

# Long term Home Parenteral Nutrition vs Intestinal Transplantation for (non malignant) severe Intestinal Failure

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Dendera

# Etiologie, complications et traitement de l'Insuffisance intestinale sévère

Pathologies	Particularités
Infarctus mésentérique : artériel versus veineux	Potentiel évolutif propre
Entéropathie radique chronique	Localisations extradiigestives
Maladie de Crohn	Traitements spécifiques
Complications postopératoires	Sepsis intra-abdominal
Pseudo-obstruction intestinale chronique (POIC)	Traitement étiologique si POIC secondaire Manifestations extradiigestives possibles
Nutrition parentérale <sup>a</sup>	
Type de nutrition parentérale	Complication principale
Complémentaire ou quasi-exclusive	Cathéter central
À l'hôpital puis à domicile	Métabolique
De longue durée (> 2 ans)	Hépatopathie
Optimisation de l'absorption	
Médicale	Chirurgicale
Solution OMS, gélules de chlorure de sodium, Octréotide (SGC type I)	Rétablissement de la continuité colique et anse jéjunale
Hyperphagie	antipéristaltique (SGC Type II)
Nutrition entérale à débit constant	Entérectomie sub-totale (POIC)
Hormone de croissance recombinante humaine	Transplantation intestin ± foie
Glucagon like peptide-2	

# HPN for (non malignant) permanent IF vs. Intestinal Tx (ITx)

- **Tailored, Specific HPN disease track**
  - *Optimized techniques for Optimized nutrition :*
    - All-in-one nutritive mixture
    - Cyclic PN as soon as PN start
    - Normo-PN-Nutrition for macronutrients (MN)
    - Micronutrients « elemental » balances...
    - Dissociate water-electrolytes  
and Macronutrients needs
    - Complete self management after full education
    - Patient as « a main contributor » of care

# HPN for (non malignant) permanent IF vs. ITx

- **Tailored, Specific HPN disease track**
  - *Optimized techniques for Optimized nutrition :*
    - HPN should not be « exclusive feeding »
    - « bowel rest » has no advantage on the long run
    - PN dependence be calibrated at « minimal macronutrients needs »
    - HPN must be viewed as « a complement » of « partial oral failure »
    - Encourage hyperphagia with frequent meals
    - Implement tube feeding to be discussed if hyporexia

# HPN for (non malignant) permanent IF vs. ITx

- **Tailored, Specific disease track HPN**

- ***Optimized care of SBS or CIPO :***

- *Better to have a very short gut than a non functioning gut*
- *Use the remaining colon as an « absorptive organ »*
- *Use rehabilitative surgery & trophic factors...*

***Eg : Two 2125 ml night infusion per wk after Teduglutide<sup>TD</sup>  
in a very SBS : half duodenum - 6/7 of remaining colon !  
i.e., a 50% reduction of PN volume & calories vs. baseline***

# Adult IF-HPN : causes of death

<b>Mortality : n= 27</b>	<b>30%</b>
<b>Cause of death :</b>	
<b>KT &amp; non-KT Sepsis :</b>	<b>27%</b>
<b>Hepatopathy :</b>	<b>22%</b>
<b>Metachrone cancer :</b>	<b>15%</b>
<b>Evolution of primary disease :</b>	<b>15%</b>
<b>Metabolic complications :</b>	<b>8%</b>
<b>others :</b>	<b>13%</b>
<b>Total :</b>	<b><u>100%</u></b>

90 adult Patients; HPN duration : 45 (6-198) mo  
Cavicchi M et al Ann Intern Med 2000

# Survival of adult HPN-IF patients

Survival : 2 yrs	98 (96-100)%
4 yrs	80 (71- 89)%
6 yrs	65 (53- 77)%
8 yrs	56 (42- 70)%

\* Age was the **only significant** variable :

For age :	< 40 ans	≥ 40 ans
<b>6 yr- Survival</b>	<b>84(71-97)%</b>	<b>53(35-71)%</b>
* p <.001		<b>4.9(CI95%1.8-13.2)</b>

90 adult Patients; HPN duration : 45 (6-198) mo  
Cavicchi et al Ann Intern Med 2000

# HPN for (non malignant) permanent IF vs. ITx

- Variables to look at :

