0 and 221 months (median 4 months). We categorized the clinical outcomes into four groups and evaluate clinical outcomes.

Results: A total of 75 patients underwent the operation including enterostomy, bowel resection and venting gastrostomy. In terms of histopathology, 56 patients were a neuropathy, 11 patients were a myopathy and 3 patients showed both results in specimen. In contrast, we could not abnormal finding of enteric neuron and muscle in specimen of six patients. The overall mortality of primary CIPO was 10.5% (8 of 76). Neuropathic type CIPO patients showed better prognosis than myopathic type patients in significant ($p < 0.008$). Furthermore 41 patients and 21 patients categorized as a good and poor outcome group in respectively. The patients who experienced a home parenteral nutrition (PN) had tendency with poor clinical outcomes due to recurrent hospitalization.

Conclusion: In recent, the clinical outcome of CIPO improved because of an early diagnosis, proper surgical treatment and multidisciplinary management. In this study, we showed an acceptable clinical outcome even though many well-known morbidities.

Disclosure Statement

The authors have no conflicts of interest.

P4.17 - Ten years Dutch nationwide intestinal transplant program: A retrospective overview and prospects for the future, regarding intestinal failure and intestinal transplantation in adults (2009 – 2019)

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Introduction: In the Netherlands there is only 1 intestinal transplant (ITx) program and 2 centers for home parenteral nutrition. The number of patients as possible candidates for ITx, referred by different centers, is growing. Still the number of ITx is small. With this overview we want to present the case mix and complexity in adults over the last decade.

Methods: The nationwide online Dutch Registry of Intestinal Failure and Transplantation (DRIFT) was started (2011) to monitor intestinal failure patients, which combines data from patients of the University Medical Center Groningen (UMCG) and three more Dutch centers. In this retrospective overview we present a small but complex group of patients who were referred to or already known by the UMCG since November 2009 till now.

Results: During this last decade, 37 adult patients were referred to our nutritional support team for possible screening regarding ITx. After a first interview at the UMCG, 14 patients were not screened because enteral feeding or autologous reconstruction was possible. Others lacked condition or feared decreasing quality of life after transplantation. 23 patients were screened, of which ten patients were rejected after screening because of medical or psychological reasons. Eventually, only ten adult patients underwent ITx (of which 1 multivisceral transplantation, 2 ITx with abdominal wall, 2 ITx with kidneytransplantation) and three patients are still on the waiting list all with intestinal failure associated liver disease (IFALD) and severe venous access problems.

Conclusion: Over the last decade, a nationwide multidisciplinary approach of intestinal failure has proven to be successful so that only a limited amount of patients needed a transplant. However, the complexity in ITx candidates is increasing with more severe venous access problems and IFALD.

P4.18 - Strategies developed to support families facing intestinal transplantation

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Introduction: A child / young person facing an Intestinal Transplant can be extremely difficult for families. It involves meeting a new team and hospital at a time when medical care of the child is challenging. An MDT approach has been demonstrated to benefit the family and help to ensure they are adherent to treatment and care. Working in partnership is essential to ensure children and young people receive the best care.

Our aim is to describe the strategies we have developed to meet the needs of our intestinal transplant families, children and young people.

Methods: Introducing families to our transplant MDT at the time of transplant assessment, ensuring they understand team members' roles and responsibilities.

Giving families regular opportunities to meet with different members of the transplant team to gather information and ask questions. Provide families with information both written and verbal to empower and encourage them to participate in the discussions with healthcare professionals. Daily communication with the family is done in their own language via interpreters.

Establish links with the local support network early and ensure they are kept up to date with treatment and care plans. Eg Shared care consultant, community nursing teams

Support the parents to communicate with the nursery / school as appropriate. Discuss return to school plans and educational care plans to ensure the child / young person can resume their education.

Behavioural contracts to establish families understand their roles and responsibilities.

Signpost families to support services e.g. Children's Liver Disease Foundation, Multi Organ Transplant Support,

Family support team advice parents / carers on welfare benefits, housing issues and financial support in the form of grants available.

Investigate and discuss opportunities for respite and other support services available in the local area.

Summary: Feedback from families is that they feel part of the team looking after their child. They are able to confidently voice their opinions and concerns. Fostering a culture of parent and healthcare professionals working together is required to ensure children and young people's needs are met.

Future Development: Further development of unit website, links for families to use prior to admission to orientate them to the unit and staff and development of apps.

P4.19 - Incidence and severity of acute cellular rejection in the recipients of small bowel transplantation in Taiwan

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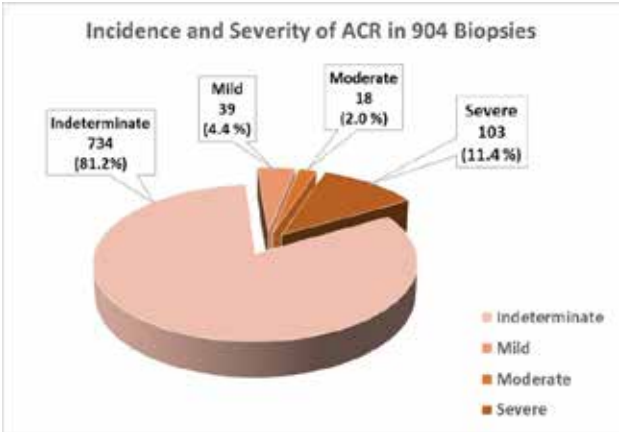
Introduction: Intestinal transplantation is considered as the ultimate life-saving treatment for the patients with irreversible end-stage intestinal failure. The 5-year survival rate is currently around 60% according to international results. Post-transplantation episodes of acute cellular rejection, systemic infection, and, in later stages, chronic rejection are the major prognostic factors for the survival of recipients and grafts. In this research we analyzed the histological findings and the outcomes among the 22 cases of isolated intestinal transplantation in our institute in Taiwan.

Methods: Patients received intestinal transplantation were under periodical graft surveillance by intestinal biopsy through ileostomy. The biopsy histology reports from the 22 cases of intestinal transplantation were retrospectively reviewed and analyzed by IBM SPSS software. The use of data was approved and under the supervision of Institution Review Board (IRB) of Far Eastern Memorial Hospital, New Taipei City, Taiwan.

Results: The 1, 3, and 5-year patient survival rates of intestinal transplant recipients in our institute are 83.7%, 72.2%, and 66.7%, respectively. During year 2007 to 2017, the total amount of biopsies taken from these 22 cases is 904. In these biopsy reports, 734 biopsies (80.9 %) were reported as indeterminate for acute cellular rejection (ACR), 39 biopsies (4.3%) as mild ACR, 18 biopsies (2.0%) as moderate ACR, and 103 biopsies (11.4%) as severe ACR (Figure 1). Among the 22 cases, 15 cases (68.2%) had been diagnosed as ACR, in which 6 were reported as mild rejection, whereas the other 9 as moderate to severe rejection. Furthermore, 10 cases within these 15 ACR cases (66.7%) developed ACR in the first 3 months after transplantation.

Conclusion: In our series of small bowel transplantation, the incidence of acute cellular rejection was 68.2%, which is comparable with other American and European centers. Scheduled graft surveillance with histological inspection greatly helped the monitoring of rejection episodes and the subsequent timely treatments for the patients.



P4.20 - Ten years trends in intestinal transplantation in the United Kingdom

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NHS Blood and Transplant

On behalf of the UK national intestinal transplant programmes

Introduction: Intestinal transplantation in the UK has been centrally commissioned at four centres since 2008; two paediatric centres (Birmingham Children's Hospital and King's College Hospital) and two adult centres (Cambridge Addenbrooke's Hospital and Oxford Churchill Hospital). The programme has evolved; this study describes the trends over the last 10 years. Mandatory data are collected centrally by National Health Service Blood and Transplant (NHSBT).

Methods: All patients were included who were registered for or received an intestinal transplant. These were classified as: bowel only (small bowel +/- colon/abdominal wall/kidney, BO), multi-visceral (liver, small bowel, pancreas +/- stomach/kidney/colon, MV), or modified multi-visceral (small bowel, pancreas +/- stomach/kidney/colon/abdominal wall, MMV)) between 1 April 2008 and 31 March 2018 were extracted from the UK Transplant Registry held by NHSBT. Trends in age, diagnosis, transplant type and survival post-transplant were analysed.

Results: During the decade, 196 intestinal transplants were performed nationally with an annual increase from 16 in 2008/09 to 26 in 2017/18. Since 2011/12 more transplants have been performed in adults than children, with 65% in adults during the latest year compared with 38% during 2008/09. BO transplants represented 72% of all transplants performed in 2010/11 compared with 27% in the latest year, due to increases in both MV and MMV transplants.

There were 251 registrations onto the transplant list, of which 45% were for short-bowel syndrome, 15% motility disorders, 9% tumour, 9% re-grafts, 6% mesenteric thrombosis, 5% intestinal failure associated liver disease, 4% primary mucosal disorders and 5% other identified causes. Short-bowel syndrome has been reported less in recent years.

Of patients placed on the waiting list, 78% were transplanted. One year post-transplant patient survival rates are 78% (69%-85%) and 85% (73%-92%) for adults and children respectively.

Conclusion: The UK programme transplants 14-26 patients per year, with a trend over time towards adult patients, multi-visceral transplants and away from short-bowel syndrome.

P4.21 - Experimental model of Brain death donors in rats: A match control study of cold ischemic injury and morphometrical changes between brain death and live donors for intestinal transplant

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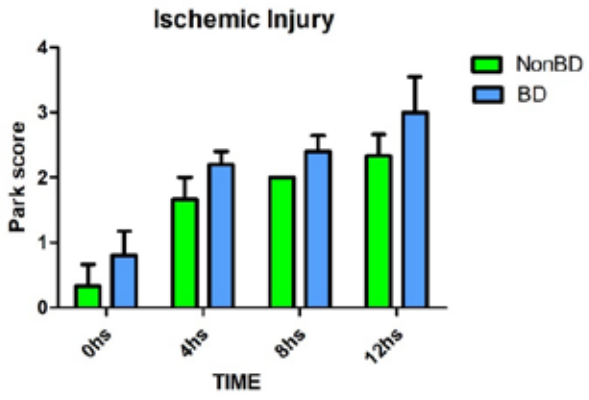
Introduction: Experimental intestinal transplantation (ITx) in rats is a widely used tool in the study of ischemia reperfusion injury and rejection. Even so, live donors are used in the majority of these protocols. With the aim of generate a model closer to the clinical reality, our study intends to introduce brain death (BD) protocol to analyze the impact of biological processes associated with ITx.

Methods: Wistar rats between 280 - 330g were used, divided into two groups, Brain Death (BD n=5) and Non BD (n=3). Anesthetic induction was with isoflurane at 5%, maintenance was initially with a mask and then endotracheal 2/2.5% with AV (50 RPM - 2.5 TV). Arterial and venous lines are placed for blood pressure and fluid therapy manage. In the BD group, through a skull trepanation, a 4F balloon cannula is subdurally placed, and insufflated at 1ml/h flow rate. When Cushing reflex is observed, BD diagnosis is performed by the apnea test. The rat remains under BD for 2 hours, handling the MAP between 70 and 140 mmhg. NonBD group is ventilate assisted for 2 hours.

Afterwards, the graft is flushed with cold saline, harvested and preserved in HTK (Custodiol®) at 4°C. Then, sampled at 0, 4, 8, 12 and 24hs for H&E staining. For histological damage was used Park-Chiu scale. Using ImageJ® morphometric variables were measured. 207 V/C units in 5 individuals of BD group and 169 (3 individuals) for NonBD at 0, 4 and 8hs, Villi and Crypt height and width (VH, VW, CH and CW), with a minimum 10 and maximum 20 V/C units for each sample. In addition, the villus/crypt index (VCI) was calculated.

Results: A minor injury in the Non BD group was observed: 0hs NonBD=0.33 (±0.58) vs BD=0.8 (±0.84); 8hs NonBD= 2 (± 0) vs BD= 2.4 (±0.55); 12hs NonBD= 2.33 (±0.58) vs BD= 3 (±1.2).



Higher scores of focal damage were reached faster in the BD group: BD= 4 (±1) at 8hs vs NonBD= 3.67 (±1.53) at 12hs.Morphometric values (µm) were higher under BD at 0hs for VH, VW and CH, ($p=<0.001$). Decreasing VCI was observed in both groups at different times (BD: $p=<0.001$; NonBD: $p=<0.005$).

Morphometric Values for V/C units.

	BD 0hs	NBD 0hs	BD 4hs	NBD 4hs	BD 8hs	NBD 8hs
Villi High	154,60 ±41,47	107,50 ±17,29	120,80 ±17,98	119,40 ±11,93	110,80 ±13,95	97,05 ±14,98
Crypt High	56,92 ±16,76	46,81 ±11,09	54,84 ±11,74	46,50 ±7,11	52,41 ±11,20	43,15 ±7,81
Villi Width	85,89 ±13,89	80,11 ±17,11	43,55 ±16,69	34,88 ±8,54	34,62 ±9,6	40,96 ±22,21
Crypt Width	15,75 ±3,25	17,51 ±4,02	17,39 ±1,23	17,66 ±2,66	16,13 ±3,08	15,98 ±3,62
VCI	2,64 ±0,65	2,77 ±1,03	2,20 ±0,51	2,58 ±0,62	2,11 ±0,52	2,23 ±0,65
V/C measured	n=65	n=58	n= 65	n= 61	n=90	n= 50

Conclusions: We could establish a reliable BD model in rats for the study of its impact on the intestine transplantation graft. Our study shows that BD introduced subtle histopathological differences compared to ventilated controls. Future studies will be focused in the consequences of these changes analyzing the impact on graft function after the engraftment.

