INTESTINAL FAILURE, REHABILITATION & TRANSPLANTATION: Indications, Techniques and Outcomes

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Short Bowel/Gut Syndrome

Short Bowel Syndrome

DEFINITIONS

Intestinal Failure

Condition resulting “from obstruction, dysmotility, surgical resection, congenital defect, or disease associated loss of absorption and is characterized by the inability to maintain protein-energy, fluid, electrolyte or micronutrient balance”.

Intestinal Failure
Functional Causes

- Chronic Intestinal Pseudo-obstruction
- Adhesions
- Fistulae

Intestinal Failure
Mucosal Causes

- Microvillous inclusion disease
- Tufting enteropathy
- Congenital neuroendocrinopathy

Intestinal Failure
Surgical Causes (ADULT)

- IBD
- Trauma
- Volvulus
- Mesenteric venous thrombosis
- Mesenteric arterial thrombosis
- Embolic phenomenon
- XRT
- Adhesions
- Fistulae
- Tumor (GIST, Desmoid; FAP)

Intestinal Failure
Surgical Causes (CHILDREN)

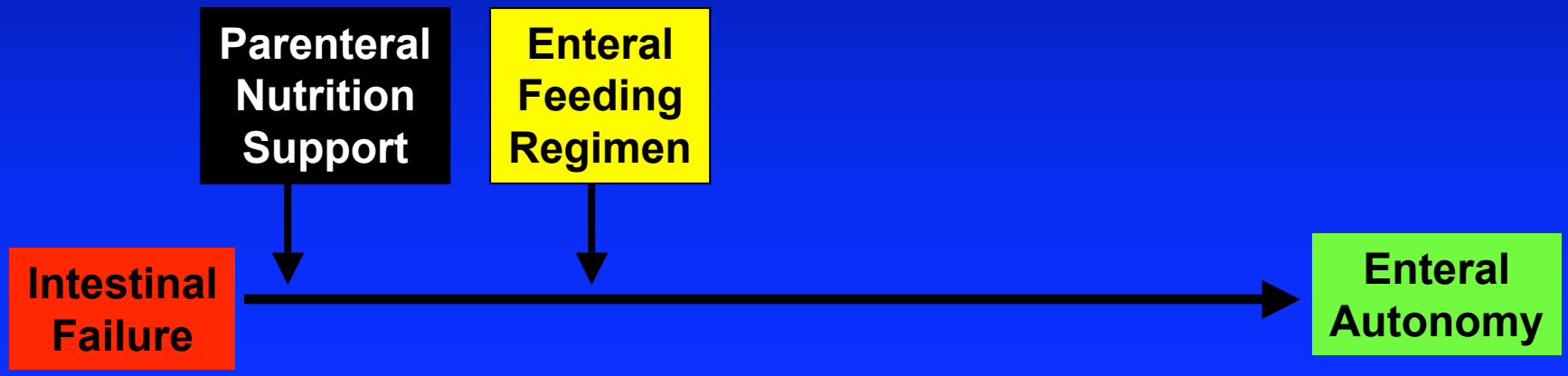
- In utero volvulus
- JI atresia
- Gastroschisis
- Omphalocele
- Meconium ileus
- Hirschsprungs Disease
- NEC
- Post-Natal volvulus
- Pseudoobstruction

The Journey

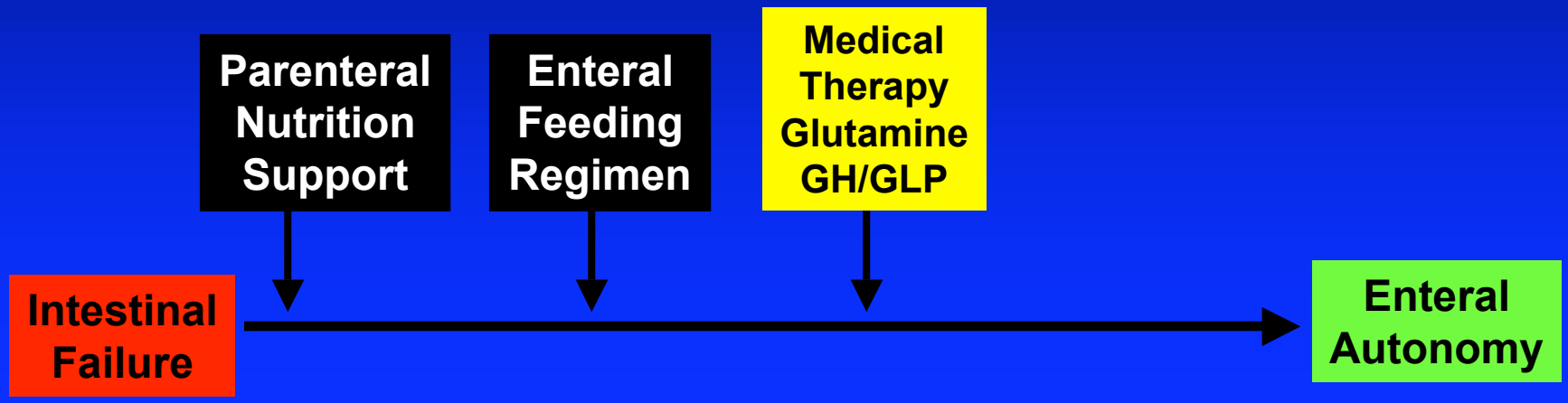
The Journey


Parenteral Nutrition Support
Intestinal Failure
Enteral Autonomy

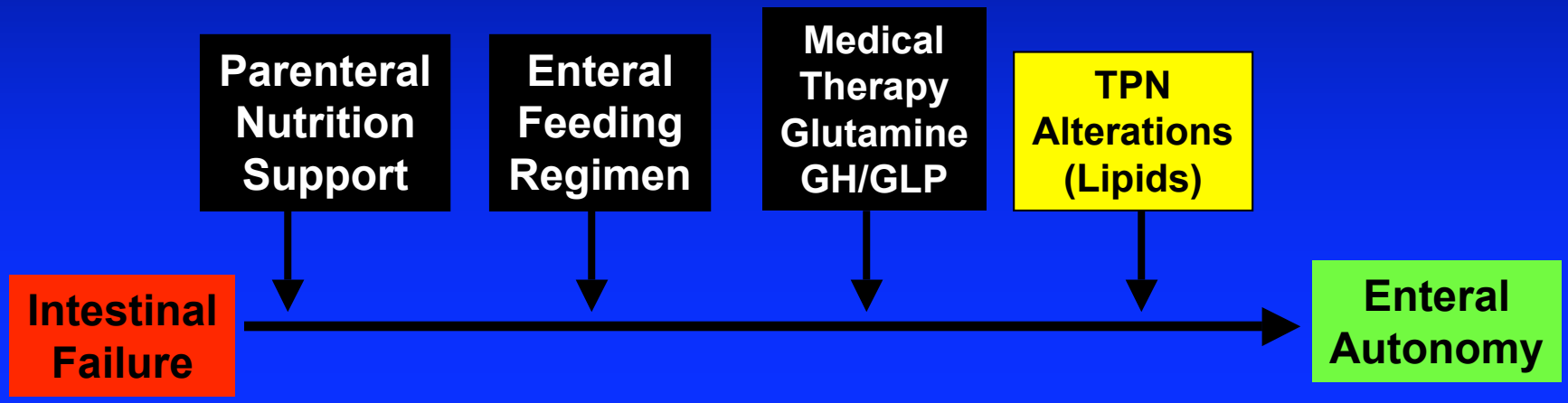
The Journey


Parenteral Nutrition Support
Enteral Feeding Regimen
Intestinal Failure
Enteral Autonomy