## – *Survival*

- Disease categories
- Degree of PN dependence (5L vs 30L / Wk) and of enteral (oral) autonomy :
  - » %absorbed :  $REE \times 1.5$
- Quality of life (QOL) and the will to live
- Team expertise

**Table 1.** Factors Adversely Influencing the Outcome of Long-Term Parenteral Nutrition Therapy.\*

Factor	Source of Data
<b>Affecting survival</b>	
Age >60 yr at institution of therapy	Messing et al. <sup>4</sup>
Jejunioileal length <50 cm	Messing et al., <sup>4</sup> Chan et al. <sup>5</sup>
Dysmotility	Scolapio et al. <sup>6</sup>
Radiation enteritis	Howard and Malone <sup>7</sup>
More severe obstruction	Messing et al. <sup>4</sup>
Longer treatment	Howard and Malone <sup>7</sup>
<b>Affecting rehabilitation</b>	
Jejunioileal length <50 cm	Wilmore et al. <sup>2</sup>
Absence of ileocecal valve	Wilmore et al. <sup>2</sup>
Mucosal disease	Wilmore et al. <sup>2</sup>
Dysmotility	Scolapio et al. <sup>6</sup>
Abdominal-wall defect in children	Thakur et al. <sup>8</sup>

**Survival**

Age > 40

Jejunal < 50 (ischemia)

Scleroderma

...

Impossibility to eat

No

**Rehabilitation**

J-I<35; J-C<60,Js<100

See above

....

If impossibility to eat

...

# HPN outcome in adult :

## Risk factors for death in SBS

- **For post-surgical short bowel syndrome :**
  - **Specific conditions :**
    - Age : yes (in every study) better in younger patients < 40yr
    - Learning curve for HPN : yes in expert centers
    - Remnant anatomy in SBS : yes for < 50cm especially in jejunostomy patients (SBS Type I) : arterial mesenteric infarction
    - Impossibility to eat (chronic [organic] occlusion...) : yes
    - ? Drugs, such as opiates : expert opinion
    - ? Degree of PN dependence (5L vs 30L / Wk) : see anatomy
    - Other : in expert centers death rate is not linked to HPN per se but mostly to the underlying condition

# HPN outcome in adult :

## Risk factors for death in CIPO

- **For chronic intestinal motility disorders :**
  - **Specific conditions :**
    - Age : yes better in younger patients < 20yr
    - Learning curve for HPN : yes in expert centers
    - SBS (J-C) in CIPO : not a worsening factor in adult
    - Impossibility to eat : yes aggravate the outcome
    - ? Drugs, such as opiates : worsen in expert opinion
    - ? Degree of PN dependence (5L vs 30L / Wk) : see eating
    - Other : in expert centers death rate is not linked to HPN per se but mostly to the underlying condition

# Rehabilitation in (*PN dependent*) SBS

Intervention	Absorbé			Poids de selles (%)
	kcal (%)	DER (gain %) <sup>a</sup>	Protéines g/kg par jour	
Hyperphagie+ : 1,6 vs 2,3 DER (n = 14)	NS	+ 33	1,3 vs 0,75	-11 (NS)
Nutrition entérale par sonde nasogastrique vs Oral <sup>b</sup> 1,9 vs 1,6 DER (n = 15 ; NS)	82 vs 65	+ 35	1,4 vs 0,8	+6 (NS)
Nutrition entérale par sonde nasogastrique + oral vs oral <sup>c</sup> 2,5 vs 1,6 DER (n = 9)	75 vs 65	+ 55	1,3 vs 0,8	+ 25 (NS)
GHRH 2,1 vs 1,9 DER (n = 12 ; NS)	54 vs 40	+ 28	0,8 vs 0,5	-8 (NS)
Glucagon like peptide-2 recombinant (Ingesta : ?) (n = 16)	NS	NS	NS	-22 (750 g/jour)
Continuité colique 1,6 DER (n = 64)	66 vs 50	+ 33	—	-36 (500 g/jour)
Anse jéjunale anti péristaltique <sup>d</sup> 1,7 DER (n = 28)	69 vs 58	+ 21	0,9 vs 0,75	-3 (NS)

# Perspectives

- To day & to morrow :
  - Diet to be optimised : ***hyperphagia is cornerstone***
    - Tube feeding for ‘non hyperphagic’ patients
  - Routine gastro treatment :
    - PPI, slowing transit,
    - Sequential antibiotics if occlusive episodes
    - SBS type I : sequential Octreotide decrease by 30%(H<sub>2</sub>O-Na) stoma output
  - Nutritional treatment :
    - Vitamins (D, E,A...), minerals (Mg, Ca ...)
  - **Reestablish colonic continuity**