P4.22 - Reporting on outcome measures in pediatric chronic intestinal failure: a systematic review

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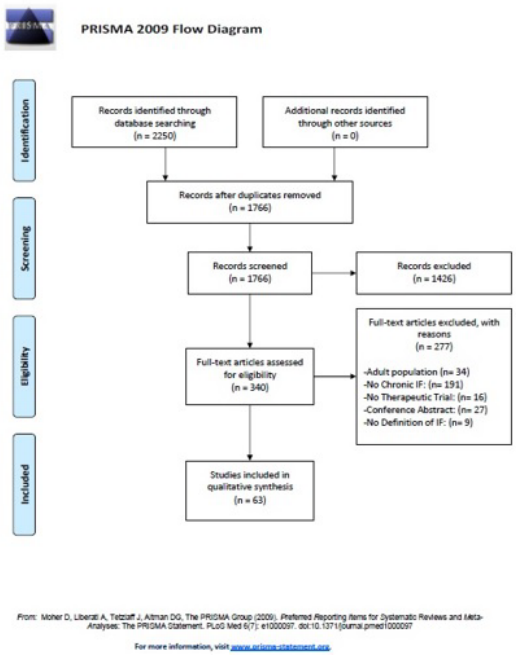
Introduction: Standardized outcome measures provide the ability of comparing outcomes of different clinical trials. Furthermore, standardized outcome measures offer the possibility of reducing potential reporting bias and increase the reporting of patient relevant outcomes. The aim of this study is to systematically assess how definitions and outcome measures are defined in therapeutic trials of children with chronic Intestinal Failure (IF). These results will be used as first step in the development of a Core Outcome Set (COS).

Methods: MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched from inception till august 2018. Studies were included if it was an original interventional study or observational study with a control group, concerning children from 0-18 years of age old with chronic IF and concomitant parenteral nutrition use, and a definition of IF was provided. No language restriction was used. Outcomes were mapped to one of the five core areas from the OMERACT 2.0 filter. The Delphi List, Newcastle Ottawa Scale for non-randomized studies, or the quality assessment tool for before-after studies (National Heart, Lung, and Blood Institute) were used to assess the quality of included studies.

Results: A total of 1766 articles were found of which 63 studies fulfilled our inclusion criteria (figure 1). 47 studies (75%) did not report any definition of IF. Of the 16 studies (25%) which reported a definition of IF, 5 different definitions were found. A total of 106 different outcomes were reported. The four most reported outcome measures were: mortality (n=23), growth (n=22), liver enzymes (n=18), and parenteral nutrition weaning (n=18). The majority (n=63; 59%) of reported outcomes was mapped to the pathophysiological manifestations core area from the OMERACT 2.0 filter. 17 studies (27%) predefined a primary outcome of which central line related infection was the most frequently used (n=5). Quality of reporting was considered low in most studies (n=47; 75%).

Figure 1. PRISMA flow diagram displaying the number of studies identified and the number of studies included after screening.



Conclusion: Heterogeneity exists in the definitions of IF, and outcome reporting in research concerning pediatric chronic IF.

P4.23 - Prevalence of Vitamin D Deficiency and Response to Oral Vitamin D Supplement in Children with Short Bowel Syndrome Receiving Home Parenteral Nutrition

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Introduction: Children with short bowel syndrome (SBS) are prone to have vitamin D deficiency or insufficiency due to poor oral intake, malabsorption. In this study, we evaluated vitamin D status of pediatric patients with SBS receiving home parenteral nutrition (PN)

Methods: During two years of study period, we retrospectively reviewed pediatric patients with SBS who had been on home PN for more than six months. Vitamin D level (25-hydroxyvitamin D, 25-OHD) was checked on routine outpatient visit and categorized into normal, insufficiency, or deficiency.

Results: Eighteen patients with SBS included. There were fifteen patients with vitamin D deficiency at least once during study period, and two patients with vitamin D insufficiency. No difference in risk of vitamin D deficiency or insufficiency according to the primary cause of SBS. Followed by supplement of vitamin D, the 25-OHD level of 40% of vitamin D deficiency group had been shown improvement to insufficient status. The rest of patients received high oral doses of vitamin D yet remained in deficient status.

Conclusion: Vitamin D deficiency and insufficiency are common in children with SBS on home PN. Routine surveillance and high dose oral supplement are important for these patients. Large multicenter research is needed to establish the optimal method and dose of vitamin D supplement.

P4.24 - Evaluation Of Clinical And Safety Outcomes After Conversion From Brand-Name To Generic Tacrolimus In Adult Intestinal Transplant Recipients

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Introduction: The introduction of generic immunosuppressants may offer an opportunity for cost savings in intestinal and other solid organ transplantation if equivalent clinical outcomes to the branded counterparts can be achieved.

Methods: At our center 14 clinically stable adult intestinal / multivisceral transplant recipients were switched from Prograf (®) to Adoport (®) starting from 1st January 2018: 8 male and 6 female; 11 of them underwent isolated intestinal transplant, 3 of them multivisceral transplant (1 associated with abdominal wall transplant). After the immunosuppression switch we conducted an acute monitoring with regard to safety and efficacy: acute cellular rejection on intestinal biopses and tacrolimus C0 levels were checked every 3 months. Pre conversion tacrolimus level was compared to those revealed at 3, 6, 9 and 12 months after conversion; at the same timepoint an intestinal endoscopy and biopsy was performed.

Results: After 1 year of follow up from the conversion, tacrolimus C0 levels did not canged (pre conversion mean level 5.1 ng / mL ± 1.8 vs 4.8 ng / mL ± 1.7, 5 ng / mL ± 1.7, 5.1 ng / mL ± 1.9, 5.2 ng / mL ± 1.9 respectively at 3, 6, 9 and 12 months after tacrolimus conversion). Survival was 100% of the patients. No episodes of ACR or enteritis or other complication were collected. No patient reverted back to gtand name tacrolimus.

Conclusion: Our clinical experience as well as research data showed that the use of generic tacrolimus results in comparable trough concentration. Given the lack of adverse events reported and the cost savings recognized, conversion from brand name tacrolimus to generic one should be encouraged also in intestinal transplant recipients

P4.25 - Serial Transverse Enteroplasty in Children with Short Bowel Syndrome

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Introduction: Serial transverse enteroplasty (STEP) is an intestinal lengthening procedure used for short bowel syndrome (SBS) that was first introduced in 2003. This study aimed to report clinical outcomes in children who underwent the STEP procedure at our institution.

Methods: STEP procedures were performed according to the guidelines of Kim et al. Since March 2008 at our hospital, five children dependent on parenteral nutrition (PN) underwent the STEP procedure. Pre- and post-STEP clinical outcomes were reviewed retrospectively.

Results: Our cohort included three girls and four boys with SBS. The causes of SBS were jejunoileal atresia (2), necrotizing enterocolitis (4), and total colonic aganglionosis (1). The median age on STEP was 37months (range, 7–59). STEP procedures were performed 1.71 times / patient, three times in one patient, three patients for two times, and one times for four patients. Intestinal length was increased in all cases. There were no perioperative complications and no evidence of intestinal leak or obstruction. Three patients have been completely weaned from PN. Other three patients have remained on PN, but their PN requirement has been decreased. In one patient with total colonic aganglionosis with small bowel involvement, the PN requirement has not been changed.

Conclusions: STEP is a simple bowel-lengthening procedure associated with promising early PN weaning and decrease in PN requirement. But in case of SBS caused by total colonic aganglionosis, it may not be so helpful. Further data from a multicenter registry are needed to evaluate its long-term efficacy and proper candidate.

P4.26 - Outcomes of three genetic syndromes with intestinal failure (IF), short bowel syndrome (SBS), intestinal failure associated liver disease (IFALD) and parenteral nutrition (PN) dependency, treated in our Intestinal Rehabilitation Program (IRP). Children's National Medical Center Washington DC

Clarivet Torres, Vahe Badalyan, Parvathi Mohan

Children's National Medical Center

3 y old boy with deafness, hypotonia, ichthyosis, osteopenia, IF, chronic enteropathy, initially on PN now on J tube feedings, secondary to MEDNIK syndrome. He had IFALD stage 4 fibrosis, now with normal conjugated bilirubin (CB). Liver biopsy with no iron or copper (Cu) deposition, low Cu quantification, presented with feeding intolerance, persistent diarrhea, dehydration, metabolic acidosis and AKI. Treated with high dose of zinc acetate to avoid accumulation of Cu (brain and liver). He had multiple admissions due to enterocolitis, sepsis and severe anemia related to low Cu. His initial target blood Cu level was ~20's but it was increased to ~40 mcg/dLto minimized complications. He was started on jejunal feeds of amino-acid (aa) based formula; with control of sepsis was able to wean off of PN, now tolerating oral feeds.

10 y old male with SBS, PN and G/J tube dependent due to multiple congenital atresias, TTC7A gene mutation. History of hypogammaglobinemia, bone marrow transplant and IFALD stage 4 fibrosis, now with normal CB. History of multiple surgeries to correct his intestinal (I) obstruction, left with 75 cm of bowel, a Santulli ostomy and a surgical G and J tube due to severe dysmotility. He had multiple I. strictures dilated endoscopically. He has tolerated progressive advances of J tube feedings decreasing PN needs from 100% to 35%.

3y old male with adrenal insufficiency and IF initially on PN , now G tube dependent, secondary to congenital osmotic diarrhea related to PCSK1 mutation. His IGF-1, IGF-BP3, Prolactin, TSH, free T4, and MRI of the pituitary were normal. He had history of multiple CLABSI and diabetes Insipidus needing vasopressin during sepsis episodes; enterocolitis and severe metabolic acidosis due to B2 deficiency. His diarrhea persisted on all formulas and he was placed on PN and on a custom formula (amino acid powder, microlipids, electrolytes), but due to his low B2 this formula was changed for aa based formula via G tube, tolerating progressive advances of enteral nutrition, with PN wean. He now takes >50% of caloric needs via PO and the rest as nighttime GT feeds. Although obesity is observed in PCSK1 his weight is at the 50% and height at the 10%.

Patients with complex genetic syndromes and diverse nutritional and electrolyte needs can be successfully managed and transitioned from PN to enteral feeding as was done in our IR program, with a multidisciplinary collaborative approach.

P4.27 - Short Bowel Produced By Intestinal Ischemia Associated With Hypobaric Hypoxia At Height. National Hospital Guillermo Almenara Irigoyen. Lima Peru.

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Introduction: We describe a series of cases of patients with short bowel, who had intestinal ischemia due to height (hypobaric hypoxia). It has been suggested that polyglobulia and hypoxia can lead to a decrease in splanchnic oxygenation and precipitate intestinal ischemic events. The descent at sea level can reduce the risk of thrombosis and finally, after intestinal rehabilitation therapy, ensure that patients can undergo autologous gastrointestinal reconstruction (AGIR).

Patients: 3 adult male patients, with short bowel anatomical who suffered from intestinal ischemia and underwent massive intestinal resection. The patients had in common being males, adults, living in valleys above 3000 meters above sea level, presenting haematological and / or endothelial diseases with levels of polyglobulia up to 60% of hematocrit.

The patients underwent a thrombotic profile, angio-TEM and echocardiogram to determine hematological alterations, atherosclerosis of splanchnic vessels or impaired cardiac function. No abnormality was found in any of them. The hematological and coagulation values, initially altered by the anti-coagulant medication, were reversible.

Discussion: These ischemic events due to physiological changes, polyglobulia and activation of coagulation factors (factor VII), have been described in patients living above 2800 meters above sea level.

We believe that patients may have presented ischemic events aggravated by endothelial damage and polyglobulia, in the territory of the mesenteric artery. Intestinal ischemia due to hypobaric hypoxia is a rare entity that usually develops in adult males who live above 3000 meters above sea level, its prognosis is good after massive bowel resection and short bowel syndrome can be resolved with intestinal rehabilitation therapy and AGIR.

P4.28 - Renal function outcomes in paediatric intestinal transplant recipients

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Background: Renal dysfunction after intestinal transplantation is a well recognised complication. Calcineurin inhibitors have a direct impact on the kidney with post-operative day 7 tacrolimus associated with kidney function at 1yr. Catheter related sepsis, prolonged usage of intravenous fluid, parental nutrition, diabetes and graft failure have all been associated with chronic kidney disease.

Methods: Review of first-time paediatric intestinal graft recipients at a single centre between August'09-June'18. CKD was defined as Cystatin-C(CysC)>1mg/l measured at baseline, 6mths,1yr,2yr and 5yr post-transplant. Demographic and data associated with CKD post-transplantation were collected (Tac lvls at POD 7,3,6 and 12mths). Immunosuppression protocol consisted of Basiliximab induction then maintenance with tacrolimus and prednisolone +/- sirolimus. Target tacrolimus levels were between 12-15µ/L in the first 3wks, 8-12µ/L 3wks -3mths, 5-8µ/L out to1yr post transplantation. Statistical analysis was applied when appropriate, and analyses performed using SPSS.

Table 1: Cystatin C and Tacrolimus level following intestinal transplantation

	Tacrolimus level *(median (IQR))*	Cystatin-C mg/l *(median (IQR))*	CKD (Cystatin-C >1 mg/l) *(%)*
Baseline	-	1.01 (0.83, 1.18)	38%
POD 7	13.4 (9.7, 17.7)	-	-
3 months	8.2 (6.4, 9.9)	-	-
6 months	6.9 (5.7, 8.8)	1.51 (1.1, 1.87)	68%
12 months	6.3 (4.9, 7.6)	1.17 (0.86, 1.42)	38%

Results: 21 paediatric patients(53% male; 43%short gut syndrome, 38%paediatric intestinal pseudo-obstruction), median age of 5 yrs(4,7.8) underwent either isolated intestinal(43%), liver and intestinal(28%) or multivisceral transplantation(29%). 38% continued with tacrolimus and steroids alone, 57% sirolimus added. 4 patients required re-transplantation at a median time from first transplantation of 33.5mths (3.5,80). 4 patients died at a median time of 9.5mths(4.8,16). CysC level of all patients at baseline was 1.01(0.8,1.2), with 38% of children having evidence of pre-existing CKD (CysC lvl 1.16(1.1,1.5). There was significant association with CysC level at 6mth and Tacrolimus lvl at 3mths, r=-0.5 p=0.03. CysC lvl improved between 6mths and 1yr post transplant. No significant association was found between CKD at 6mths or 1yr and type of immunosuppression, prolonged use of intravenous fluids, parental nutrition, diabetes, graft failure, line sepsis or Tac lvl POD 7.

Conclusion: Renal dysfunction is already prevalent at the time of intestinal transplantation therefore continuing close monitoring of renal function and tacrolimus levels is advisable. In our cohort renal dysfunction peaked at 6mths post transplant then improved following titration of tacrolimus level. A larger prospective study is required to identify paediatric variables that effect renal function following intestinal transplantation.