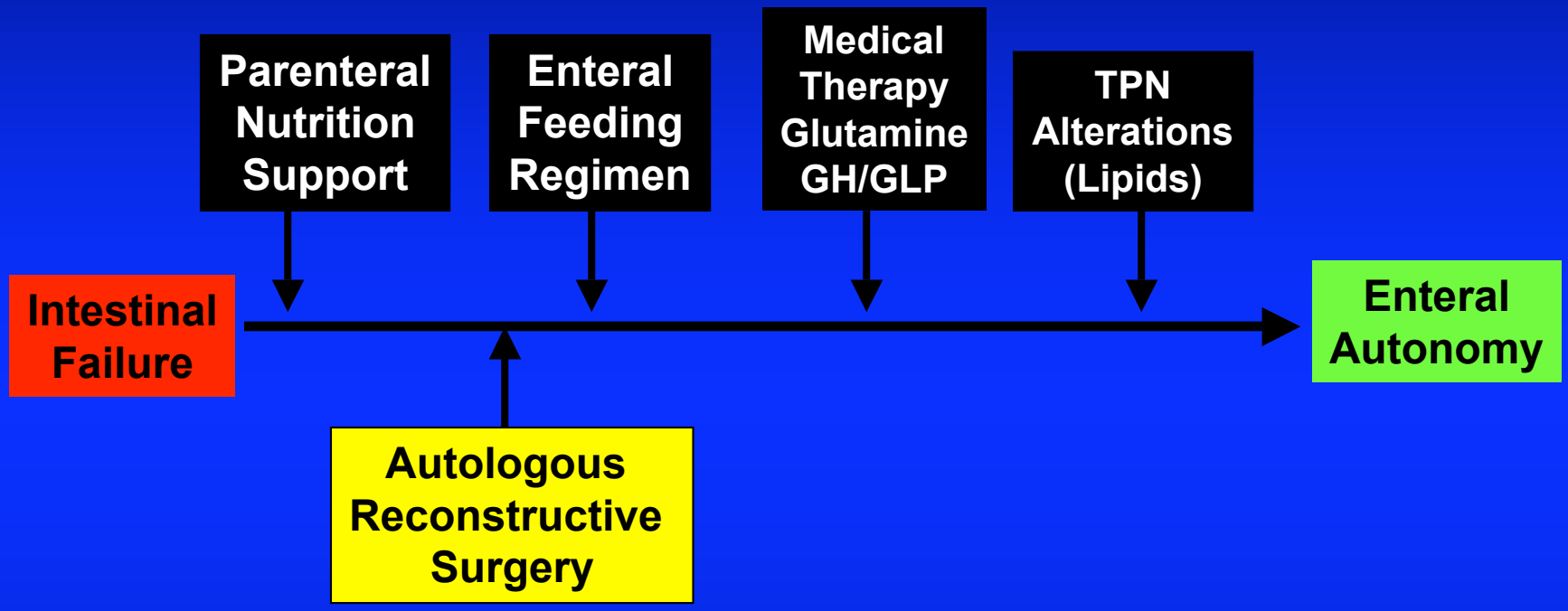
The Journey


Parenteral Nutrition Support
Enteral Feeding Regimen
Medical Therapy Glutamine GH/GLP
Intestinal Failure
Enteral Autonomy

The Journey


Parenteral Nutrition Support
Enteral Feeding Regimen
Medical Therapy Glutamine GH/GLP
TPN Alterations (Lipids)
Intestinal Failure
Enteral Autonomy

The Journey


Parenteral Nutrition Support
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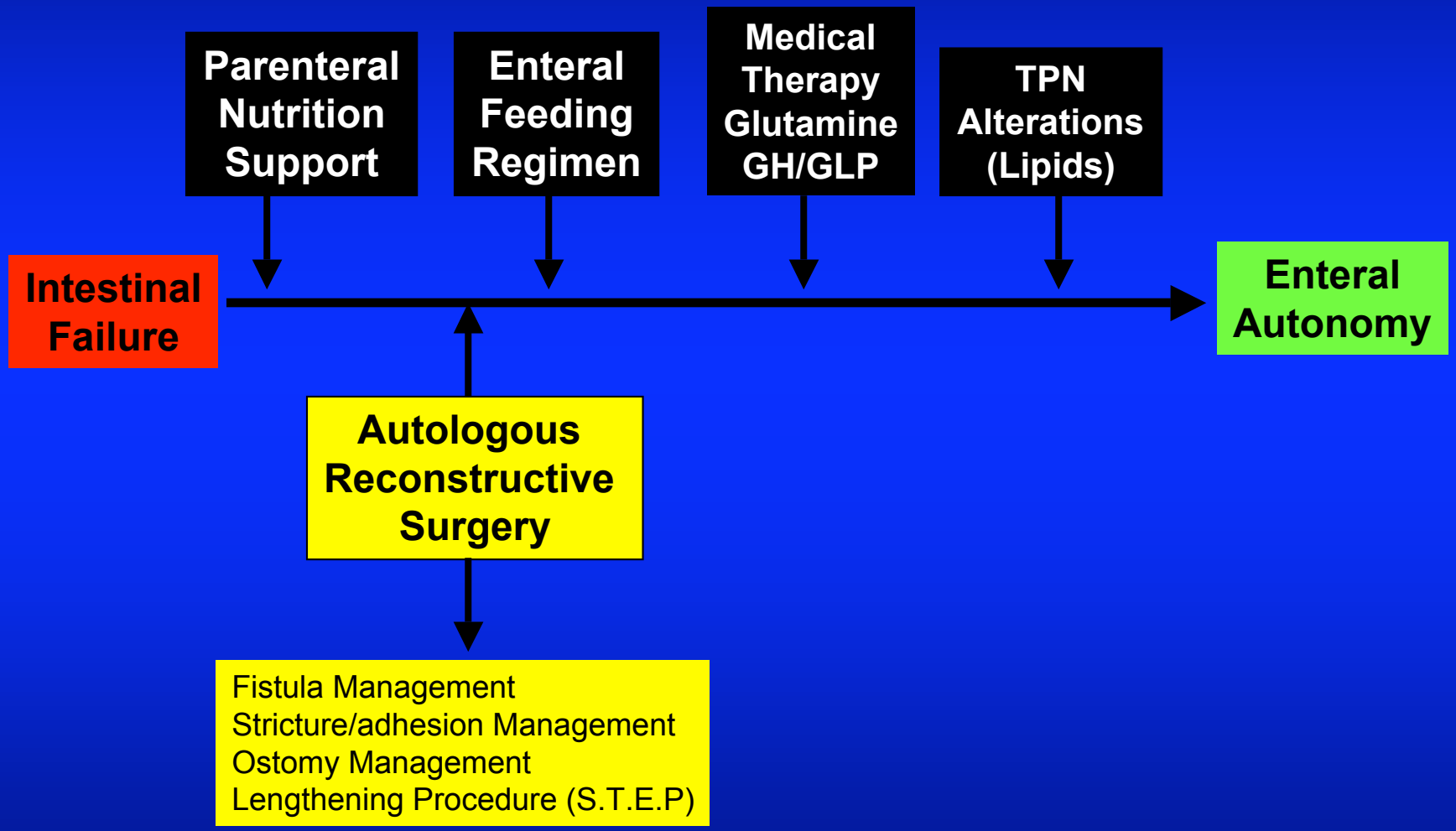
Enteral Autonomy
Autologous Reconstructive Surgery

The Journey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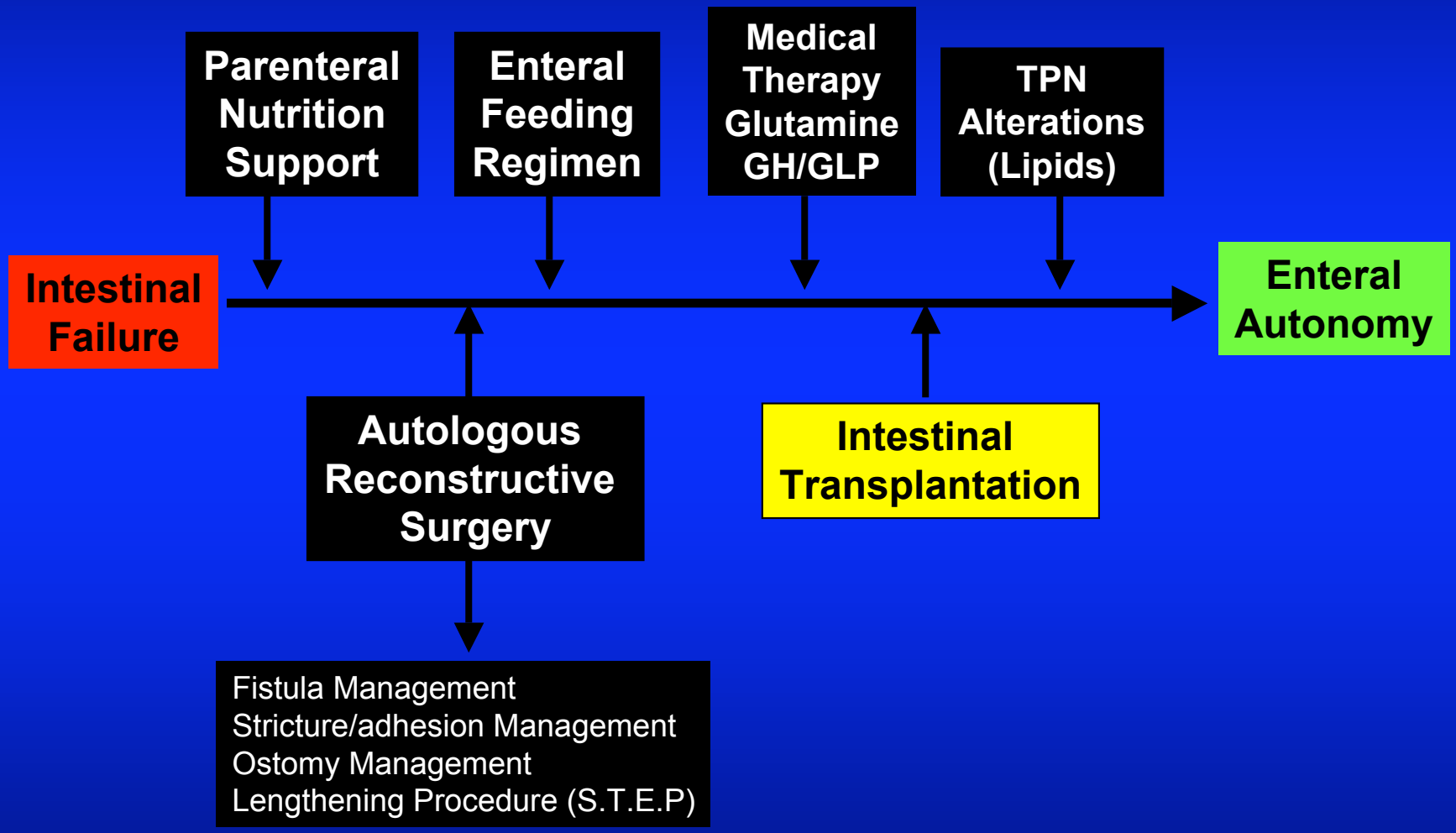
Enteral Autonomy
Autologous Reconstructive Surgery
Fistula Management
Stricture/adhesion Management
Ostomy Management
Lengthening Procedure (S.T.E.P)

The Journey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Autologous Reconstructive Surgery
Intestinal Transplantation
Fistula Management
Stricture/adhesion Management
Ostomy Management
Lengthening Procedure (S.T.E.P)

Parenteral Nutrition Support

LONG-TERM PARENTERAL NUTRITIONAL SUPPORT AND INTESTINAL ADAPTATION IN CHILDREN WITH SHORT BOWEL SYNDROME: A 25-YEAR EXPERIENCE

RUBÉN E. QUIRÓS-TEJEIRA, MD, MARVIN E. AMENT, MD, LAURIE REYEN, RN, FAYE HERZOG, RN, MICHELLE MERJANIAN, MD, NANCY OLIVARES-SERRANO, MD, AND JORGE H. VARGAS, MD

Objective To analyze the outcome of children with short bowel syndrome (SBS) who required long-term parenteral nutrition (PN).