# Perspectives

- To morrow : indicate
  - *Cocktail of enteric trophic factors* (exclude *malnutrition* because of '*resistance to neuropeptides*').... and
  - *Rehabilitative surgery* : reverse jejunal segment in SBS type II
  - Extensive small bowel resection in some severe CIPO
- **Transplantation if HPN fails with above strategy**

# Guts\*

ADAM HAS EATEN THE APPLE

EVE HAS EATEN ADAM

THE SNAKE HAS EATEN EVE

THIS WORLD IS THE OBSCURE INTESTINE

...

*Ted Hughes (1930-1998, Theology)*

\*Guts

# Guts\*

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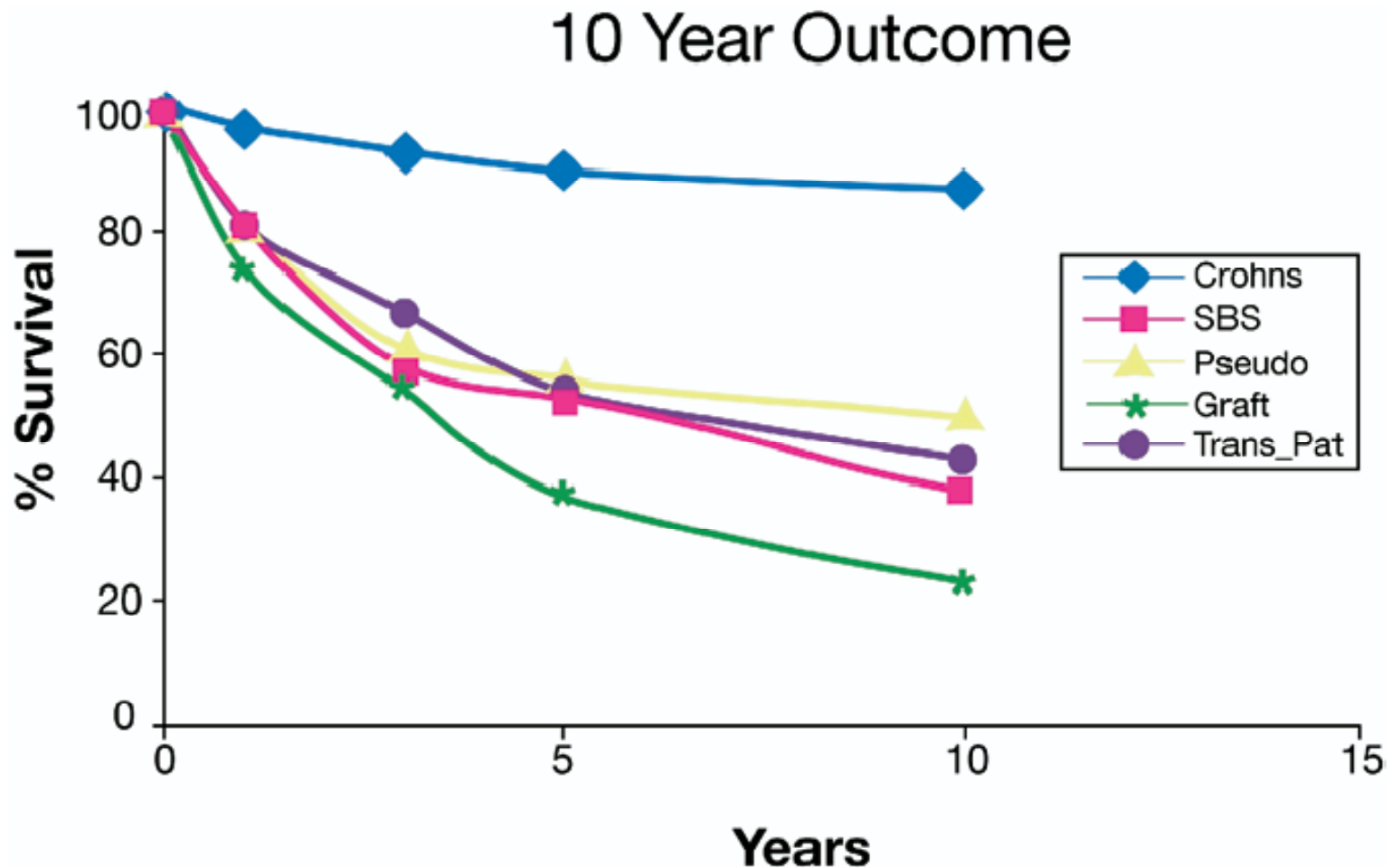
THIS WORLD IS THE OBSCURE INTESTINE