P4.29 - Vedolizumab for chronic allograft enteropathy? A case report

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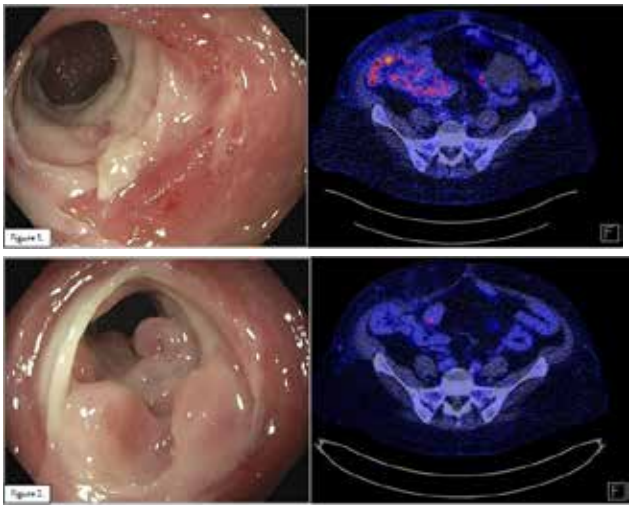
Introduction: Chronic allograft enteropathy (CAE) is the main cause of intestinal graft loss two years post transplantation. Clinical course is insidious and silent, and medical treatment is disappointing. While its physiopathology is mostly unknown, the golden standard for the definitive diagnosis of CAE is histopathological analysis of the resected graft. In CAE there is atrophy of the mucosa with fibrosis and remarkable vasculopathy of middle-sized arteries. Vedolizumab, a humanised anti-$\alpha 4\beta 7$ integrin antibody, is currently in use for inflammatory bowel disease (IBD). The proposed mechanism of action involves selectively blocking active immune cells from the acquired immune system from entering the intestinal mucosa. More recently, an effect on innate immune cells has also been described. In this case report, we show the first known use of vedolizumab to treat a patient with CAE.

Methods and Results: A 54 year old woman,15 years post-transplant, presented with in the annual routine ileocolonoscopy ischemic ulcers and a stricture in the terminal ileum which could not be passed by the scope. A consequent PET-CT scan showed inflammatory signs in the graft (Figure 1). Mucosal biopsies showed crypt distortion and slight increase of fibrosis in the lamina propria and inflammation suggestive for CAE. HLA antibodies, PCR for EBV and CMV were all negative. Treatment with methylprednisolone (1 gram/day for 3 days) was not successful. Due to the lack of specific medical treatment for CAE, vedolizumab was started under a standard IBD scheme (300 mg I.V. at weeks 0, 2, 6 and every 8 weeks thereafter), in addition to maintenance immunosuppression. After 16 weeks (4 infusions), a follow-up colonoscopy and PET-CT scan (Figure 2) showed almost complete resolution of the mucosal inflammation, although the stricture remained. It was therefore decided to do a surgical resection of the stenotic area and continue treatment with vedolizumab.



Conclusion: This case report shows promising effects of vedolizumab in a patient with CAE. With our case study we intend to study the physiopathology of CAE to further understand how vedolizumab can play a role to extend graft survival in an otherwise deleterious condition.

P4.30 - Accelerated transition - a patient centred approach

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Addenbrooke's Hospital

Introduction: Transition from paediatric to adult services should usually be conducted in a staggered manner, giving the young person time to adapt to the changing environment and healthcare professionals[1]. Occasionally, rapid transition in an acute setting is required and we describe here an unusual case in which this occured.

Method: A description of a challenging case that required urgent transition from paediatric to adult services in the acute clinical setting of a seriously ill child needing multivisceral transplantation.

Results: CS, a 15 year old male was admitted to a paediatric ward with life-changing diagnoses (nephrotic syndrome, recurrent pancreatitis, cholangiopathy and hypogammaglobulinaemia). Due to his age and requirement for multivisceral transplant he was cared for by multiple specialist teams across paediatric and adult services, coordinated by the paediatric WellChild nurse. Weekly MDT's were held, with discussions about his medical status, plans for transition, social care and educational needs.

It was agreed that the young person should formally transition to the adult medical and surgical teams at the point of transplant. A document including chronology of patient journey, family perspectives and fears and anxieties, was prepared for staff in ICU/HDU/ward areas. Following his transplant aged 16 years 11 months, support was provided to the patient and family from the WellChild nurse and adult transplant specialist nurses.

Conclusions: Despite occuring under urgent circumstances and entirely in hospital, this transition process was a success. This was due to the engagement and dedication of the staff involved across many aspects of paediatric and adult care. The patient and his family remained at the centre of all discussions and plans, which at times included very difficult decision making.

MDT working encouraged development of new relationships, knowledge of roles and processes within different services.

For the paediatric team it has highlighted the need for a WellChild paediatric transition nurse.

For the adult team it has given much insight into the transition process and the need for transition expertise. Particular lessons learned included how important the emotional wellbeing of the entire family is and how the inpatient environment on the adult ward had to be adapted to accomodate the family.

Overall we "Got it right" for CS and his family[1].

Reference:

1. DOH document: Transition: Getting it Right for Young People (2006)

P4.31 - Cystatin c as a marker of renal function in children on home parenteral nutrition

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Introduction: Well known complications of children with intestinal failure (IF) on home parenteral nutrition (HPN) include sepsis, central access loss, liver disease, pulmonary embolism, metabolic disturbances and bone disease. Renal abnormalities are less understood. Estimation of glomerular filtration rate (eGFR) from serum creatinine, height and a proportionality constant (Schwartz Formula) is the current gold standard in children[1]. Cystatin C (CysC) is freely filtered by the glomerulus, reabsorbed by tubular epithelial cells and measured in serum[2]. The aim of this study was to investigate the incidence of renal disease (RD) comparing eGFR and CysC.

Methods: Children receiving HPN > two years were identified from a tertiary IF clinic and data recorded prospectively from 2017 to 2018.Underlying IF aetiology, duration and proportion of PN were recorded. CysC was measured and eGFR calculated in 2017 and 2018. Normal renal function was defined as CysC < 1 mg/L or eGFR > 90 ml/min/1.73 m².

Results: The underlying IF diagnosis was short bowel syndrome in 15/45, enteropathy in 8/45, motility disorder in 14/45, 6/45 were post bone marrow transplantation and 2/45 had Crohn's disease. 24/45 patients received HPN for 2-5 years and 21/45 for 5-10 years, 4/45 were weaned off PN, 4/45 were on total PN. In 2017 26/45 children had a normal CysC compared to 36/45 with normal eGFR, 19/45 (42%) had an abnormal CysC compared to 9/45 (20 %) with abnormal eGFR. In 2018 30/45 patients had a normal CysC compared to 40/45 with normal eGFR, 15/45 (33 %) had an abnormal CysC compared to 5/45 (11 %) with abnormal eGFR.

Conclusion: RD is associated with HPN. A higher proportion of RD is diagnosed by CysC compared to eGFR (p = 0.02/2017; p = 0.006/2018).

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2. Roos JF, Doust J, Tett SE, Kirkpatrick CM. Diagnostic accuracy of cystatin C compared to serum creatinine estimation of renal function in adults and children – a meta analysis. Clin Biochem 2007; 40: 383-391

P4.32 - Digestive autonomy in patients with intestinal failure after small bowel transplantation

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12 de Octubre Hospital

Introduction: Home parenteral nutrition (HPN) and all the complications related to it, used to be the only option in patients with intestinal failure. Nowadays small bowel transplant (SBT) is an answer to these patients.

Methods: From December 2004 to January 2019 we have assessed 105 patients as potential candidates, the majority of them not eligible; and have performed 31 transplants in 29 patients (21 IT and 8 MVT).

Results:

Short bowel syndrome (SBS) was found in 60% (18 / 29) of the patients.

Potential candidates for SMT were malnourished, with a mean pretransplant BMI of 22.2, average weight of 61.6kg and pre albumin values around 21.7mg / dl. 64% of the patients required total HPN before the SBT and almost 86% had several HPN-related complications due to it (6% thrombosis of major venous access, 37% catheter -related infections, 28% sepsis, refractory balance alterations.

After SBT the patients in our study reached a mean BMI of 23.7,mean weight of 67.8kg and pre albumin values around 26.7mg / dl. All recipients achieved satisfactory oral nutritionat about post-transplant day 12. Almost 80% of the patients required parenteral nutrition support during the first two months post-transplantation.

SBT recipients will need some form of parenteral nutrition support for an average period of 27 months including the time before and after the SBT.

One year after undergoing transplantation, all recipiets will achieve a complete digestive autonomy and only 8,3% will need fluid replacement therapy.

Conclusions: Small bowel transplantation is a life-saving procedure for patients with intestinal failure who develop complications related to parenteral nutrition, and it is the most effective treatment in terms of complete digestive autonomy acquisition for these patients

P4.33 - Operational tolerance can be achieved after intestinal transplant: first report and mechanistic analysis

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Introduction: Transplantation tolerance is a highly sought and rarely achieved state in clinical medicine. Defined as long-term stable and acceptable graft tolerance without immunosuppression and with an otherwise competent immune system, tolerance maximizes graft survival and function and decreases organ demand without the negative side effects of immunosuppression. While there have been prior reports of tolerance after liver and kidney transplantation, we herein report and mechanistically characterize the first case of tolerance after intestinal transplantation.

Methods: Intestinal transplantation was performed using our standard method. Immunosuppression for induction was thymoglobulin and steroids and for maintenance was tacrolimus. Graft and blood lymphocytes from the patient, 8 stable intestinal recipients, and 8 healthy controls (blood only) were analyzed using flow cytometry. Recipient T cell responses to donor and third party antigens were assessed by Pleximmune (proprietary).

Results: We performed intestinal transplantation on a 14-year old male for severe pseudo-obstruction. Subsequently lost to follow up, he presented 7 years post-transplant and 3.5 years after stopping all immunosuppression with no graft problems. Biopsy showed pristine allograft histology. Given his history of GVHD, we hypothesized that central tolerance was mediated by chimerism. However, serial peripheral chimerism studies did not show donor chimerism. Thus, we speculated that he had peripheral tolerance mediated by regulatory T cells (Treg). This was confirmed by flow cytometric analysis showing that, compared to both sets of controls, the patient's blood and graft had higher levels of naïve and lower levels of effector memory CD4 / CD8 as well as higher Treg percentages. Demonstrating immunocompetence, recipient T cells robustly produced IL-17, TNF-α, and IFN-γ when stimulated by PMA / IO and highly upregulated antigen-specific CD154 expression in response to CMV and EBV antigen stimulation ex vivo. Critically, donor-specific hyporesponsiveness was confirmed by 2-fold higher CD8+CD154+ T cell response to 3rd party vs. donor lymphocytes in mixed lymphocyte reaction.

Conclusion: This represents the first report of tolerance after intestinal transplantation. Mechanistic analysis demonstrates that peripheral tolerance mediated by increased Tregs and decreased effector memory cells in both graft and blood appears to play a role.

P4.34 - Long term use of Teduglutide (TED) for Type III Intestinal Failure (III-IF) in Adults Patients (pts). A single center experience.

Hector Solar, Mariana Doeyo, Gabriel Gondolesi, Adriana Crivelli

Hospital Universitario Fundacion Favaloro

Introduction

III-IF is a highly invalidating condition which requires long term parenteral nutrition (PN).The most frequent cause is post-surgical short bowel syndrome (SBS). Less than 50% of pts would be able to reach rehabilitation within 2 years. Favorable outcomes rely on, post-surgical intestinal length (PSIL), anatomy type (PSAT) and the presence of ICV. Over the last years the use of TED has changed the course of this disease, challenging the classically accepted predictors for favorable outcome.

Aim:

Report the experience using TED for Type III-IF in adults, single and first center experience in Latin America.

Material and Methods:

Data from TED treated pts from 2014 to 2018 was collected and analyze, including: Age, gender, PSIL: a): < 50cm., b) 51-99 cm., c)>100 cm; PSAT: 1) terminal jejunostomy, 2) jejuno-colonic anastomosis and 3) jejuno-ileo-colonic anastomosis; freedom from PN survival and comparison of outcomes to previous reports, and drug adjustments made over time, were analyzed using SPSS v20.

Results:

Twelve adult pts have been treated since 6/2014. 11 received AGIRS. Mean age: 40.5 years, 50% male; 7/12 had PSIL: a). Six pts had PSAT: 3); five: 2) and only one: 1). Mean PN volume during admission was 20.37 +/- 5.72 (range: 10-28) Lt/week. All patients received standard treatment for SBS, and most of them could reduce PN volume to 12.5 +/- 4.73 (range:6-21) Lt/week. 7/12 pts are currently PN free, three of them with PSIL: a) and four with PSIL:b). Compared to the 2015 report, the percentage of pts able to achieve intestinal autonomy increased from 74 % to 83%, and from those in the PSIL a) group PN independency grew from 0% to 33%, and in the PSIL b) group went from 67% to 91%. Results are shown in table (1) and figure (1). Two pts are currently off PN, and off TED; and 1 of them has been able to sustain a successful pregnancy; 2 pts have been on every other day doses due to abdominal bloating and discomfort for 14 and 7 months respectively, sustaining weight and urine output.

Patient	AGIRS	Age/Gender	PSIL/PSIA	PN Vol. hospital discharge (Lt)	PN Vol at beginning of treatment (Lt)	Time of treatment with GLP2 (weeks)	Actual PN2 volume (Lt)	Initial Weight/ Actual Weight (kg)
1	Yes	24 / F	00 / 3	21	10	28	0	63.7/61.5
2	Yes	39 / F	15 / 2	15.5	12	54	0	48.4/43.5
3	Yes	39 / M	75 / 2	28.5	10	5	0	82/86.4
4	No	48 / F	100 / 1	21	21	24	10	67/63
5	Yes	30 / F	00 / 2	10	10	12	0	50.1/44.6
6	Yes	18 / M	16.5 / 3	10	10	24	0	51/49.9
7	Yes	64 / M	25 / 3	28	18	30	0	70/67.5
8	Yes	30 / F	00 / 2	21	6	12	0	56/49.7
9	Yes	31 / M	15 / 3	21	17.5	9	10	53.1/51.5
10	Yes	40 / M	5 / 2	21.5	17.5	8	15	58.2/62
11	Yes	50 / F	10 / 3	21	10	8	6	46.5/48.6
12	Yes	66 / M	22 / 3	28	8	4	8	63.5/53.8

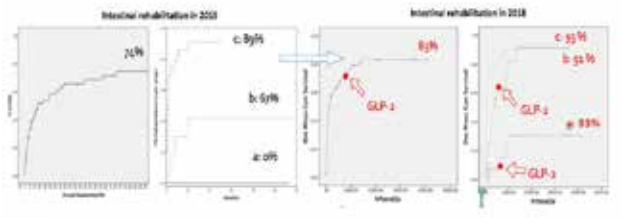

Figure 1

Conclusions:

TED is the first gut hormone commercially available proven to enhance intestinal rehabilitation in patients with SBS and III-IF. The use of TED in this very selective initial group of patients validates previous reports performed in developed countries. It adds the concept of using it after AGIRS, allowing not only to recover intestinal sufficiency but also to reduce the time to achieve it, even with unfavorably anatomy.