Study design Retrospective analysis of children (n = 78) with SBS who required PN >3 months from 1975 to 2000. Statistics: univariate analysis, Kaplan-Meier method, and Cox proportional regression model were used.

Results We identified 78 patients. Survival was better with small bowel length (SBL) >38 cm, intact ileocecal valve (ICV), intact colon, takedown surgery after ostomy (all $P < .01$), and primary anastomosis ($P < .001$). PN-associated early persistent cholestatic jaundice ($P < .001$) and SBL of <15cm ($P < .01$) were associated with a higher mortality. Intestinal adaptation was less likely if SBL <15 cm ($P < .05$), ICV was removed, colonic resection was done (both $P < .001$), >50% of colon was resected ($P < .05$), and primary anastomosis could not be accomplished ($P < .01$). Survival was 73% (57), and 77% (44) of survivors had intestinal adaptation.

Conclusions SBL, intact ICV, intestinal continuity, and preservation of the colon are important factors for survival and adaptation. Adaptation usually occurred within the first 3 years. Need for long-term PN does not preclude achieving productive adulthood. Patients with ICV even with <15 cm of SBL and patients with SBL >15 cm without ICV have a chance of intestinal adaptation. *(J Pediatr 2004;145:157-63)*

OUTCOME PREDICTORS

SURVIVAL

- SMALL BOWEL LENGTH
- ILEOCECAL VALVE
- COLONIC RESECTION
- ENTEROSTOMA
- PN COMPLICATIONS
- PN LIVER DISEASE

ADAPTATION

- SMALL BOWEL LENGTH
- ILEOCECAL VALVE
- COLONIC RESECTION
- ENTEROSTOMA
- CHOLECYSTECTOMY
- #INFECTIONS
- TIME ON TPN

TPN Complications

Catheter Sepsis
Catheter Occlusion
Vascular thrombosis
Cholelithiasis
Liver Disease
Bone Disease
Nephrolithiasis
Renal Function
Death

Survival on TPN

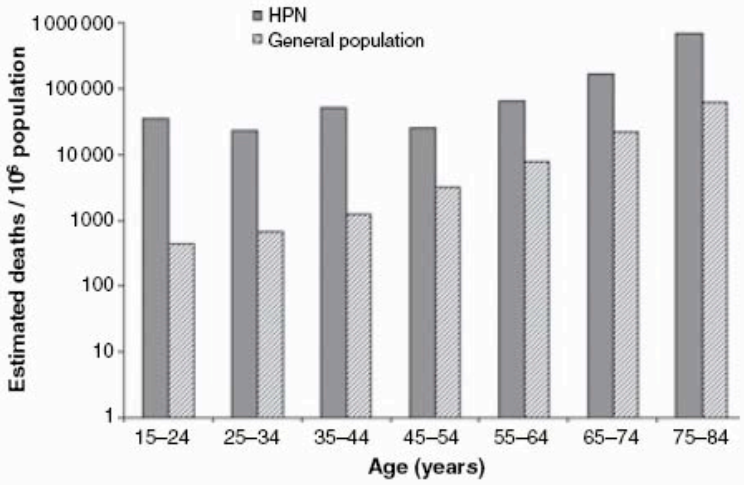


Figure 1. Mortality rates of patients receiving HPN compared with general population.

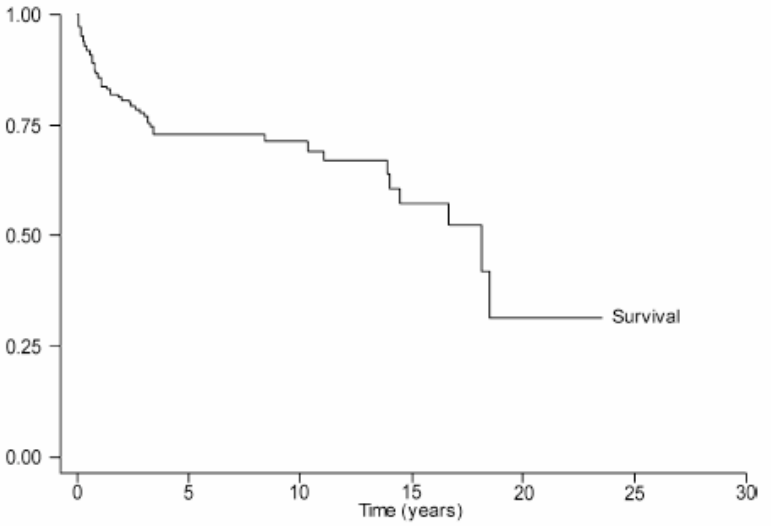


Figure 2. Kaplan–Meier plot of survival.

Aliment Pharmacol Ther 2006

TPN Alterations to Minimize Complications

Minimization of TPN Complications

- Optimize enteral feeding
- Eliminate sepsis
- Line care
  - Vanco and ampho Locks
  - Ethanol locks
- Identify coagulation disorders
- TPN formulation alterations

Fish Oil Emulsions
Omegaven®

Prospective, Case Controlled Trial of 24 weeks of Intravenous Fish Oil in Children with Intestinal Failure Associated Liver Disease

Kara Calkins*[1], Stephen Shew[2], James Dunn[2], Douglas Farmer[2], and Robert Venick[1,2]

[1]Department of Pediatrics, [2]Department of Surgery
University of California, Los Angeles