**But does transplantation bring Light ?**

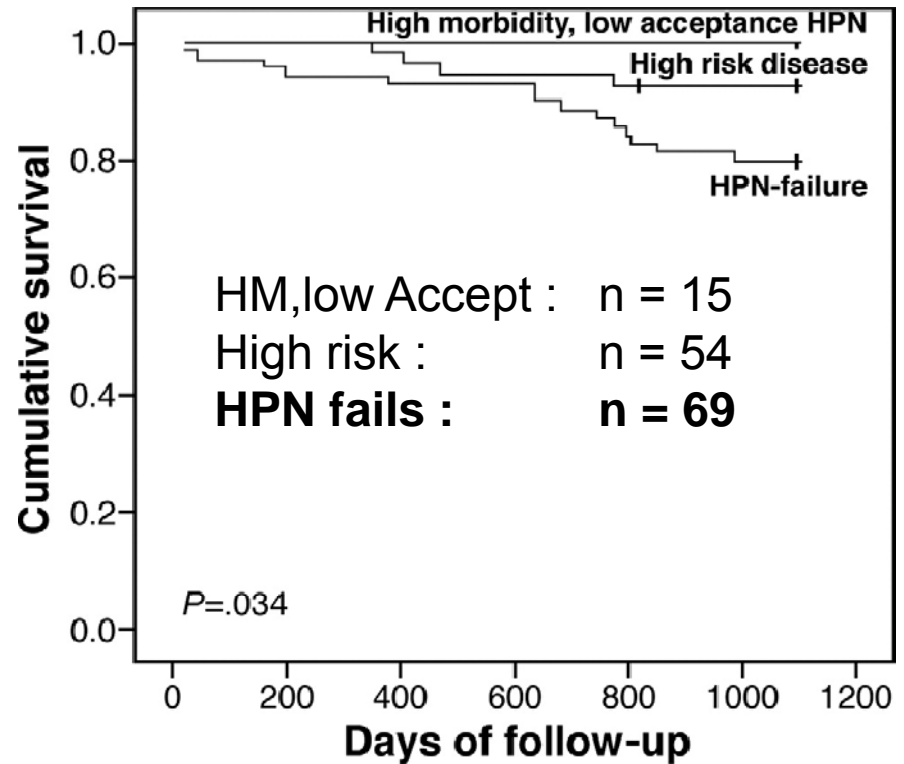
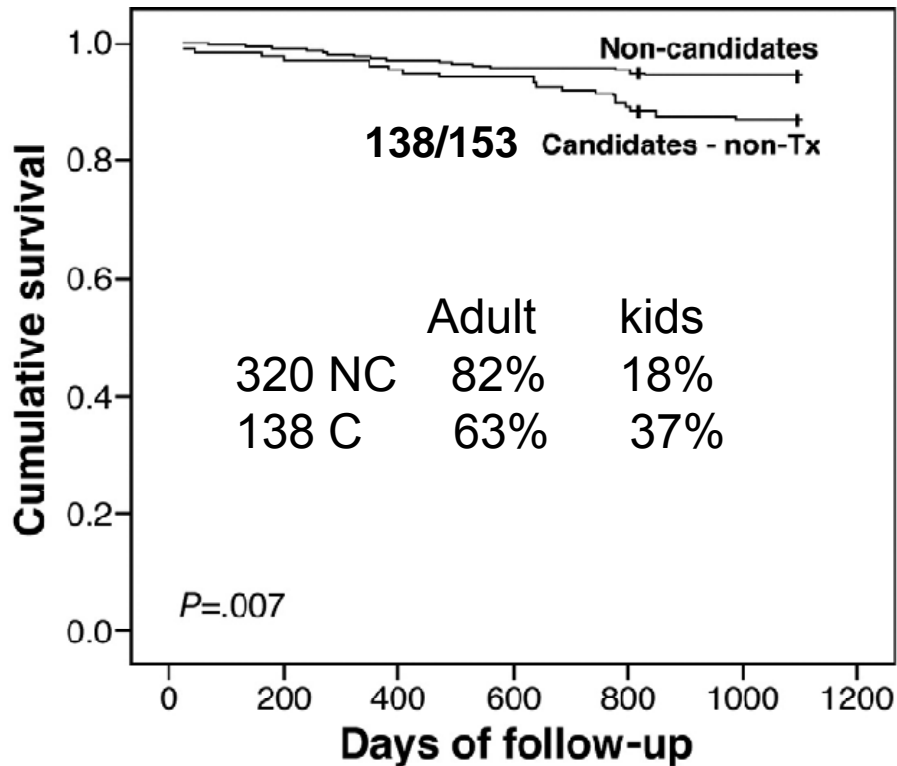
*Ted Hughes (1930-1998, Theology)*