P4.35 - Children with complex intestinal failure benefited from the expert multi-disciplinary review- A retrospective study

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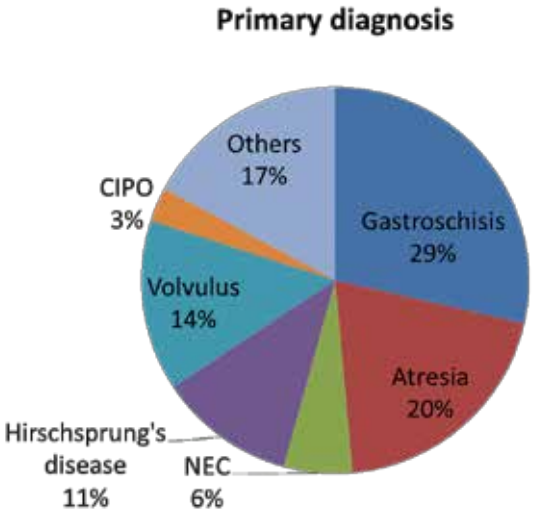
Introduction: Home parenteral nutrition service was established at Birmingham Children's Hospital since 1987. Since then, the service has grown and the unit provides a second opinion to local, national as well as international complex intestinal failure (IF) patients. There is limited literature looking into the benefits of a multi-disciplinary team (MDT) in intestinal failure. This study aims to provide some initial data.

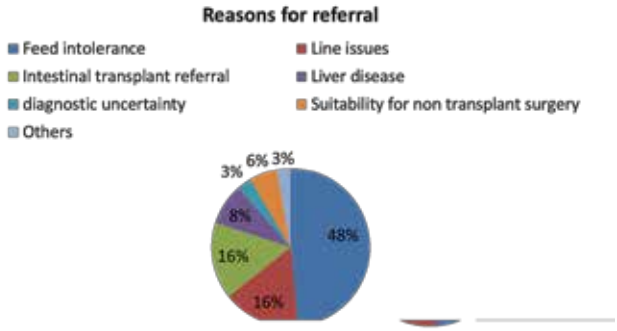
Methods: We did a retrospective data analysis over a 4-year period from January 2015 to December 2018 of all the children who have been discussed in our monthly multi-disciplinary IF planning meeting. We analysed their background diagnosis / reasons for referral / main advice given by the nutritional support and intestinal failure team (NSIF team) and their outcome as of January 2019.

Results: Over this period we had given our input for 61 patients with 70 consults with a male to female ratio of 1.8:1.

There were 4 non-UK referrals, 56 (80%) external UK referrals and 10 (14%) internal referrals. The median age at presentation was 5years, ranging from 1month to 16years.

As of January 2019, 19% had either come off parenteral nutrition (PN) or had reduced PN. 4% had small bowel transplant. One patient died post-transplant and the other whilst awaiting transplant. We are not aware of the outcome in 42%. 31% had no change in their clinical outcome.





Conclusion: Gastroschisis is one of the most common referred diagnoses, despite necrotising enterocolitis (NEC) being the most common reason for home parenteral nutrition. This might reflect difficulties faced by the clinicians dealing with complex gastroschisis possibly with dysmotility. The most common reason for referral was feed intolerance or non-progression. 19% either came off PN or had PN reduced after MDT advice / actioning, signifying the importance of obtaining advice from centres with IF expertise. 42% unknown outcome signifies more regular communication with the referral teams to determine the value of the meetings for the parent site.

P4.36 - Transition from pediatric to adult intestinal transplant services: a multidisciplinary collaboration for development of a successful transition program

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Introduction: Thanks to increased knowledge in how to treat children undergoing intestinal or multivisceral transplantation, the number of patients graduating from pediatric to adult care is expected to increase. To this date, 9 intestinal pediatric transplantations have been performed with a 5 year survival, close to 90%. Three patients have transitioned to adults. Intestinal and multivisceral transplanted are fragile patients. According to our experience they don´t mature normally. They risk pain-killer addiction and reduced psychological well-being. In addition, adolescence is a period of increased search for independence and rebellious behavior. Previous studies of young transplanted adults show that the transition process may manifest as non-adherence and lack of engagement with medical services. There are reasons to believe that these findings are highly applicable to young adults with intestinal or multivisceral graft. At Sahlgrenska University Hospital a multidisciplinary, intestinal failure center (TSC) including adult and pediatric care has been founded. This unique organization provides new opportunities to develop an adapted, person-centered transition program, aiming to ensure a successful transition.

Methods: We have used our experience from the transition process of liver transplanted adolescents and modified the program to intestinal or multivisceral transplanted patients. We have established two new roles - transition coordinators; one at the children hospital and one at the adult hospital. These two nurses are responsible for the overall transition process and collaborate closely. Once a month a multidisciplinary conference is held at TSC and the transition coordinators can report progress, discuss patient problems and update the individual transition plan. A set of screening instruments to identify symptoms, evaluate wellbeing and assess adherence has been agreed.

Results: Preliminary findings from this work is reported. The team conferences enables effective decisions and improved team work. The transition coordination provides security for the patient, the parents and the team. The screening instruments improve assessment, dialog and education in patient contact.

Conclusion: This transition program and new unique organization contribute to a higher level of adherence to both long-term medication and lifestyle changes, and thereby increase chances for improved quality of life and graft survival.

P4.37 - Extra-Intestinal Manifestations of Children with Genetically Confirmed Microvillus Inclusion Disease

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Objectives: Microvillous inclusion disease (MVID): congenital disorder caused by MYO5B or STX3 mutations. Pathognomonic features are severe intractable diarrhoea and malabsorption due to intestinal brush border atrophy, accumulation of lysosomal granules and microvillus inclusions in the apical cytoplasm of enterocytes. All epithelial tissues express MYO5B but gut involvement is classically described.

Method: Two males: A, 2-year-old Pakistani and B, 12-month-old Kuwaiti with MYO5B mutation.

Results: Patient A: Neonatal secretory diarrhea with high fluid and electrolyte requirements, deteriorated on feed introduction. Duodenal histology: blunted villi, hyperplastic crypts, loss of surface epithelium, goblet cell depletion and apoptosis. Periodic acid–Schiff (PAS) and CD10 staining suggested MVID, confirmed by electron microscopy (EM). Genetics: homozygosity of MYO5B gene: c.1087C>T mutation. He was discharged on home parenteral nutrition (PN) at 10 months with ongoing high volume and sodium demands, gradually worsening diarrhea and minor transaminitis in his first year but otherwise stable liver function. Annual PN screening showed low TMP/GFR (0.89mmol/L), elevated cystatin C (1.27mg/L), biochemical evidence of renal tubular leak and radiological signs of rickets but no nephrocalcinosis. Fanconi syndrome was diagnosed. Currently on 24hr PN (250ml/kg) with large amounts of electrolytes, phosphate, acetate with over 20 watery stools/day. He was referred for small bowel (SB) transplantation.

Patient B: Neonatal watery diarrhea and severe acidosis with feed introduction. He was commenced on PN, tertiary referral to London at 2months; arriving in poor nutritional status, marked conjugated hyperbilirubinemia and transaminitis. SB mucosal biopsies demonstrated total villous atrophy, focally vacuolated superficial epithelium and few intraepithelial lymphocytes. PAS and CD10 staining suggested MVID confirmed by EM. Genetics: compound heterozygosity for MYO5B gene mutations; c.1576C>T; p. and c.2111del; p. variant. Liver biopsy: lobular cholestasis, hepatocyte giant cell transformation and bridging fibrosis. He currently tolerates small amount of an amino-acid based formula and 170ml/kg/day PN with 10-hours break; with stable diarrhea (6-7/day). Due to severe liver injury and long term PN, he is being assessed for combined liver and SB transplantation.

Conclusion: MVID has variable phenotypes, with other organ involvement such as liver and kidney apart from the gut.

P4.38 - Bleeding episodes following intestinal transplantation- think outside the box

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Introduction: In intestinal transplantation (ITx), bleeding from the intestinal tract is a rare complication and the differential diagnosis include infection, rejection, and PTLD. We report on a case series with bleeding from ectopic varices

Methods:

Case 1: 15 year old girl (intestinal pseudo-obstruction) presented with bleeding from the stoma, 8 years after Liver ITx . Graft biopsies excluded rejection and PTLD. An upper GI endoscopy (UGIE) showed no evidence of active bleeding. Repeat UGIE 3 wks later showed a cluster of varices at the upper graft anastomosis . ATIPPS was performed which stopped the bleeding. Two mths after TIPPS, she had recurrent bleeding from the jejunal varices, despite an patent TIPPS. She developed multi-organ failure and she eventually died.

Case 2: A 8 year boy (MVID), presented with malaena & splenomegaly 4 years after isolated ITx. CT Angio revealed a patent portal vein & intra-abdominal varices in small bowel. A further UGIE revealed varices at upper graft anastomosis and were injected with thrombin. A TIPPS was performed, which stopped bleeding. He developed multiorgan failure and subsequently died.

Case 3: 3 year old girl (gastroschisis) presented with recurrent intermittent bleeding from the stoma 1 year after Liver ITx. A initial UGIE showed no bleeding point and graft biopsies were normal . Video-capsule endoscopy done showed no varices. CT angio could not pinpoint the location of bleeding, but demonstrated occlusion of porta-caval shunt. Due to ongoing blood transfusion requirements, a further UGIE showed varices at the junction of the upper graft anastomosis. The child continues to have intermittent episodes of bleeding but the family has declined a definitive surgical option.

Discussion: The bleeding episodes in our children originated from the ectopic varices that developed at level of the upper graft anastomosis due to altered hemodynamics following portacaval shunt blockage in two liver ITxgrafts . In the child with isolated ITx, it was due to progression of liver disease and possibly because of adhesions from repeated abdominal surgeries, which then predisposes to the development of collaterals at the upper graft anastomosis.

Conclusion: Ectopic varices should be in the differential diagnosis of children presenting with bleeding episodes following ITx especially when the graft biopsies are normal.

P4.39 - Citrate-taurolidine lock solution: impact on the incidence of catheter related bloodstream infections in children with intestinal failure receiving home parenteral nutrition

Juliana Resende do Nascimento, Heitor Pons Leite, Larissa Resende dos Santos, Keilla Mayumi Uchoa, André Ibrahim David, Maria Fernanda Carvalho de Camargo

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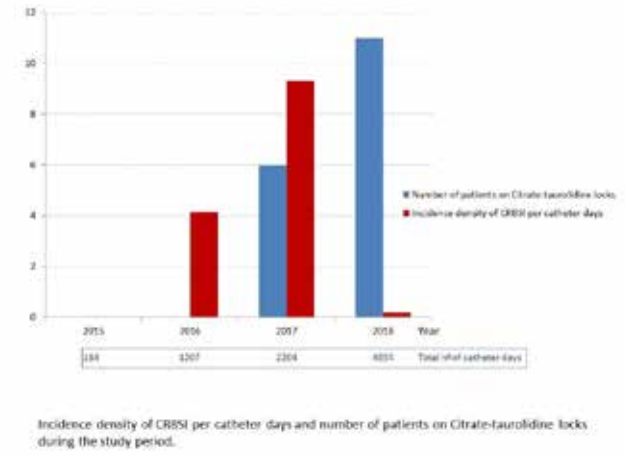
Introduction: The use of central venous catheters (CVC) for parenteral nutrition (PN) administration has increased survival rates and allowed patients with short bowel syndrome who are dependent on long-term PN to be discharged for home care. However, catheter related bloodstream infection (CRBSI) remains as a major complication of long-term PN and is associated to increased morbidity, mortality, length of stay and hospital costs. Several lock solutions have been used to prevent CVC contamination. Among them, the citrate-taurolidine solution (composed of 2% taurolidine and 4% citrate), which is unique by reducing the biofilm formation of bacterial cells and avoiding bacterial adhesion and clotting in the catheter. We aimed to identify the rates of CRBSI before and after the use of the citrate-taurolidine solution in de-hospitalized children receiving home PN.

Methods: This was a prospective cohort study in 11 children with intestinal failure (IF), mean age 35.4 months (12.7), receiving home PN and followed-up at a center for intestinal rehabilitation between July 2015 and November 2018. The rate of CRBSI was calculated for each patient by the incidence density ratio, defined as number of infections per 1,000 catheter-days. The citrate-taurolidine solution began to be used from March 2017 onward. The primary outcome was the variation in the rate of CRBSI before and after use of citrate-taurolidine lock solution.

Results: The median time on PN was 26.4 months (interquartile range 15.2 - 32.9). The mean number of catheter days per patient before and after taurolidine were 178 (interquartile range 32 - 85.5) and 238 (interquartile range 203 - 386) days, respectively. There were 13 episodes of CRBSI before and only one episode after the use of citrate-taurolidine line locks. The incidence density of pre-taurolidine CRBSI was 5.7 and of post-taurolidine was 0.3 per 1000 catheter days. The main microorganism identified was Staphylococcus epidermidis.

Conclusion: The rate of CRBSI was greatly reduced after the citrate-taurolidine use; this lock solution should be the first choice in reducing CRBSI in children with IF receiving home PN.



Incidence density of CRBSI per catheter days and number of patients on Citrate-taurolidine locks during the study period.

P4.40 - Severe hypothyroidism and metabolic encephalopathy in a child receiving long-term home parenteral nutrition without selenium

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Introduction: Selenium is essential in the protection against oxidative stress, for optimum immune response and for thyroid hormone biosynthesis and metabolism.

We describe a case of chronic selenium deficiency with severe hypothyroidism and metabolic encephalopathy in a child with ultra-short bowel syndrome receiving long-term home parenteral nutrition (PN) without selenium supplementation.