*Supported by NIH grant T32GM75776-6

PROSPECTIVE FO COHORT

Satisfies Inclusion Criteria

↓

FO
Omegaven™ 1 gm/kg/d IV
X 24 weeks or until death/transplant

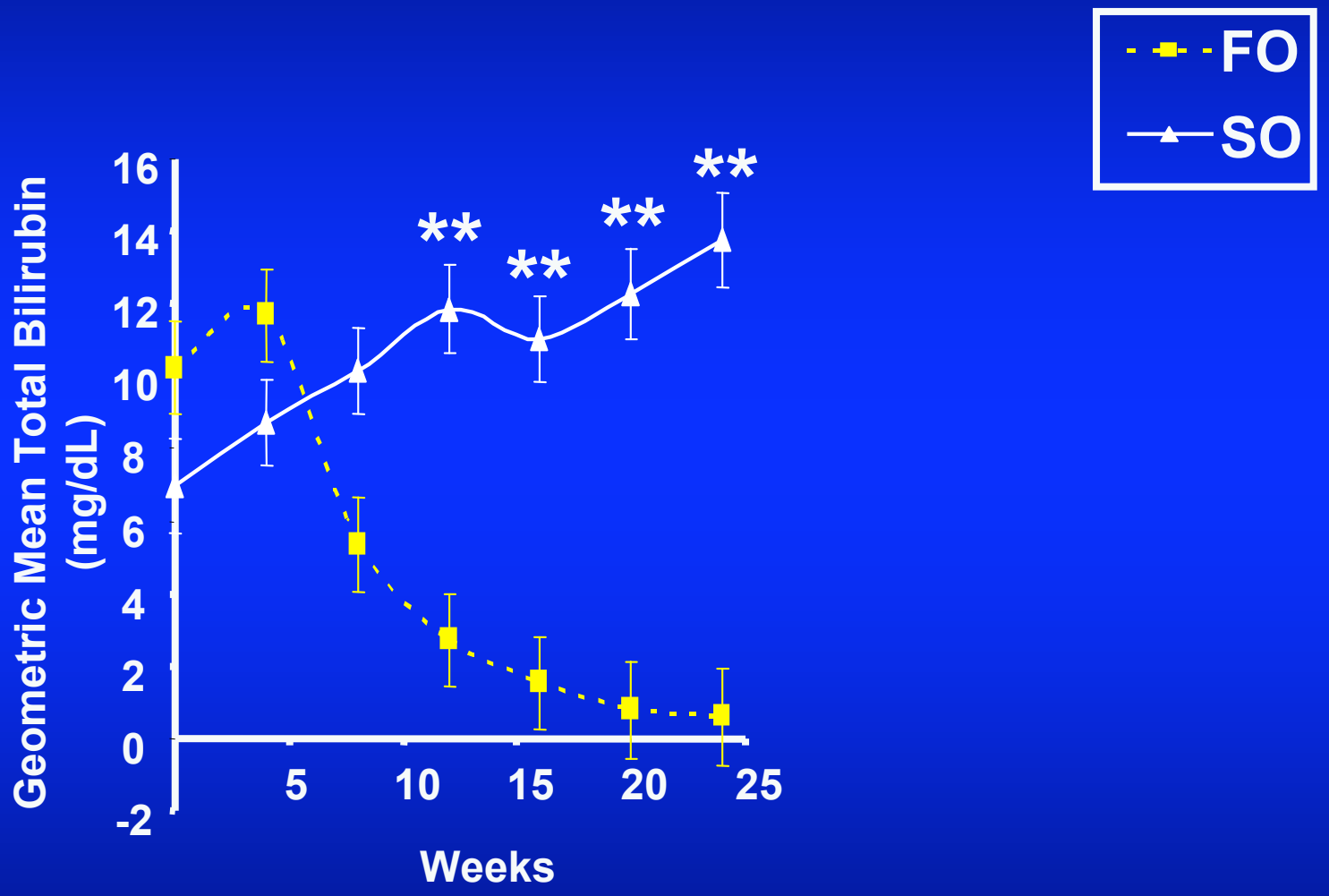
RETROSPECTIVE SO COHORT

Satisfies Inclusion Criteria

↓

SO
Intralipid™ 0.5 – 4 gm/kg/d
x 24 weeks or until
death/transplant

BILIRUBIN



**p-value<0.0001

Medical Therapies for adaptation

Glutamine and Growth Hormone

"In the last decade, most IF research has been focused on exploring the potential of these substances as supportive IF treatment. However, clinical trials so far have ***not demonstrated reproducible or meaningful*** clinical benefits with the use of glutamine or growth hormone."

C. Tee, K. Wallis, S. Gabe, Clin Exp Gastro 2011

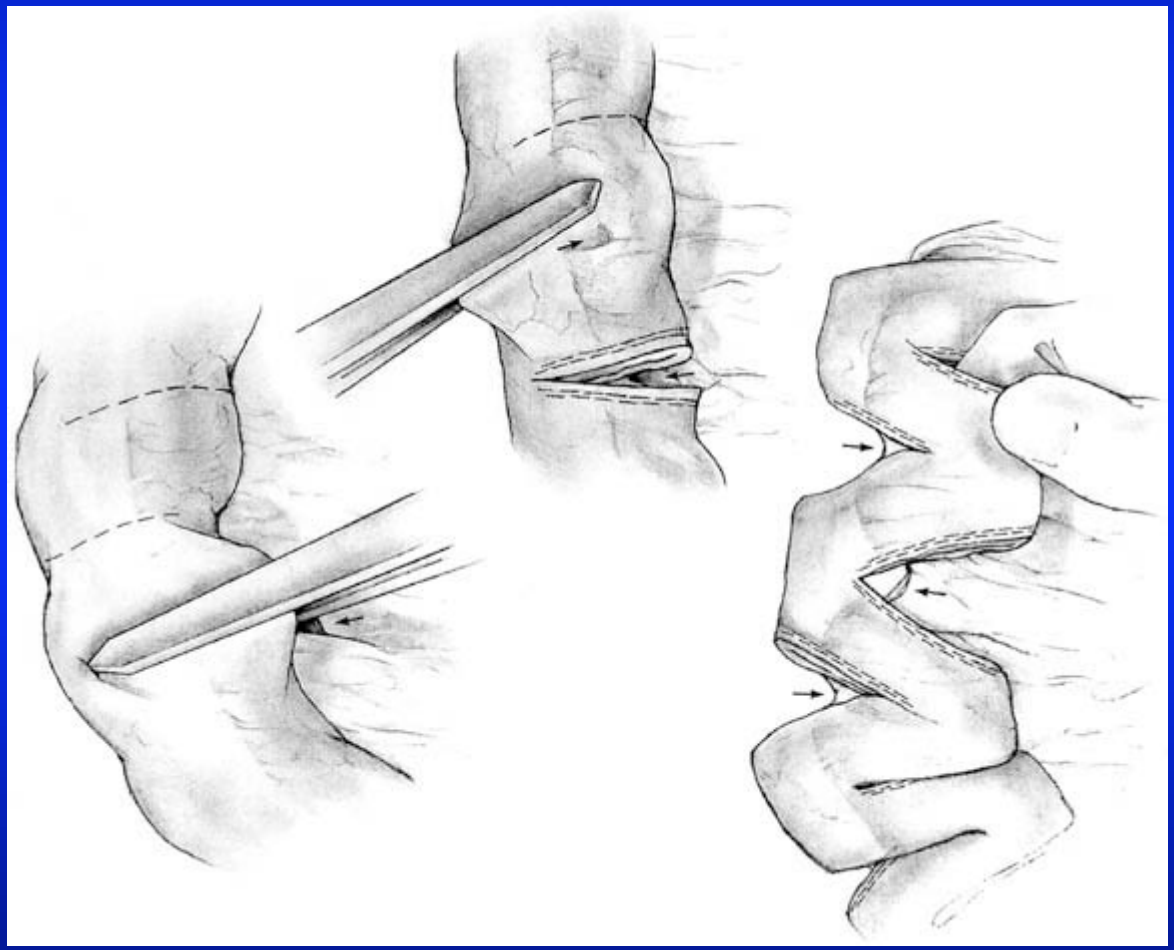
Glucagon-like Peptide 2 (GLP2)

- Gattex ® (teduglutide)
- FDA approved
- 24 week phase 3 trial
- 63% vs 30% achieved a 20% reduction in tpn at 24 weeks

Surgical Therapies for adaptation

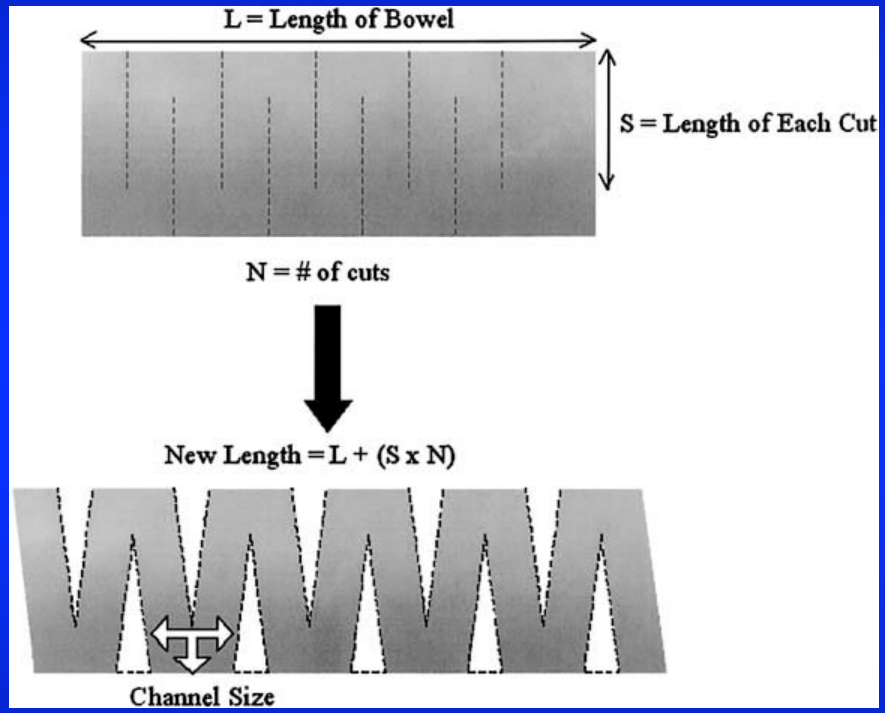
STEP

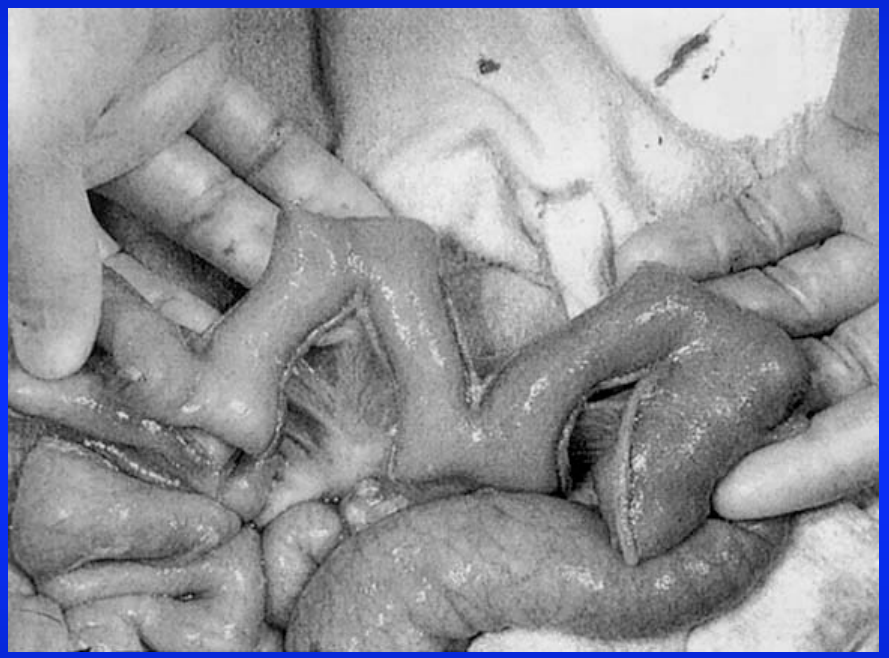
STEP



Kim et al., JPS 2003

STEP


L = Length of Bowel
S = Length of Each Cut
N = # of cuts
New Length = L + (S x N)
Channel Size