\*Guts

# HPN vs Intestinal transplantation



From Jeejeebhoy et al HPN in Canada; IF book 2006.  
& Freeman RB et al Am J Transplant 2008; 8: 958-76.



**Population :** , Multicentre, 3 yr prospective survival,  
deemed permanent Intestinal failure : **weaned 72(15%)1/3 after 3yrs,**

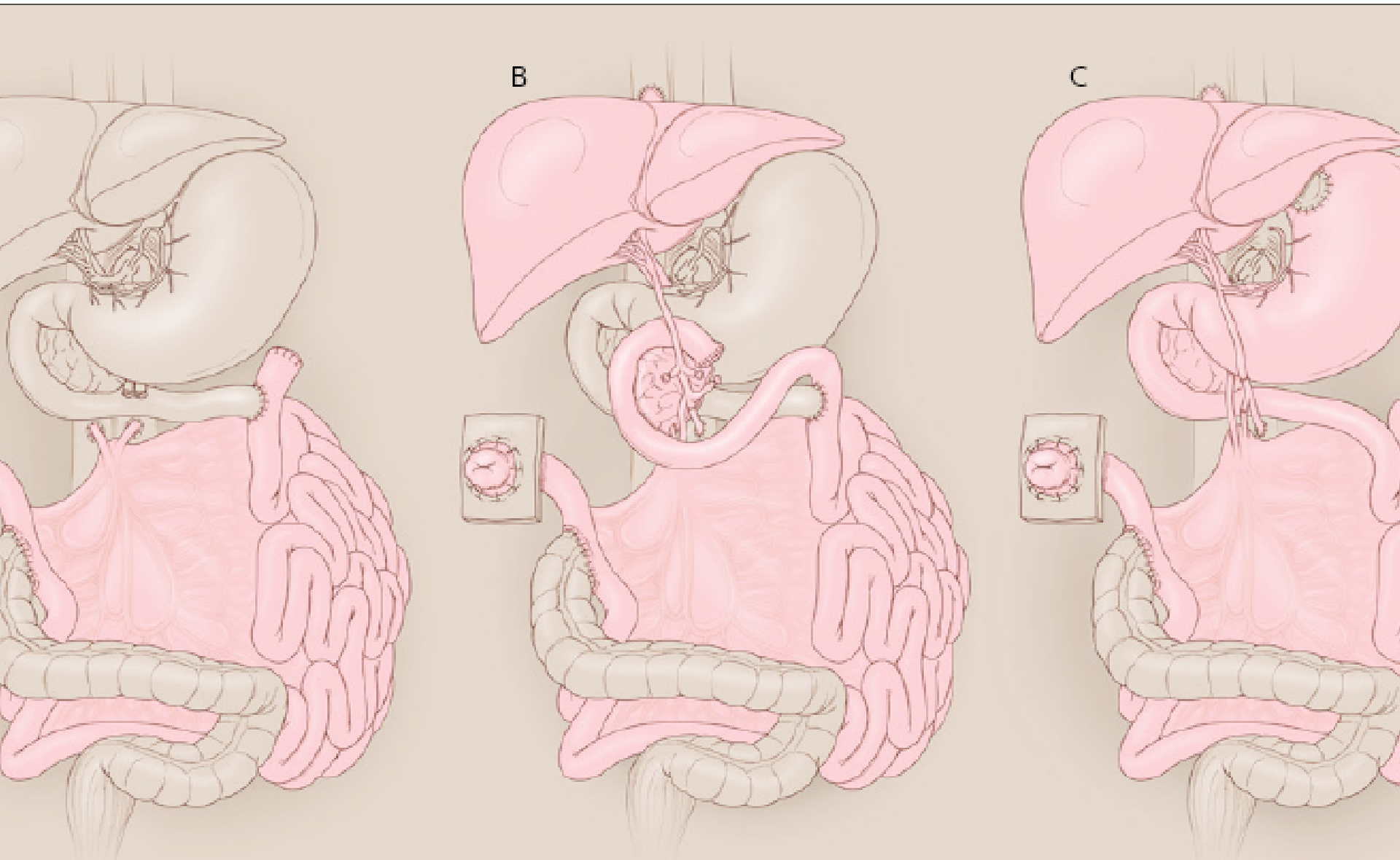
	Adult : 359 (76%),	Ped : 114 (24%)	total
473 patients			
SBS	276 (77%)	61 (53%)	71%
Motility	62 (17%)	30 (26%)	19%