Methods: The patient is a 4-year-old girl, born prematurely at 26 weeks of gestation, birth weight 670g. At the 13th day of life she was diagnosed with necrotizing enterocolitis and required exploratory laparotomy. There was necrosis of the small bowel and need of extensive resection, with 3 cm of small bowel and half of colon remaining. After the surgery, she was started on exclusive PN containing a fixed dose of multi-trace element solution but lacking selenium, probably due to drug shortage. After a one-year hospitalization, she was discharged and continued to receive PN at home. At 3 years old she presented with converging strabismus and regression of motor development. Initially she had inability to ambulate, which worsened until she couldn't walk, sit and talk. At that time, she was diagnosed with decompensated hypothyroidism, requiring T3 and T4 replacement therapy.

Results: At the age of 3 years 8 months, she was referred to our intestinal rehabilitation center for investigation. On examination she had an edematous face, muscle weakness, irritability and depigmented hair. Plasma selenium levels were undetectable. The diagnosis of encephalopathy and myxedema secondary to severe selenium deficiency was made. Intravenous selenium repletion therapy was initiated (4 µg / kg / day), followed by 2 µg / kg / day as maintenance and, as selenium plasma levels normalized, the need of T3 replacement was reduced until it was discontinued and maintenance treatment with levothyroxine isolated was initiated. She was discharged from hospital to home care four months later at the age of 4. After selenium levels restored to normal, neurological signs improved progressively and growing hair was repigmented. She continues to receive physio, speech and occupational therapy and she is progressing well.

Conclusion: Chronic selenium deficiency caused severe hypothyroidism and metabolic encephalopathy in a child receiving exclusive long-term home PN without selenium. Patients on long-term PN need selenium supplementation to avoid serious clinical manifestations of deficiency.

P4.41 - Intestinal Transplantation in children, evolution of its applicability over the last 12 years in a single center.

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Introduction: Intestinal transplantation (ITx) has been accepted worldwide as a valid treatment for intestinal failure when other options for medical o surgical rehabilitation have failed and severe complications related to intestinal insufficiency have emerged.

The aim of this study is to show how the prevalence and indications for ITx evaluation and ITx in children have evolved over the last twelve years in a single Intestinal Rehabilitation and Intestinal Transplant Program in Argentina.

Material and methods: This is a retrospective review of a prospectively filled database, from March 2006 to December 2018, including every patient <18 years of age with intestinal failure that was referred to this Program. Demographic data, diagnosis, indication for evaluation and indication given according to evaluation are analyzed. Patients were divided into three periods for analysis and comparison: 1= 2006-2009; 2= 2010-2013 and 3= 2014-2018.

Results: A total number of 102 Pediatric patients with chronic IF were referred to the Unit over the studied period (41 patients in Period 1, 36 patients in period 2 and 25 patients in period 3). From the total number, 66 patients were referred for ITx evaluation and are analyzed here; 23 were female, the primary diagnoses were: intestinal atresia (12); long segment Hirschsprung's (11); gastroschisis with atresia (9); no neonatal volvulus (8); gastroschisis (8); NEC(6); perinatal volvulus (4); CIPO (3); microvillous inclusion disease (2); others (3). At the time of ITx evaluation the mean age was 38 months (SD±44), their mean time on PN was 29 months (SD± 37). Table 1 shows indications for ITx evaluation divided by period and Table 2 shows the treatment implemented / patient's clinical course after the evaluation was completed.

Table 1. Main reason for ITx evaluation

Year of ITx evaluation	ITx eval (n)/ Pts referred (n)	CVAL*	IFALD**	Hydroelectrolytic disorders	Recurrent Sepsis	Other
2006-09	28/41 # & ¶	12 (43%)	6 (22%)	8 (28%)	1 (3.5%)	1 (3.5%)
2010-13	28/36 #	17 (61%)	7 (25%)	2 (7%)	1 (3.5%)	1 (3.5%)
2014-18	10/25 & ¶	8 (80%)	2 (20%)	0	0	0

*CVAL central venous access loss, **IFALD intestinal failure associated liver disease.
 # (p ns)
& (p 0.02)
¶ (p 0.003)

Table 2. Treatment implemented/patient's clinical course after ITx evaluation

Year of ITx evaluation	Transplanted	Contraindication due to Lack of CVA*	Dead or worsening of clinical condition	Drop out from WL** due to improvement	Family refusal for ITx	No ITx indication	Change of Center	Currently on WL**
2006-09 n=28	15 #	3	4	2	1	2	1	0
2010-13 n=28	10	2	5	1	5	4	1	0
2014-18 n=10	2 #	1	2	1	0	3	0	1

*CVA central venous accesses, ** WL waiting list.
 # p 0.03

Conclusions: The number of ITx evaluations and the indication of ITx have suffered a significant decrease since 2013. The number of patients excluded from the WL due to clinical deterioration and number of deaths while on WL reflects both, late referrals and scarcity of pediatric donation. Loss of central venous accesses continues to be the main indication for ITx referral and lack of venous accesses has been the main cause for contraindication of ITx in this program.

P4.42 – Teduglutide: Intestinal rehabilitation in children, our initial experience.

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Background and aim: Teduglutide (TED), a synthetic analog of glucagon-like peptide 2, has been recently approved by the European Union to promote intestinal rehabilitation in pediatric patients with chronic intestinal failure secondary to short bowel syndrome. We aim to present the first series of paediatric patients treated in Argentina.

Material and methods: This is a retrospective review of a prospectively filled database, including every patient <18 years of age treated with TED at a single Intestinal Rehabilitation and Transplant Unit. Demographic data, diagnosis, nutritional status, parenteral support as % of the basal metabolic rate (no protein Kcal), intestinal anatomy, outcome and adverse effects are presented.

Results: From a total of 62 children with short bowel syndrome followed in the Unit, 4 patients started treatment with TED (dose 0.05 mg / kg / d, administered subcutaneously once a day). Table 1 shows baseline data and Table 2 follow up data.

Table 1. Parenteral support and patients' data when TED* treatment was started

Patient Sex	Diagnosis	Intestinal Anatomy	Age when TED* started IF duration (Years)	BMI/Age Height/Age Z-score	PN** support •No protein Kcal •# infusions/week •Liters/week
1 M	Atresia IIIA Imperforate anus	Type 3 A 20 cm jejunum + 3 cm Ileum ICV present Whole colon	6 6	1.32 -3.66	80% 6/7 8.1
2 M	Mid gut volvulus	Type 2 A 30 cm jejunum Transverse colon	17.1 11.4	-0.68 -2.01	98 % 6/7 9.0
3 M	Gastroschisis and atresia	Type 2 A 8 cm jejunum Transverse colon	12.7 12.7	-0.27 -1.70	83% 7/7 14.7
4 F	Trauma	Type A 15 cm jejunum Transverse colon	12.9 2.7	0.28 0.30	79% 6/7 14.4

*TED teduglutide, ** PN parenteral nutrition

Table 2. Patients data at last follow up visit and adverse events registered

Patient	Week of treatment	PN support No protein Kcal # infusions/week Liters/week PN Reduction (%)	BMI/Age Height/Age Z score	Adverse effects
1	101	0 0 0 100%	0.97 -2.61	Upper respiratory tract infection Injection site bruises
2	44	0 0 0 100%	-1.3 -2.02	None
3	14	72% 6/7 12.9 28%	-0.43 -1.61	Pharyngitis Epigastric pain Injection site bruises
4	8	73% 5/7 11.7 27%	0.73 0.28	Abdominal pain Dark color of urine

Conclusions: TED treatment was well tolerated and has allowed, up to last follow up, achieving intestinal autonomy in half of the treated patients, and a significant PN requirement reduction in the rest. The four treated patients had been chronically PN dependent, and had failed other medical or surgical alternatives to reach intestinal autonomy.

P4.43 - Evaluation of accessibility to intestinal failure therapy and transplant, in a center from an emergent economy country

Liliana Marta Martinez, Carolina Rumbo, Maria Ines Martinez, Gabriel Eduardo Gondolesi

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Introduction: In Argentina the health care (HC) is provided by a multi-payer system including both, State and Private HC organizations. Chronic IF care is provided by both systems, but intestinal transplant (ITx) is only offered in the private structure. In Argentina, chronic IF was officially included among the visceral disabilities (VD) in 2011. The Federal Government grants a certificate to individuals with VD; this benefit allows them not only the full access to HC coverage including PN and ITx, but also gives them free admission to public transportation and provides them a pension. In addition, VD is not an impairment to get employment in a public or private work. In spite of the existence of a theoretical adequate access to VD certificate, there is still a lack of knowledge and education on how to obtain it, becoming a barrier, delaying or precluding its accessibility.

Aim: To analyze the accessibility to IF therapy and ITx in our center and to measure the impact of the social worker intervention

Material and methods: This is a retrospective review of a prospectively filled database with IF patients that were evaluated for ITx at our Intestinal Failure, Rehabilitation and Transplant Unit, from March 2006 to December 2018.

Patients were divided in three categories according to their HC coverage and it was recorded for each patient when IF was diagnosed and when ITx evaluation was performed:

1) Patient's paid health insurance (PHI): a) Private insurance (PI); b) Employer and Union sponsored plans (EUSP)

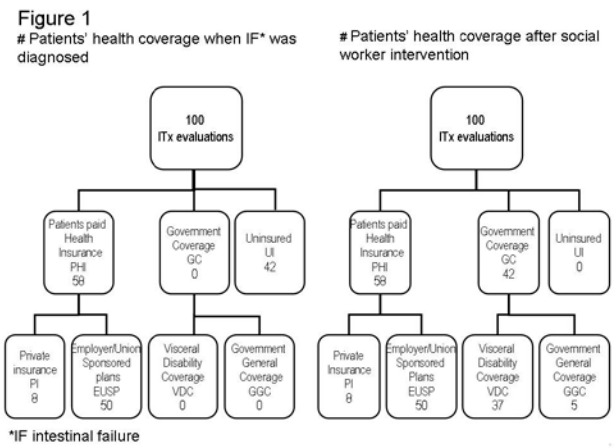
2) Government coverage: (GC) a) Visceral Disability coverage (VDC) b) General government coverage (GGC)

3) Uninsured (UI)

Results: A total of 100 patients were analyzed (Figure 1): when IF was diagnosed, 58 had PHI (50 [86%] PI and 8 [14%] EUSPI) and 42 patients were UI.

Due to social worker intervention, when referred for ITx evaluation, all the UI patients could obtain GC (37 patients [88%] got VDC and 5 [12%] got GGC), in order to have access to IF treatment including ITx.

Figure 1



Conclusions: Although many of the IF patients had PHI when IF was diagnosed, a high percentage had no coverage and due to specialized social worker intervention they could obtain GC, allowing them to get appropriate treatment for their medical condition. Rare diseases require a multidisciplinary approach for the diagnosis, treatment and the suitable use of the available social resources to obtain adequate access.

P4.44 - Transhepatic central venous catheter placement for long-term parenteral nutrition in a patient 10 years after intestinal transplantation: a case report

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Introduction: Patients with end-stage intestinal failure require long-term total parenteral nutrition (TPN) via central venous access; however, recurrent episodes of line sepsis and multiple replacements of central venous catheters may cause venous thrombosis, resulting in loss of all central venous access. Herein, we report our experience in a patient with end-stage central venous access failure 10 years after intestinal transplantation.

Case report: A 12-year-old girl with intestinal failure due to allied disorders of Hirschsprung's disease underwent deceased intestinal transplantation. The proximal end of the intestinal graft measuring 320 cm in length was anastomosed in an end-to-end fashion to the recipient's duodenum and the distal end was brought through the abdominal wall as a single-barrel ileostomy (cold ischemia time, 7 h 18 min; warm ischemia time, 43 min). Venous outflow from the intestinal graft was conveyed into portal venous circulation. At the time of transplant, left internal jugular vein was the only patent central venous access and all other central veins were occluded by frequent episodes of catheter-related infection resulting in venous thrombosis. After the transplantation, she suffered multiple bouts of enteritis both from cytomegalovirus and bacterial infection and acute cellular rejection, which eventually lead to intestinal graft failure. She was forced to go back to long-term TPN. Thereafter, her left internal jugular vein got occluded and a computed tomography scan revealed her left hepatic vein to be the only patent central vein that was accessible percutaneously. We placed a Broviac catheter in the left hepatic vein via percutaneous and transhepatic route, 9 years after transplantation. The catheter was displaced accidentally 8 months later, and we safely exchanged the catheter under the same approach. At the time of this report, her oral intake is limited to fat-free liquid diet. She now weighs 27 kg and is on tacrolimus (target trough level, 2-3 ng/ml), prednisolone 5 mg QD, and mycophenolate mofetil 1000 mg QD. She is currently under evaluation for intestinal retransplantation.

Conclusion: Transhepatic central venous catheter placement is a viable option in a patient with end-stage central venous access failure; however, its long-term management to prevent accidental removal has yet to be defined.

P4.45 - Infective Endocarditis as a complication of central venous catheters used for Home Parenteral Nutrition: experience from a national Intestinal Failure Centre

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Introduction:, The management of intestinal failure (IF) requires the safe and sustained delivery of parenteral nutrition (PN) via long-term central venous catheters (CVCs). Infective Endocarditis (IE) is a recognised complication of indwelling CVCs in a number of medical conditions, for example, the incidence of IE was 483 per 100 000 person-years in haemodialysis patients, while it was 6.5 per 100 000 person-years in the general US population. Indeed, recent ESPEN guidelines on the management of acute (type 2) and chronic (type 3) IF highlight IE as a potential complication. However, there are no published data on the incidence and outcomes of IE in patients with IF.

Methods: This is an observational study conducted on all patients with type 2 or 3 IF admitted to a national IF Unit between January 2010 and December 2017. Patients with transthoracic(TTE) and/or transoesophageal(TOE) echocardiography evidence of IE were identified from a prospectively maintained IF database and hospital coded procedures. The diagnosis of IE was based upon Modified Duke's Criteria, with positive blood cultures, together with a characteristic vegetation appearance on echocardiography, in combination with expert cardiology review. Details of organisms, heart valves involved and antibiotics prescribed were extracted from the patient notes, together with appropriate clinical outcomes.