International STEP Registry Data

HB Kim, MD
Boston Children's Hospital

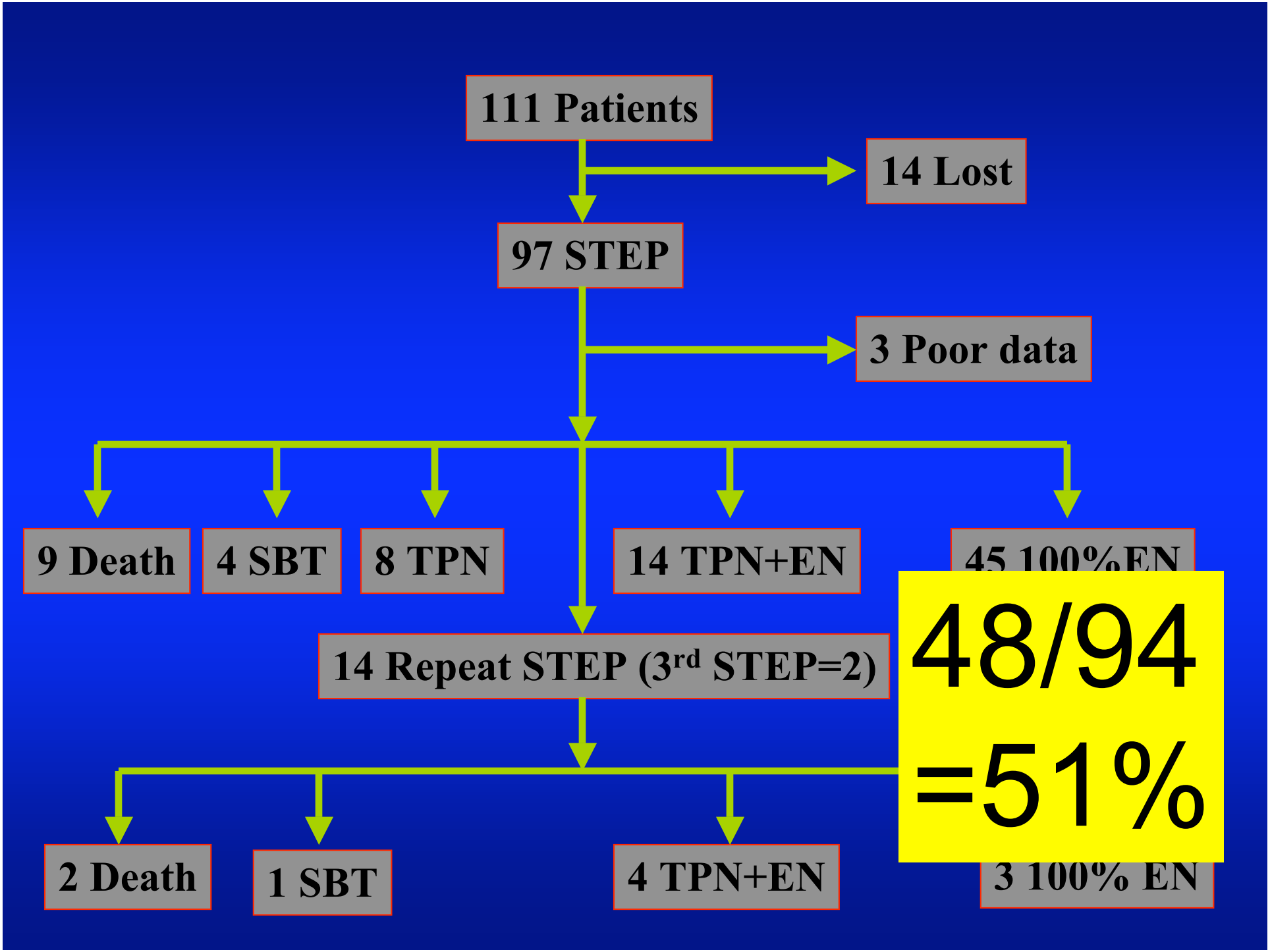
Pediatric Intestinal Failure and Rehabilitation Symposium (PIFRS)

Chicago, IL 2010

STEP Registry

- 111 patients
- 9/2004 – 1/2010
- 50 worldwide centers

HB Kim, MD


111 Patients
14 Lost
97 STEP
3 Poor data
9 Death
4 SBT
8 TPN
14 TPN+EN
45 100%EN
14 Repeat STEP (3rd STEP=2)
48/94
=51%
2 Death
1 SBT
4 TPN+EN
3 100% EN

Transplantation

July. 28. 2009. 7AM. At UCLA
Mr. WanChao Wu had a small bowel
transplant by Dr. Farmer. & his team

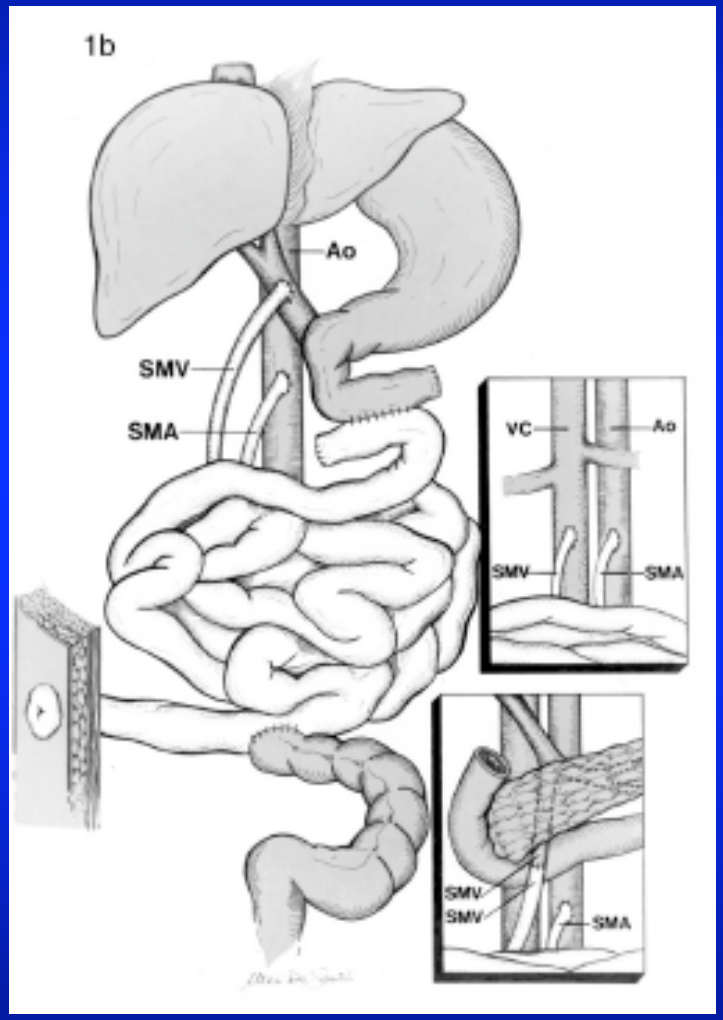
Intestinal Transplantation Indications

Irreversible **Intestinal Failure** associated with one or more life-threatening complications:

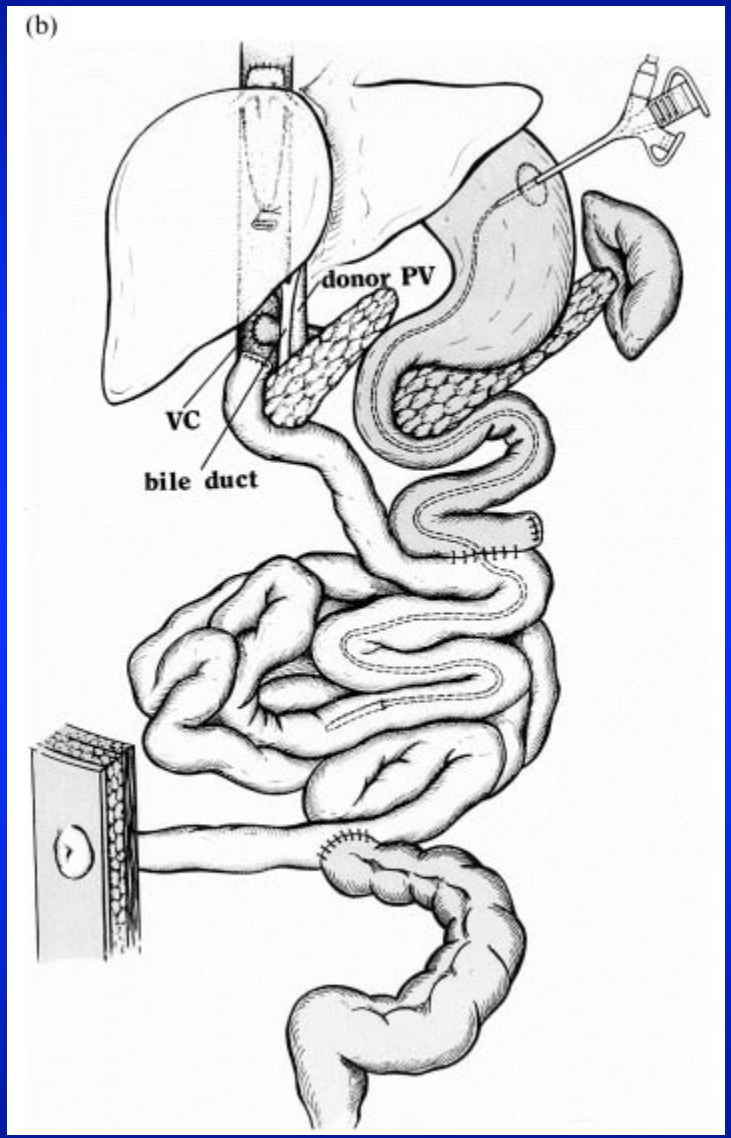
- Liver Disease
- Loss Vascular Access
- Recurrent Catheter Sepsis
- Complex fluid and electrolyte management
- Non-reconstructible GI Tract