Results: 332 of 432 patients with indwelling CVCs admitted during the study period underwent a total of 534 echocardiograms. 513 TTE and 21TOE were performed. 2 patients were diagnosed with IE both involving native aortic valves and both visible on TTE and TOE. One patient (diagnosed with Enterococcus faecalis IE) had type 2 IF at admission from a referring hospital for ongoing treatment for IE with persistent pyrexia, splinter haemorrhages and regurgitant murmur; clinical symptoms resolved with IV Amoxicillin and Gentamicin but valve replacement was required due to severe Aortic Regurgitation. The second patient (Coagulase-negative Staphylococcus with type 3 IF) was admitted with a CRBSI, low grade pyrexia and intermittent rigors and treated with IV vancomycin and currently remains under cardiology follow up pending potential valve replacement.

Conclusions: CVC-associated IE is a very rare complication of CVCs implanted for types 2 and 3 IF. However, as noted in our case series, the potential morbidity associated with this condition means that a high index of suspicion should be maintained.

P4.46 - Pediatric Intestinal Retransplantation: Outcomes In A Referal Center

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Purpose: Intestinal retransplantation is required in more than 10% of long term survivors, especially in those who underwent isolated intestinal transplantation. However, no clear guidelines are available regarding indications, type of graft and immunological management. Our aim is to report our experience after retransplantation in children.

Material and methods : A retrospective study of pediatric intestinal retransplantation performed in our center in the last 15 years (2003-2018) was conducted.

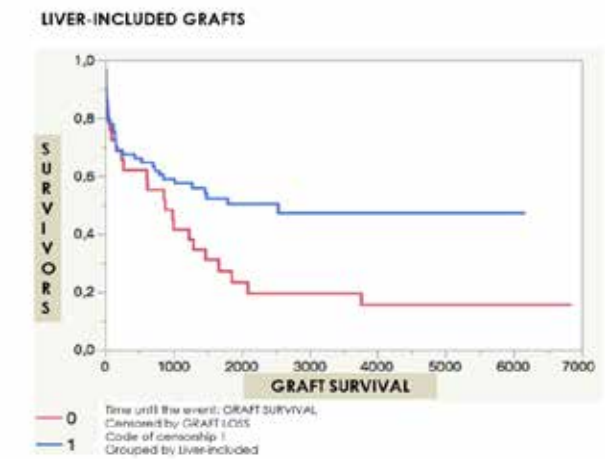
Epidemiological and anthropometric data, number of grafts received by each patient and the type of these with or without liver inclusion, causes of graft loss and recorded DSA data were analyzed.

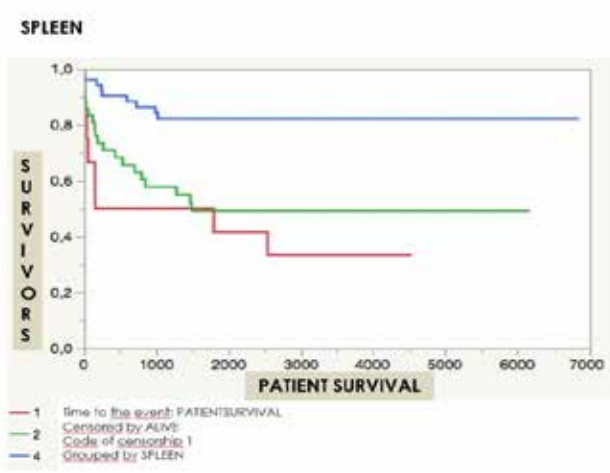
Results: A total of 18 patients were retransplanted (male predominance, mean age of 5.5yrs), 12 of them twice and 6 three times, totaling 42 grafts implanted. The liver was included in the graft in 22 (4 liver-intestinal -CLSB- and 18 multivisceral -MV-). Overall survival after 5yrs was similar in children undergoing transplantation compared to our general series (63 vs 73%).

Regarding the type of graft, survival after 1 and 5yrs for isolated bowel and liver-including grafts was 20% and 0% vs. 68 and 61% respectively ($p<0.05$).

Preformed DSA were present in 6 cases (14%), 3 of them lost their second grafts. And 2 patients (5%) developed de novo DSA and lost their non-liver included grafts (SB).

Conclusions: Retransplantation in children had long term outcomes similar to the main series. Liver-including grafts showed much better survival. Preformed or the novo DSA had negative impact on graft survival that was attenuated by the presence of the liver. Further studies are warranted to provide better understanding of the role DSA on these patients.





P4.47 - Case Report Of The First Successful Patient Of Isolated Small Intestine Transplantation At Sao Paulo University Hospital

Andre Lee [1], Flavio Galvao [1], RAFAEL PINHEIRO [1], ALICE SONG [1], LILIANA DUCATI [1], RYAN FERREL [2], RUBENS MACEDO [1], WELLINGTON ANDRAUS [1], MARIANNA HOLLANDA ROCHA [1], Lucas Lee [3], Luiz Augusto Carneiro D'Albuquerque [1]

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Objective: The case report about the longest survival of small bowel transplantation and their perioperative complications

Material and method: Male, 22 years, which began in childhood due to a pyloric hipertrophic estenosis and subsequently evolves with intestinal oclusion leading to several procedures in the correction of intestinal fistulas and adherences, resulting in six surgical procedures and ultrashort bowel syndrome by several intestinal resections The patient was submitted at first to parenteral nutrition (PN), in second time to intestinal transit reconstruction and finally isolated intestinal transplant The evaluation parameters were: various blood test including liver, kidney function and electrolytes level, radiological exams, ultrasound, echocardiography, vascular color doppler, endoscopy, colonoscopy and daily evaluation by multidisciplinary team

Results: The patient presented severe malnutrition and was unable to walk with Body Mass Indice (BMI)=11,18 Kg / m2, B1 hypovitaminosis (Beriberi) characterized by cardiac disfunction, thrombosis of various central veins caused by recurrent infections and liver test show moderate cholestasis After six months of nutritional support and three months on post operative period of intestinal reconstruction , the BMI increased to18,1 Kg / m2 and return of normal cardiac function Then was submitted a Isolated Intestinal Transplantation on the fourth day of december / 2017, presenting the following complications: kidney failure, lymphatic fistula, jejunal bleeding and pericardial effusion. But he weaned from NP completely in two months after transplant and reached independent oral feeding.

Conclusion: This case teaches us that despite several severe perioperative complications mainly malnutrition, many central line infections with thrombosis, considered initially palliative treatment, however had excellent evolution and good quality of life until this moment.

P4.48 - Evaluating psychological support services available for intestinal failure patients nationally

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Introduction: New Zealand (NZ) has a population of 4.9 million with a publicly funded health system. The NZ Health Strategy 2016 requires care to be delivered close to home. A multidisciplinary team approach for patients with intestinal failure (IF) is widely accepted and a standard of care (SOC) endorsed by NZ National Intestinal Failure Service (NIFS), this includes access to psychological support services. Clinical network (CN) feedback indicated aspects of the SOC were unable to be delivered due to variability and availability of psychological care. In order to advocate for appropriate services, it was necessary to understand the current psychological and psychiatry services for IF patients.

Method: A web based survey was developed to identify psychological services, referral pathways, appropriateness and desired levels of service provision for IF patients in NZ. The survey contained questions allocated to five categories including occupation details, current psychological care services, access to psychological care and NZ NIFS SOC. The survey was sent to 502 members of the NZ NIFS CN in August 2017. Responses were collated and analysed using Microsoft Excel to identify themes and regional variance.

Results: Forty-one clinicians from 13 of 20 District Health Boards (DHB) completed the survey representing a response rate of 8.2%. Of note, most DHBs contribute multiple staff to the CN and collated responses were sent on behalf of their DHB. Responses confirmed that there is a lack of psychological care services available nationally. This applied equally to both adult and paediatric IF services. It is particularly concerning that respondents identified mental health deficiencies as a reason that 2 of the 10 NZ NIFS SOCs could not be met. Themes highlighted include inconsistencies in availability and adequacy of services between and within DHBs. There is a lack of knowledge of access and referral pathways available for psychological care services.

Conclusion: Findings highlight a disparity in provision of psychological care services in NZ which represents a risk to the NZ Health Strategy 2016 close to home model of healthcare. Every IF patient requires appropriate psychological care as a minimum SOC. Whilst acknowledging that current services have limited capacity the NZ NIFS will continue to advocate for the provision of appropriate and equitable psychological care and engage the CN to identify local psychology and psychiatry services in their DHB.

P4.49 - Home Parenteral Nutrition : www.Necker-HPN-traveling.com

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Introduction: In France, the Hôpital Necker-Enfants Malades Home Parenteral Nutrition (HPN) program is the oldest (certified in 1984) and the largest with ~ 40% of the 380 children currently on HPN. We enrolled > 800 infants and children in our program since 1984. In 2018, it supported 156 children (ages: 3mths-17yrs): short bowel syndrome (SBS) (n=78), congenital enteropathy (CE) (n=28), total intestinal aganglionosis (TIA) (n=22) or chronic intestinal pseudo-obstruction (CIPOS) (n=17); miscell.(n=11). We try to offer the most normal life for the child, parents & siblings: family life, school attendance, physical & cultural activities..., and vacations. In France, holidays are sacred...!!. Moreover, some children have their grand-parents living outside France, especially in North Africa, the French islands (Caribean & Indian Ocean), Turkey, Portugal.... Until recent years, holidays outside of France were like an unreachable dream. Thanks to our experience of vacations within France and with our multidisciplinary approach and mutual trust with families, we crossed progressively the French borders. Nowadays, 23 different countries have been visited by 21 families.

Methods: the HPN vacations organization involves nurses, MD, pharmacists, psychologist, social worker.... It requires time and should be anticipated at least 2 months before departure. Contacts are established with airlines companies for transporting material in the aircraft both in the cabin and in the hold. Local medical and nursing contacts are established, while medical recommendations are delivered regarding emergency situations and the management of hot weather conditions.

Results: In 2018, 20 children went to foreign countries or French Islands. IF causes: SBS (n=9), CE (n=7), TIA (n=4). Children received PN 3 to 7 nights a week, with bags from the French usual provider, completed if needed by a local hospital pharmacy (n=4). Destinations were: Morocco, Algeria, Turkey, Greece, Tunisia, Caribeans, Portugal, Thailand,...Stay in the country ranged from 1 to 8 weeks. Only one child had an harmful event with a dehydration.

Conclusion: According to the very successful and enjoyable experience for the families, we do encourage an increasing number of families to do the same whenever financially possible. We suggest our colleagues and friends in charge of a HPN program to set up a "HPN travel agency"..... for offering families great holidays and happiness.

P4.50 - Sequential autologous bowel reconstruction for near-total intestinal aganglionosis

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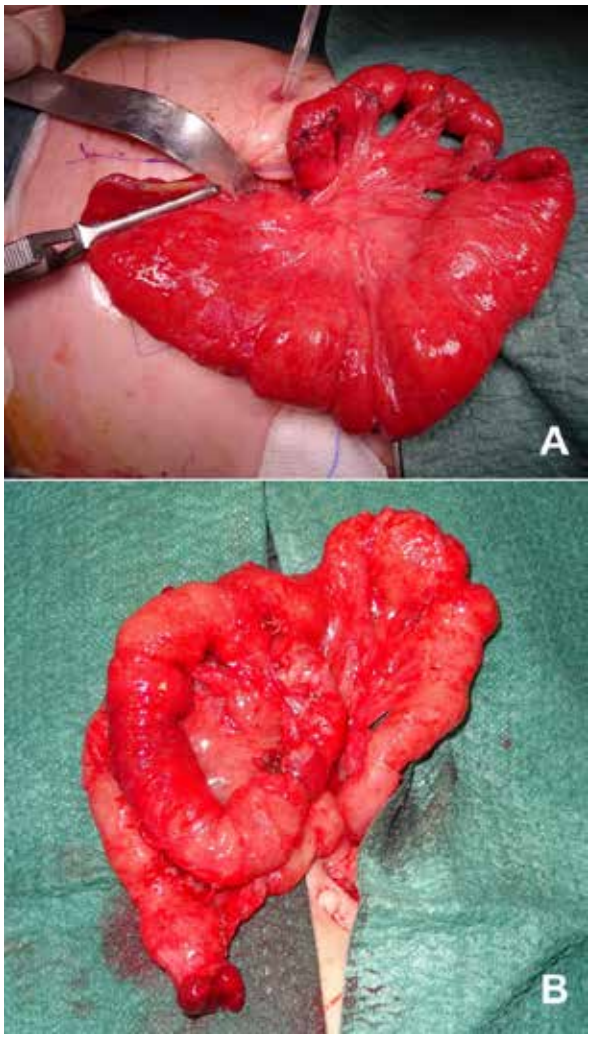
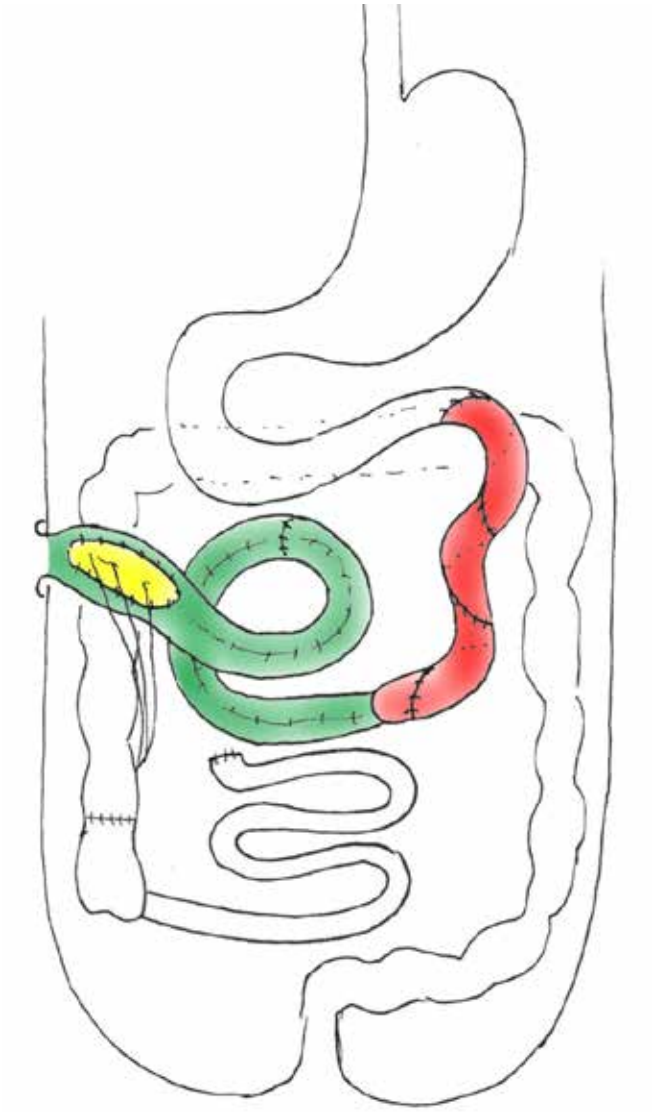
Introduction: Near-total Intestinal Aganglionosis (N-tIA) extending into high jejunum results in a severe short bowel state with large jejunostomy losses, and increased mortality from TPN/sepsis liver injury and loss of venous access, and life-long TPN dependence for those with <20cm jejunum. The alternatives are Autologous Gastrointestinal Reconstruction (AGIR) or Bowel Transplant. We present a female child who underwent Bowel Expansion, Sequential Autologous Bowel Lengthening with SILT (Spiral Intestinal Lengthening) followed by LILT (Longitudinal Intestinal Tailoring and Lengthening), and the addition of a prejejunostomy patch of aganglionic right colon, with an ongoing and improving outcome.

Methods: A 14-day old female child with N-tIA and 20cm of ganglionic residual jejunum from the ligament of Trietz, was initially treated by jejunostomy at 50cm from Treitz, retaining 30cm of aganglionic jejunum. At 15months the aganglionic jejunum was excised and the dilated proximal ganglionic 20cm were lengthened by SILT to a total of 50cm (fig1A). The stoma was closed around a 16F Pezzer catheter that was brought out onto the abdominal wall as a Tube Jejunostomy. Timed catheter clamping over 5 months induced Controlled Bowel Expansion, and was followed by LILT (fig1B) to an increased total jejunal length of 80cm.



At 29months of age 10cm of opened ascending colon was patched to the side of the distalmost jejunum just proximal to a permanent jejunostomy stoma (fig2).



Results: At 5years of age total TPN caloric requirement has decreased from 100% to 55%, and her Body Mass Index is 15.4 at the 50th centile for her age. Neurological function is normal for her age. Largely after the colonic patch her stoma output reduced from 130ml/kg to 30ml/kg.

Conclusion: Patients with N-tIA with a residual short bowel state benefit from AGIR designed to increase full thickness bowel volume and enhancing intestinal adaptation. Following controlled bowel expansion, sequential lengthening by SILT and LILT, and an ascending colon patch (endogenous GLP2?) our patient has had a 50% reduction in TPN requirement and has shown sustained physical and mental growth and an improved quality of life. We recommend management spanning several years by Sequential Autologous Gastrointestinal Reconstruction (expansion, lengthening, increased mucosal contact techniques) to enhance intestinal adaptation and absorption, and with no cut-off point for referral for Intestinal Transplantation.

P4.51 - Follow-up of nutritional status and growth in children with intestinal failure receiving long-term parenteral nutrition

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Introduction: Regular and frequent monitoring of the patient's nutritional status is necessary for optimizing nutritional support in children with intestinal failure (IF). We aimed at examining the changes in anthropometric nutritional status and identifying factors associated with this outcome in children with IF followed at a pediatric intestinal rehabilitation center.

Methods: Prospective cohort study in 13 children with IF (8 males and 5 females), mean current age of 32.9 (16.7) months. Patients were followed-up at an intestinal rehabilitation center between July 2015 and December 2018; all were receiving long-term parenteral nutrition (PN). The main primary cause of IF was necrotizing enterocolitis (6/13) and 7 patients had ultrashort bowel syndrome. Z scores of weight, height, and body mass index for age were routinely monitored at two-week intervals and compared with the WHO reference standards. Data were collected regarding the energy and protein supplied by PN and by oral/tube feeding route. Age, sex, time of follow-up, prematurity, length of the remnant small bowel, ostomy and the diagnosis of intestinal failure associated liver disease were the main explanatory variables for the outcome (Z scores of weight/age and height/age). The effect of the exposure variables on the outcomes was analyzed by generalized estimating equations.

Results: The median time of follow up was 16.5 months, with interquartile range (IQR) of 8.9 to 32.4 months. The Z scores of the anthropometric parameters increased significantly during the follow-up. Median weight/age Z score increased from -3.68 (IQR: -4.97 to -2.66) to 0.45 (IQR: -2.0 to 0.44) and mean height/age Z score increased from -3.93 (IQR: -4.66 to -2.63) to -1.12 (IQR -4.18 to -0.28). Malnutrition (based on weight for age Z score) decreased from 77% to 23% by the last assessment. Mean (SD) total energy and protein supply were 88 (23.4) kcal/kg/day and 2.3 (0.7) g/kg/day, respectively, and both decreased significantly along the follow-up period ($p < 0.001$). Mean energy and protein supply by PN were 67.6 (SD 17.5) kcal/kg/d and 1.8 (0.5) g/kg/d respectively. The increase in the anthropometric z scores was not associated with any of the clinical and demographic factors considered in the analysis.

Conclusion: There was a significant improvement in the nutritional status of children during the follow-up period. This improvement seems to occur independently of demographic factors and comorbidities.

P4.52 - Preventing catheter-associated infections in parenteral nutrition in a pediatric gastroenterology unit, 2010-2018: impact of an educational program surveying policies for insertion and care of central venous catheters

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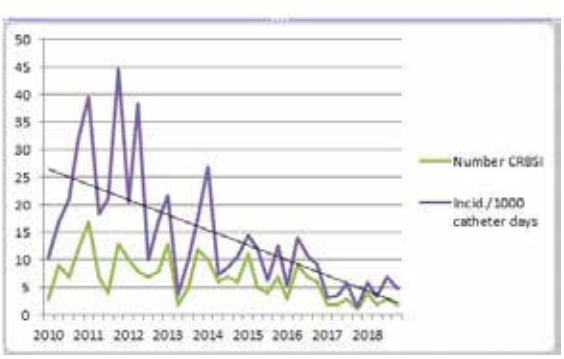
Introduction: Children hospitalized in gastroenterology units for parenteral nutrition are exposed to central venous catheters (CVC) and the occurrence of infection on CVC. These infections are a major cause of morbidity and mortality for these patients. Prevention methods aiming education of the nursing team and optimization of intravascular medical devices are implemented. The aim of this study is to assess incidence trend and to observe influence of these methods to improve health care quality.

Methods: A prospective surveillance study was performed in the pediatric gastroenterology and artificial nutrition unit of Lyon university hospital. Since 2010, any child hospitalized in the ward with a CVC for parenteral nutrition was included. The data were collected by research of bacteriological results in blood culture and discussed with the clinicians. The number of catheter days was counted by the clinicians by number of parenteral nutrition bags administered in the clinical ward. The incidence of blood-stream infections was expressed by 1000 catheter-days.

Results: The surveillance conducted since 2010 shows a constant decrease of catheter-related blood-stream infections (CRBSI) since 2012. The annual infection rate was initially superior to 20/1000 catheter days. This high incidence was following the move of the clinical unit to a new pediatric university hospital and the high turn-over of the nursing team. From 2012 to 2016, the incidence decreased constantly between 20 and 10 CRBSI/1000 catheter days. Since 2017, the incidence is inferior to 5 infections for 1000 catheter days.

Several measures of quality care improvement were implemented successively: the revision of protocols, numerous training workshops of care practices, and audits were performed. The newly recruited and interim nurses without training were not allowed to manipulate the central catheters. The catheter material was optimized by the implementation of new perfusion lines adapted to the pediatric context.

Conclusions: The surveillance of bacteremia highlights an important decrease of CRBSI in children hospitalized in gastroenterology for parenteral nutrition. The improvement of quality of care seems to be linked to this decrease: reorganization of nursing care, training workshops for perfusion line connection and manipulation, improvement of care protocols and perfusion material optimization.



P4.53 - Unusual indications for multivisceral transplantation

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Introduction: Recent improvements in intestinal rehabilitation programs allowed avoiding intestinal transplantation in many cases. Conversely, improved outcomes prompt the use of intestinal transplantation for complex intestinal pathologies not included in the classical list of indications. Our aim was to analyze our experience in some of these unusual indications for transplantation and to review their outcome when compared to the usual indications.

Methods: Retrospective review of our historical series of intestinal and multivisceral transplants (1999-2018) identifying those cases in which the initial diagnosis was not among the classic indications (short gut syndrome, motility disorders, untreatable diarrheas). Their general outcome (complications, immunosuppression, graft loss, survival) were compared with the rest of the cases, considering statistically significant a P value under 0.05.

Results: We reviewed 107 transplants, finding 9 unusual cases transplanted with an average age of 4 years (1-10). Their initial diagnoses were: 3 benign cystic retroperitoneal teratomas with SMA lesion during surgery, 1 myofibroblastic tumor involving main vessels, 1 multifocal postext IV hepatoblastoma with tumoral portal thrombus reaching beyond the splenic mesenteric junction, 1 vascular accident in an appendectomy, 1 Martínez-Frias syndrome, 1 mitochondrial disease and 1 Alagille syndrome with ileal atresia. Eight patients received a multivisceral graft and 1 an isolated small bowel. Surgical and infectious complications did not shown statistical differences with our main series. PTLD was only seen in 11% (1) and GVHD in 22% (2), being less common than in the main series but not statistically significant. The rate of rejection and retransplantation was also similar. Only the case who had an isolated small bowel graft presented rejection (11%) requiring multivisceral retransplantation. Overall patient survival was 82% with a mean follow-up of 7 years [0-13], with no differences between the groups. No tumor recurrence was observed.

Conclusion: Multivisceral transplant is a safe therapeutic option in unconventional and challenging cases in which the integrity of the intestine is affected. According to our study, these transplants present the same prognosis as the classic indications. Emerging indications, like the 9 cases reported in this work, would appeared in the future. Intestinal transplantation should be at least considered to treat these patients attended in IRUs.

P4.54 - An old technique for a new problem: Bishop Koop stoma to facilitate endoscopic surveillance

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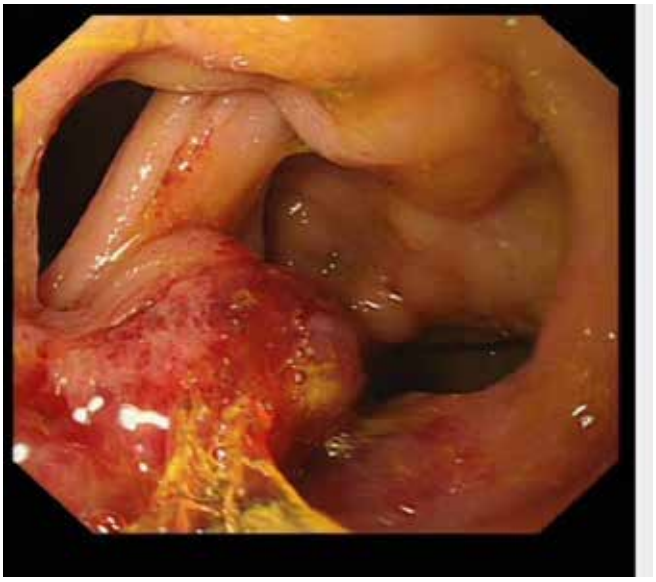
Introduction: Endoscopic surveillance of the transplanted intestine is essential for early diagnosis and successful management of graft rejection. End ileostomies are easy to survey, but patients often have high output leading to renal impairment and electrolyte disturbance. Increasingly colon inclusion has become standard of care but endoscopy via an end colostomy can be difficult and lead to failure to access the terminal ileum. In addition a standard loop ileostomy proximal to a transplanted colon does not take advantage of the fluid balance advantages conferred by colon inclusion. In 2017, we started to use a Bishop Koop anastomosis proximal to an anastomosis between transplanted and native colon.

Methods: This is a retrospective review of a prospectively held database of all intestinal-containing grafts from 2017.

Results: Since 2017, 10/20 transplants have included a Bishop-Koop stoma. In the 10 patients who did not have Bishop Koop stomas this was as a consequence of either concerns regarding the native colon at transplant (2 patients) or recipient pathology that rendered distal continuity inappropriate or technically impossible (pan proctocolectomy, ileal pouch).

Endoscopic surveillance was quicker and more comfortable for patients and ileal visualisation was possible in all cases. Two patients have subsequently undergone stoma reversal and this has proven technically easier than with our previous stoma.

Conclusion: We describe the use of a Bishop Koop stoma for patients undergoing intestinal transplantation. This has resulted in improved endoscopic surveillance, fluid balance and patient satisfaction compared to our previous use of end colostomies. Stoma reversal with the Bishop Koop is a simpler undertaking.



P4.55 - Results from a single institution pediatric intestinal transplant database: Pertinent clinical data absent from national databases

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Introduction: The United Network for Organ Sharing (UNOS) collects data before and after intestinal transplantation (ITx) from all transplant centers across the United States. While much of the information is useful, it fails to capture other data that is interesting for physicians and surgeons involved in the care of ITx patients. We present the results of a major intestinal rehabilitation (IRP) and ITx program, focusing on data that is currently not captured by the UNOS database.

Methods: A retrospective review of all ITx (both isolated small bowel and multivisceral) performed at a regional referral pediatric IRP and ITx program between 2004-2019 was performed (n=18). Clinical, surgical, and outcomes data were collected. This study was approved by the Institutional Review Board (IRB #2019-2474). Solely data this is currently not collected in the UNOS ITx database is presented herein.

Results: 18 transplants (3 multivisceral) were performed. The most common indication for ITx was recurrent infections (either central line associated bloodstream infections or small bowel bacterial overgrowth: 12/18, (67%), either alone or combined with loss of vascular access. Intestinal failure associated liver disease was the indication for transplant in 5 patients, including all 3 multivisceral transplants. Loss of vascular access was the indication in one patient. Median time to starting enteral feeds after transplant was 16.5 days [6-210], and 56% (10/18) were discharged on full enteral feeds. Fourteen of 18 patients (78%) were weaned off parenteral nutrition at some point after their transplant. Median time to initially stopping parenteral nutrition after transplant was 74 days [32-244]. Most patients underwent stoma closure (12/18, 67%), and median time to stoma closure was 297 days [122-558]. One-year survival outcomes were 89% (16/18 patients) and 83% (15/18 grafts). Ultimately, 5 grafts had to be explanted. 4/5 patients who were explanted suffered from chronic rejection, which was caused by non-compliance in 2 patients.