Intestinal Transplantation
Graft Options

Isolated Intestine Implantation



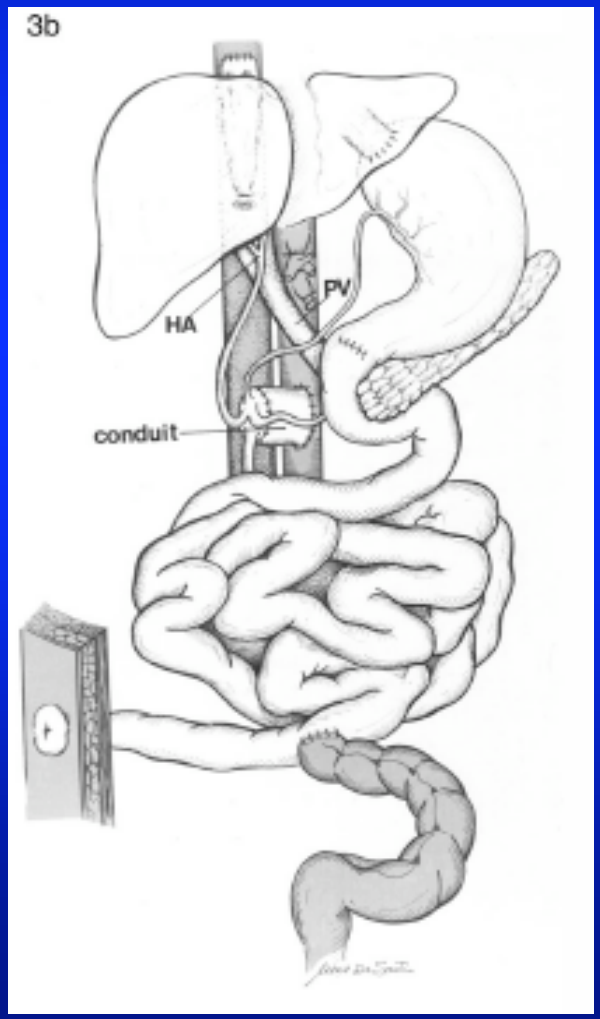
WJS 2002



COMBINED LIVER-INTESTINAL IMPLANTATION

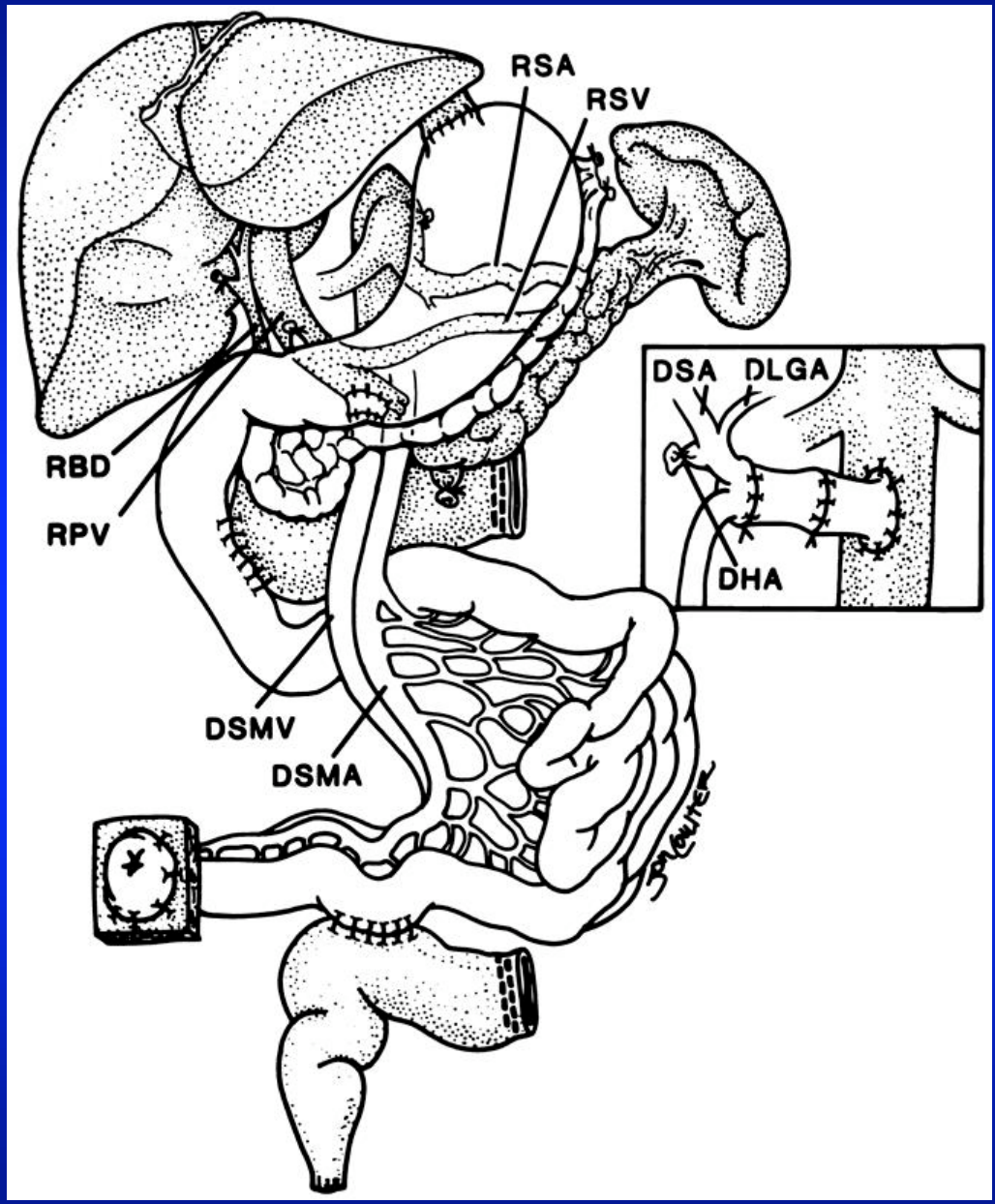
Miami Ped Transpl 1999

Multivisceral Implantation



WJS 2002

Modified Multivisceral Implantation



Ann Surg 2001

The liver, spleen and preformed antibodies are important predictors of survival after intestinal transplantation: Analysis of a single center, 20 year experience

Douglas G Farmer, Robert S Venick, Laura Wozniak, Yvonne E Esmailian, Hasan Yersiz, Kanela Artavia, Laurie Reyen, Susan Ponthieux, Erin Core, Villy Hwang, Anna Zafar, Galen Cortina, Sue V McDiarmid, Ronald W Busuttil

Intestinal Transplant Program
Dumont UCLA Transplant Center

XIth International Small Bowel Transplant Symposium
Washington, DC, September 2011

Introduction

- Short term survival after intestinal transplantation has markedly improved
  - 80-90% 1-year survival has been reported
- Medium term survival (1-5 yr) still lags
  - UNOS 5-yr survival 40-45%
  - ITR 2009 5-yr survival 50%
- Long term outcomes (>5 yr) are rarely reported

Pretransplant Predictors of Survival After Intestinal Transplantation: Analysis of a Single-Center Experience of More Than 100 Transplants

Douglas G. Farmer,[1,7] Robert S. Venick,[2] Joanie Colangelo,[1] Yvonne Esmailian,[1] Hasan Yersiz,[1] John P. Duffy,[1,3] Galen R. Cortina,[4] Kanela Artavia,[5] Khiet Ngo,[2,6] Suzanne V. McDiarmid,[2] and Ronald W. Busuttil[1]

Introduction. Outcomes after intestinal transplantation (ITx) have steadily improved. There are few studies that assess factors associated with these enhanced results. The purpose of this study was to examine peri-ITx variables and survival.
Methods. A review of a prospectively maintained database was undertaken and included all patients undergoing ITx from 1991 to 2010. The study endpoints were patient and graft survival. Data collection included 44 variables. Survival was computed using Kaplan-Meier methods. Univariate analysis was conducted (log-rank test) with significance set at *P* less than or equal to 0.20. Multivariate analysis of significant variables was conducted using model reduction by backward elimination variable selection method with significance set at *P* less than 0.05.
Results. Eighty-eight patients received 106 ITx. The majority of recipients were male, Latino, and children. The leading causes of intestinal and liver failure were gastroschisis and parenteral nutrition. Grafts transplanted were isolated intestine (24%), liver-intestine (62%), and multivisceral (14%). Overall 1- and 5-year patient and graft survival were 80% and 65%, and 74% and 64%, respectively. Significant univariate survival predictors were weight less than 20 kg, children, liver-inclusive allograft, panel reactive antibody less than 20%, absence of donor-specific antibody, negative crossmatch, warm ischemia time less than 60 min, absence of recipient splenectomy, interleukin-2 receptor antagonist induction, and era. Significant multivariate survival predictors were absence of donor-specific antibody, absence of recipient splenectomy, and liver-inclusive graft type.
Conclusion. This large, single-center ITx experience confirms a marked improvement in outcome over time. Several important factors were associated with survival, and these factors can potentially be adjusted before ITx. These findings should refocus future efforts on strategies to improve treatment and prevent graft loss.

Keywords: Intestinal transplantation, Small bowel transplantation, Multivisceral transplantation, Outcomes.

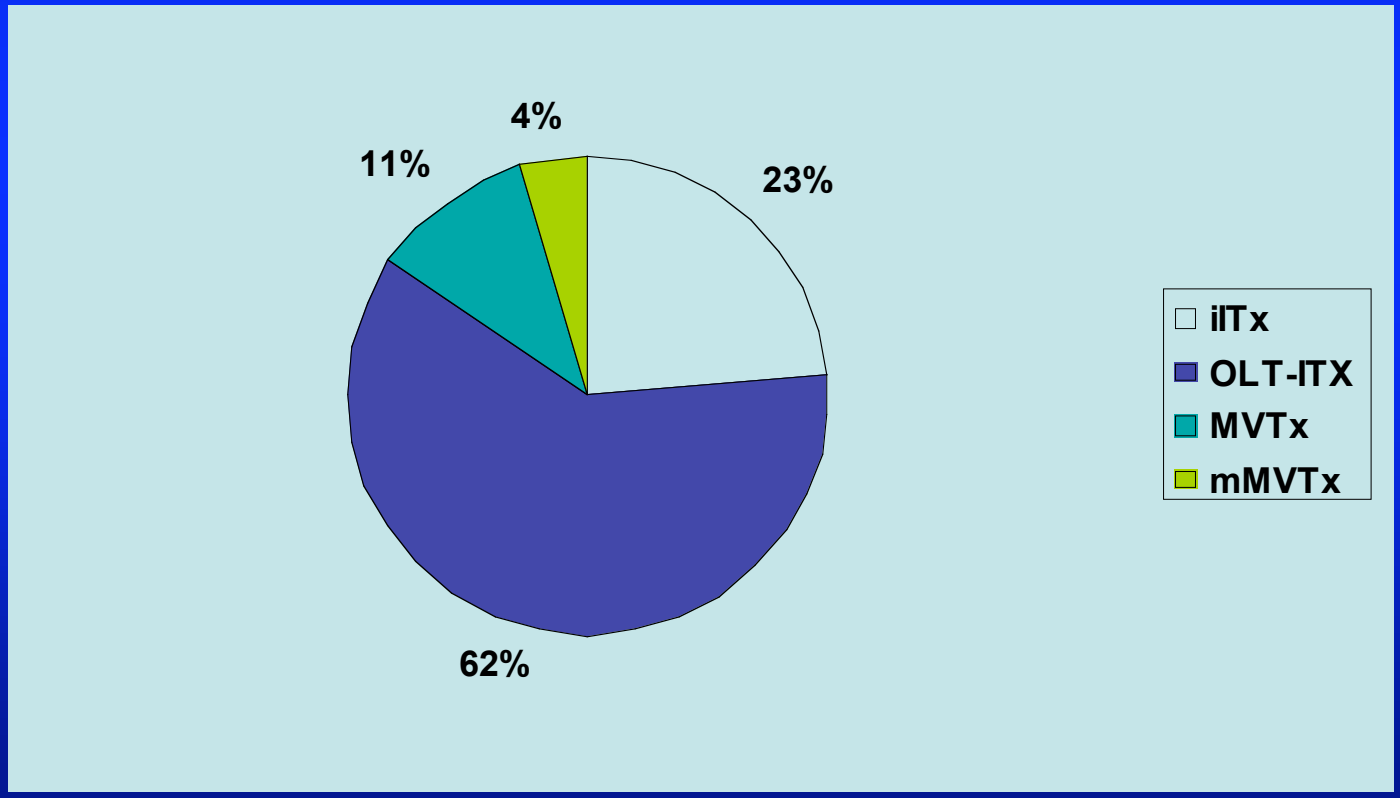
(*Transplantation* 2010;90: 1574–1580)

Results

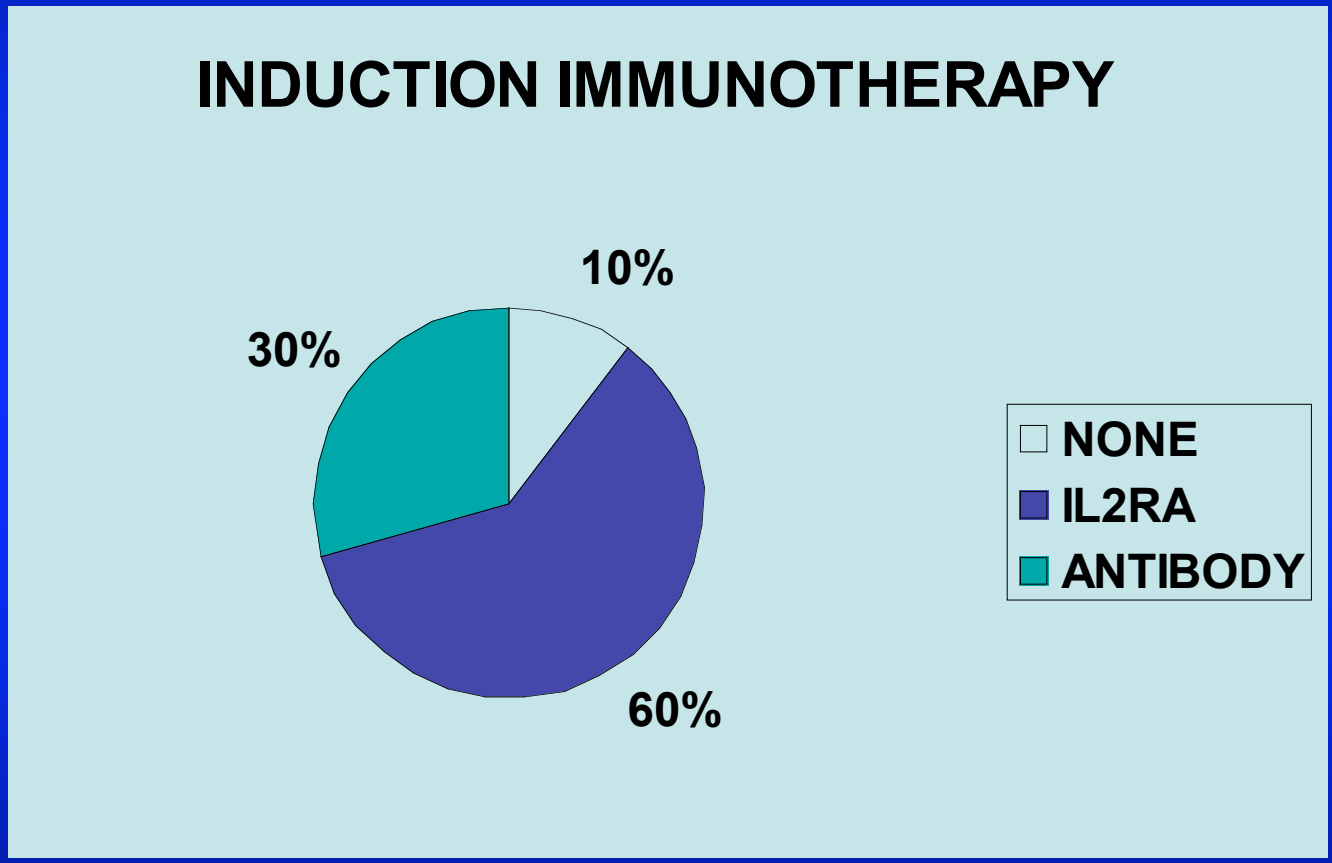
- 97 recipients
  - 59% male
  - 74% children
  - 12.1 ± 13.9 yrs old
  - Actual MELD/PELD 13.7 ± 11.3
  - Adjusted MELD/PELD 34.4 ±11.0
  - 45% hospitalized (25% ICU)
  - cGFR 109 ± 56 ml/min/1.73m^2