Conclusion: National databases provide major post-transplant outcome measures. However, much pertinent clinical data that is important for ITx medical and surgical providers but also for patients and families is not collected. A better knowledge and understanding of granular pre- and post-transplant clinical and surgical data can help better counsel and prepare families before transplant.

P4.56 - Muscle and adipose measurement of pre and post-surgical intestinal transplant patients using computed tomography to compare malnutrition diagnosis using nutrition focused physical exam

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Introduction: Sarcopenia has been defined as a low appendicular skeletal muscle mass (kg/m2) two standard deviations below the mean of a young healthy reference group (Baumgartner 1998) coupled with a concomitant loss of muscle function, or severe muscle depletion. Studies have shown that sarcopenic patients undergoing surgical resection diagnosed by computed tomography (CT) prior to surgery were at increased risk for perioperative infections, increased length of stay (LOS) and higher mortality (Moissy et al 2013, Weijs 2014). Sarcopenic obesity measured by CT imaging has been correlated with poorer outcomes in post living donor liver transplantation (Itoh S, 2016). In our institution, highly trained and experienced registered dietitians (RDs) assess muscle loss as part of the nutrition focused physical exam (NFPE) using the new guidelines to diagnose malnutrition set by the Academy of Nutrition and Dietetics and the American Society of Parenteral and Enteral Nutrition (White 2012). This practice, however, has yet to be validated. CT scans are an objective measurement of assessing skeletal muscle mass, and abdominal wall and visceral adipose (Gomez-Perez 2016), and may be useful in determining skeletal muscle loss.

Methods: Our team studied the correlation between malnutrition diagnosis via NFPE and muscle and fat mass on CT scans before and after intestinal transplantation. We also looked at the correlation of CT measurements with predicting post-operative morbidity and mortality.

Results: A total of 42 subjects were included in the study consisting of 31% male and 69% female patients. Sixty percent of subjects did not have any degree of malnutrition during the pre-transplant NFPE, while 40% had moderate to severe protein calorie malnutrition. We found a significant correlation between patients diagnosed with malnutrition and those without malnutrition in subcutaneous fat CT measurements during pre-transplant evaluation (p=0.037). We also found a significant correlation with LOS (p=0.005) and mortality (p=0.006) with patients who received multivisceral transplants versus all other types of transplant (isolated intestine, modified multivisceral, intestine and pancreas).

Conclusion: This study is the first of its kind to analyze malnutrition in the intestinal transplant population. Based on these results, it may be feasible to analyze CT measurements to assess recent patient nutriture to help identify patients with malnutrition prior to transplantation.

P4.57 - Intestinal and multivisceral transplantation at hospital das clinicas da faculdade de medicina da universidade de Sao Paulo (HC-FMUSP) - Brazil

Flavio Henrique Galvao, Andre Lee, Rafael Pinheiro, Rubens Macedo, Rodrigo Bronze, Lucas Nacif, Vinicius Santos, Daniel Waisberg, Wellington Andraus, Luiz Carneiro D'Albuquerque

Departamento de Gastroenterologia do hospital das clinicas da faculdade de medicina da universidade de Sao Paulo

HC-FMUSP is one of the world's pioneer of isolated intestinal transplantation (IIT) performed by the living legend Masayuki Okumura (1)and currently is the public Hospital reference for Intestinal and Multivisceral Transplantation (IMT) in Brazil. In 2014, HCFMUSP restart IMT program, inspired by animal research (2-6) and financed by the Government. Here we show five cases of IMT performed at HC-FMUSP.Cases: ONE A 38 years old male underwent IIT in 1968, 10 days after a massive enterectomy due to mesenteric artery thrombosis. The recipient survived for twelve days (one of the longest survival in that age) and died due to uncontrolled rejection. TWO: A 12 years old female underwent IIT in 1969, 34 days after a massive enterectomy due volvulus. The patient survived for five days and die due to uncontrolled rejection. THREE: A 33 years old, male, with a neuroendocrine tumor in the pancreas involving mesenteric vessels and multiple liver metastasis received a multivisceral graft in 2014, survived for five days and died due to uncontrolled bleeding. FOUR: 51 year old male presenting liver cirrhosis due to alcohol with a complex portal vein thrombosis (grade IV) received a multivisceral graft in May of 2015, survived for 30 days and died due to a liver needle biopsy that caused a progressive internal bleeding and liver failure. FIVE. A 21 year old male presenting short bowel syndrome due to mesenteric torsion received isolated intestinal transplantation in 2017. Intestinal reconstruction was performed four months after the transplantation and he is currently very well, gained nine Kg of body weight and accomplished total oral feeding autonomy. This case is the longer survival of isolated intestinal transplantation in Brazil (14 months). Currently we have 15 patient referral and five patients listed for IMT, three for isolated and two for multivisceral. The main obstacle for IMT in Brazil is the lack of suitable donors (7).Conclusion: HCFMUSP is world's pioneer in IMT and currently have achieved long term survival in a case of intestinal transplantation. Improvements in donor care would improve this actively in Brazil.

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P4.58 - Management and outcomes of Gastroschisis over the last decade: A US tertiary-center experience.

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Introduction: Gastroschisis (GS) is the most common abdominal wall defect requiring neonatal operative intervention and it represents one of the most costly congenital defects. It is associated with short and long-term morbidity associated with complications due to preterm birth, sepsis, need for small bowel resections, necrotizing enterocolitis (NEC), associated anomalies such as intestinal atresia (in 10 to 20% of patients with GS) and other birth defects. We report all patients with GS who were surgically treated or underwent intestinal rehabilitation (IR) at our institution in the past 10 years describing features, management and outcome.

Methods: We retrospectively reviewed patients with diagnosis of GS treated at our institution from July 2007 to January 2018.

Results: In this study a total of 91 patients with GS were identified (62% male). Median gestational age was 36 weeks (interquartile range [IQR]: 33-38).

Sixty-four patients (71%) had uncomplicated GS. Primary surgical closure in these patients was associated with earlier intestinal autonomy and shorter duration of PN in 31% of patients ($p<0.05$). In this group, introduction of feeds occurred at a median age of 23 days of life (IQR: 13-35), 90% of them received breast milk with supplemental standard infant formula.

Twenty-seven patients (29%) had complex GS; their complications include: intestinal atresia (n=12), intestinal necrosis at birth requiring bowel resection (n=10), medical NEC (n=18), bacteremia (n=14) and severe intestinal dysmotility requiring promotility medications (n=13).

All patients with complex GS initiated treatment by our Intestinal Rehabilitation Program (IRP) at a median age of 2.5 months. Upon initial evaluation, 88% of patients (n=24) were on parenteral nutrition (PN) that provided a mean of 97% of their daily calorie goal. 17 patients (71%) were weaned off PN after a mean of 7 months of IR. 7 patients (29%) remain PN dependent with a median bowel length of 34 cm, their mean daily energy requirement from PN is presently 48%, down from 90% at IRP enrollment.

Conclusion: Multiple prenatal and postnatal events affect outcomes in patients with GS. Patients with complex GS are at higher risk of morbidity. A specialized multidisciplinary IRP is crucial in the management of these patients to optimize their health related outcomes.

P4.59 - Pregnancy during long-term total parenteral nutrition in a patient with intestinal failure

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Introduction: There have been few reports on the use of long-term Total Parenteral Nutrition as the primary nutrition source during pregnancy from conception to birth.

Methods: A 30 year old female who suffered a volvulus resulting in intestinal failure required TPN as her primary source of nutrition. Given the extent of resections and no intestinal rehabilitation possible she required an intestinal transplant. During the evaluation process, she was found to be 5 weeks pregnant. It was decided to put the transplant evaluation on hold. She was transferred to the registered dietitian and physician for TPN management during her pregnancy.

Results: The patient's pre-pregnancy weight was 46kg with a BMI of 18 and was receiving 30 kcals / kg in 3 liters of TPN. Given that she was underweight and pregnant it was our goal for her gain the right amount of weight throughout each trimester. The guidelines for weight gain for underweight pregnant women is 28 to 40 pounds. The patient's calories were gradually increased from 35 kcals / kg to 41 kcals / kg by the end of her pregnancy. She gained 28 pounds during her pregnancy. Her fluid requirements increased to an average of 3500 liters of TPN daily with additional fluids for hydration used as needed. The patient's protein requirements throughout pregnancy averaged 2 g / kg. The patient had been on Intralipid from the time she was started on TPN but given a slight elevation in liver function tests as well as long-term TPN dependence it was decided to change her to SMOF lipid. She required an average of 1.6 g / kg of SMOF lipid throughout the pregnancy. Her LFT's remained stable during pregnancy with no significant increases. The patient had low adjusted calcium levels and ionized calcium levels resulting in a daily need of 50 milliequivalents of calcium gluconate in her TPN. Vitamin and mineral levels were measured every 3 months and remained normal throughout pregnancy with the patient receiving 10mL of multivitamin in the TPN and standard dose trace elements. Iron levels were low later in pregnancy in which she received a course of intravenous iron sucrose for correction. The patient had no complications during her pregnancy and delivered a healthy full-term infant.

Conclusion: When properly managed by a multidisciplinary team pregnant women can carry a successful full term pregnancy while dependent on long-term TPN. Labs, weight and outputs should be closely monitored during pregnancy.

P4.60 - Bortezomib for the treatment of chronic Graft Versus Host Disease in Intestinal Transplant recipient

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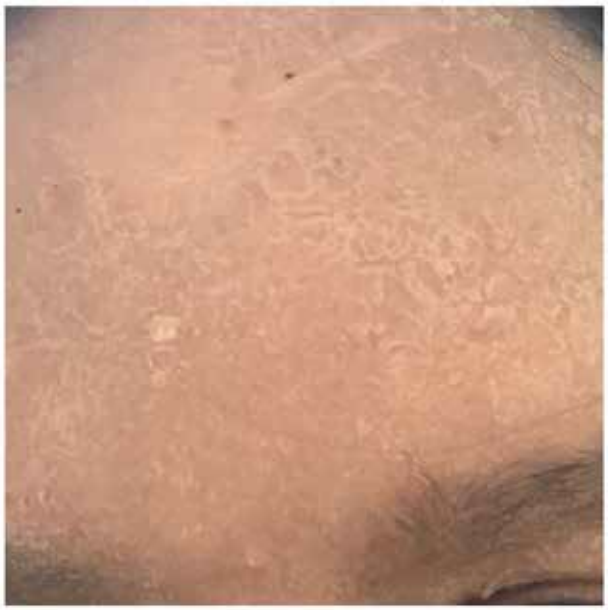
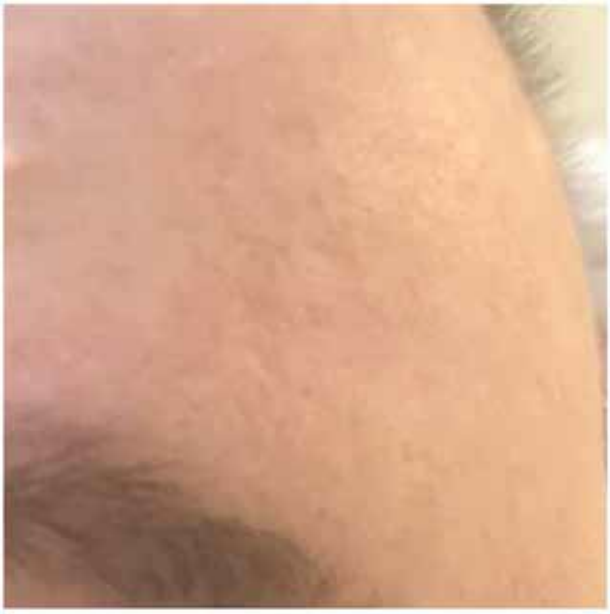
Introduction: GVHD is a disparate immunological response between host and recipient tissues. When it occurs after Intestinal Transplantation (ITx), it can be deadly. Bortezomib is a proteasome inhibitor that affects dendritic and T-cell processes essential for the development of GVHD but also decreases B cells. The use of Bortezomib at time of bone marrow transplant (BMT) in mice protected against acute GVHD. Bortezomib has been used in ITx for refractory acute rejection with donor specific antibodies. To our knowledge, we present the 1st use of Bortezomib for chronic GVHD in ITx.

Case: 25 yo female with Pseudo-obstruction as a result of Ehlers Danlos received a modified MVT. Induction immunosuppression (ISP) was Antithymoglobulin / Rituximab / Methylpred / Basiliximab and maintenance FK / Everolimus. Blood chimerism was followed serially. She developed a skin rash and persistent fevers on week (wk) 4 post transplant. Chimerism rose from 33% wk 4, 61% wk 5 and 80% wk 6. Endoscopy on wk 5 was negative for rectal chimerism and GHVD. Given ongoing symptoms, Alemtuzumab 30 mg IV x 2 was given for acute GVHD. Chimerism decreased to 1% wk 8 but again rose to 96% wk 11, fluctuating over the next month, 56-96%. A 3rd dose of Alemtuzumab was given wk 15. Chimerism decreased to 2% by 5 months (mn) post transplant.

6 mn post transplant, she developed neutropenia. Given possible bone marrow GVHD, a biopsy was done and negative. She again developed rash with alopecia but managed conservatively with prednisone. Course complicated with BK viremia (5.6 million copies) treated empirically with IVIG and decrease in ISP. 9 mn post transplant, she lost 14 pounds due to high ostomy output. Work up ruled out rejection, allergy and infection except BKV pcr + in bowel biopsy. She started Cidofovir, symptoms improved and blood BKV pcr decreased. 12 mn post transplant, liver enzymes increased and biopsy ruled out GVHD. However, she again presented with skin rash despite chimerism <5%.





14 mn post transplant, Bortezomib was given weekly x 4 for chronic GVHD. Thereafter, rash resolved in 4 weeks with no recurrence now 2 years post transplant.

Discussion: GVHD continues to be a threat to ITx recipients with high mortality. Diagnosis is notoriously difficult as biopsies tend to be negative early in the course. A strong index of suspicion is necessary, before life threatening organ involvement develop, as early treatment is key to survival. Bortezomib may be an option for chronic GVHD in ITx.