- 115 ITx
  - 6 kidney inclusive
  - 6 colon inclusive
  - 0 stomach inclusive

Results



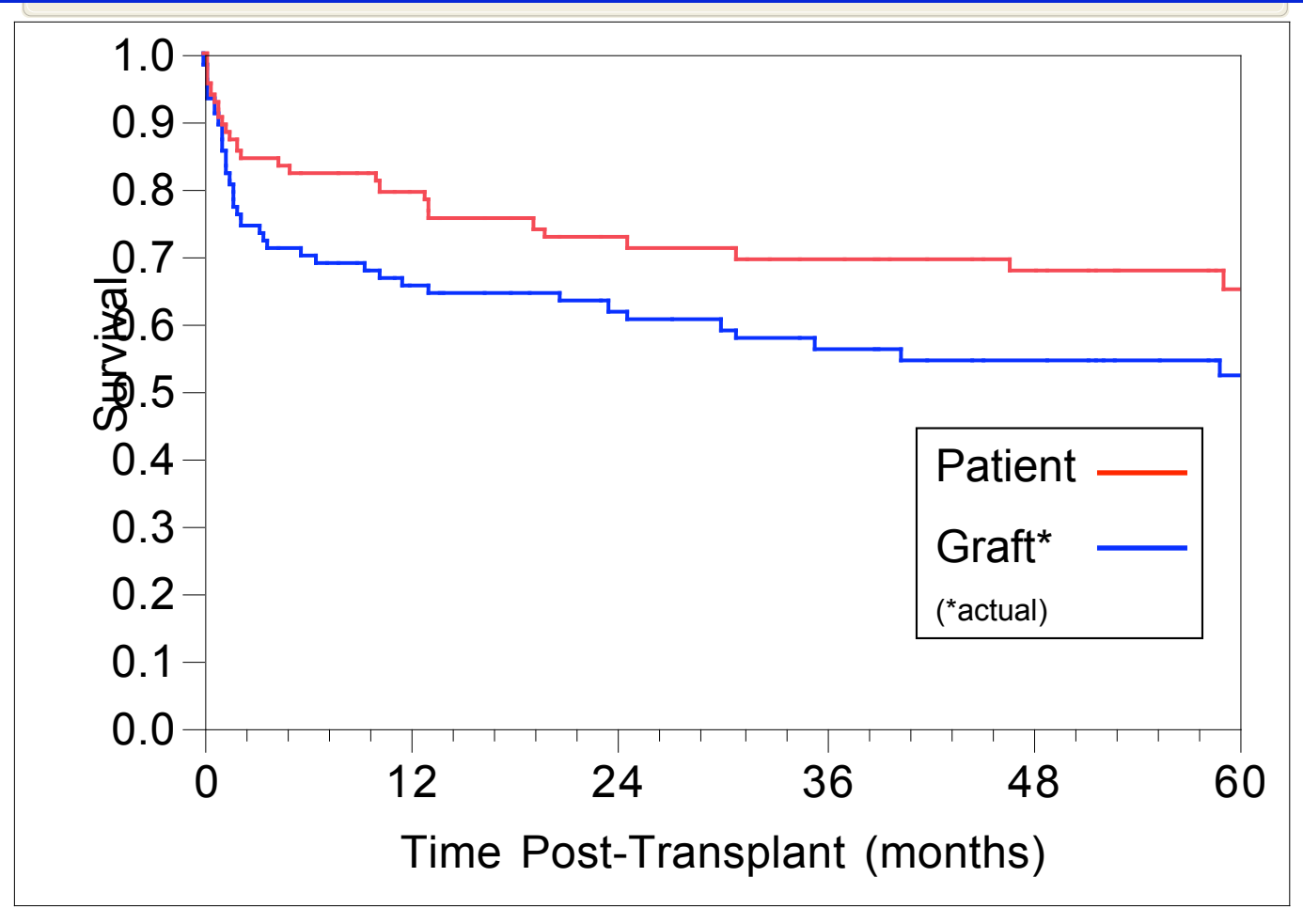
Results

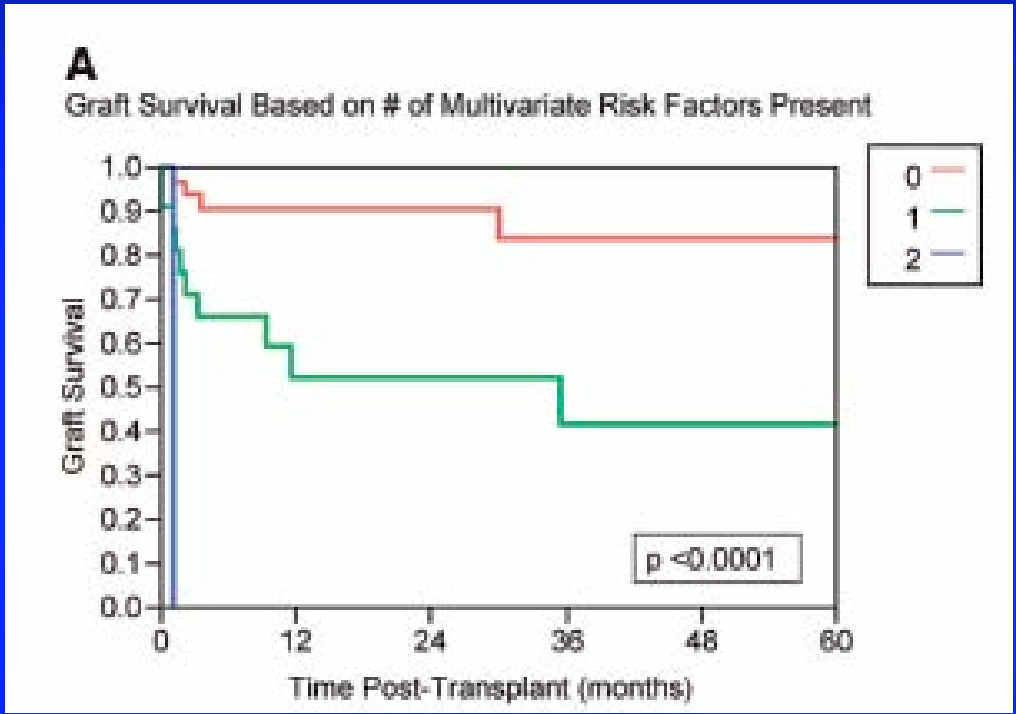


Results

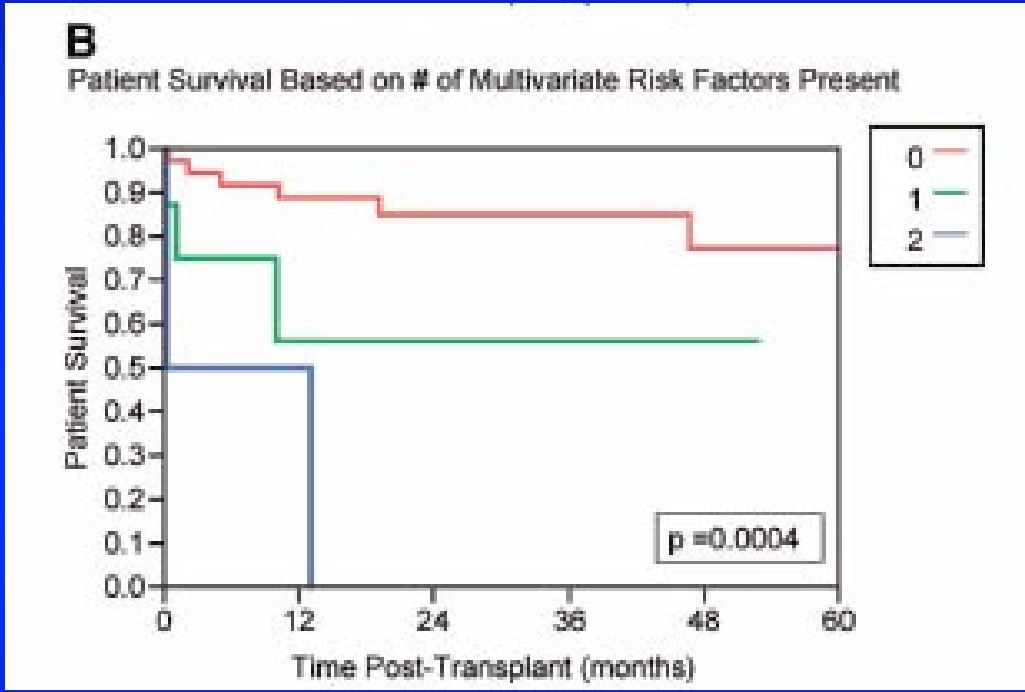
- Acute Rejection
  - 43% without ACR
  - Median 1 ACR/graft
- Chronic Rejection: 8 pt (7%)
  - 3.5 ± 2.4 yrs post-ITx
- GVHD: 3 pt (2.6%)
- Tissue invasive CMV Dz: 6 pt (5%)
- PTLD: 9 pt (8%)
- Infectious Enteritis: 70 pt (61%)

Post-Transplant Survival





0 = No risk factors
1 = DSA+ OR non-Liver graft
2 – DSA+ AND non-liver graft



0 = No risk factors
1 = DSA+ OR splenectomy
2 – DSA+ AND splenectomy

CONCLUSIONS

CONCLUSION 1

- TPN therapy required for all
- Long-term TPN management appropriate in some case
- Emphasize PN weaning
- Minimize PN associated complications

CONCLUSION 2

- Fish oil based lipid formulations appear to be safer in short-term for infants and children with early IFALD
- No long-term data
- Other emulsions in development

CONCLUSION 3

- Medical consideration should be given to the use of GLP2 analog in scientific study

CONCLUSION 4

- Surgical options should be considered in all
- STEP best applied to patients with
  - dilated small bowel segments
  - Dependent on PN for 25-75% of calories
  - Absence of advanced hepatic fibrosis/cirrhosis

CONCLUSION 5

- Reserve transplantation for patients who
  - Fail with adaptation
  - Develop 1 or more life-threatening TPN complications
  - Careful patient selection, operative planning
  - Choose the correct organs!

Thank You!