**Table 2.** Distribution of Disease States among Recipients of Intestinal Transplants.\*

Disease State	Children (N= 1031)	Adults (N= 733)
	<i>percent</i>	
Short bowel syndrome		
Volvulus	17	7
Gastroschisis	21	1
Trauma	2	8
Necrotizing enterocolitis	13	1
Ischemia	1	25
Crohn's disease	0	12
Intestinal atresia	8	0
Other	2	8
Malabsorption (mucosal defect)		
Microvillus inclusion	6	0
Secretory diarrhea	0	0
Autoimmune enteritis	0	0
Other	2	0
Motility disorder		
Pseudo-obstruction	9	9
Aganglionosis		
Hirschsprung's disease	8	0
Other	1	0
Tumors	1	15
Retransplantation	8	7
Other	2	5

Fishbein TM  
NEJMed 2009;  
361(10):998-1008

From  
[internationaltransplant.org](http://internationaltransplant.org)



**T Fishbein NEJMed 2009, 361(10):998-1008**

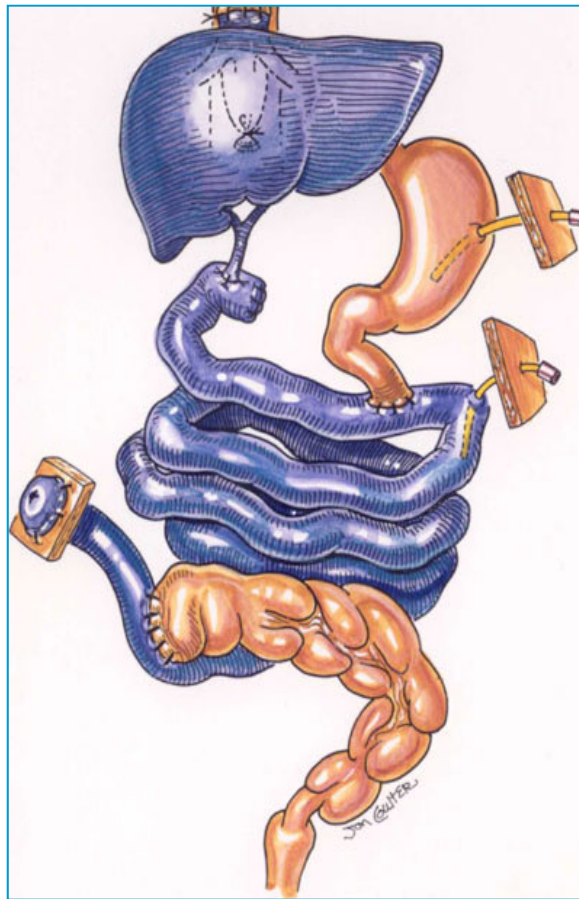
**Three Types of Transplants in Intestinal Failure.**

When the small intestine (jejunoileum) is transplanted alone, it is referred to as an isolated intestinal transplant (Panel A), with the transplant connected to the recipient's vena cava. A composite liver and intestinal transplant usually includes the duodenum and an intact biliary system (Panel B). A composite liver and intestinal transplant usually includes the duodenum and an intact biliary system (Panel C).



Isolated Ltx  
"Preemptive"

**45%**



Liver & Intestinal Tx  
Irreversible fibrotic L

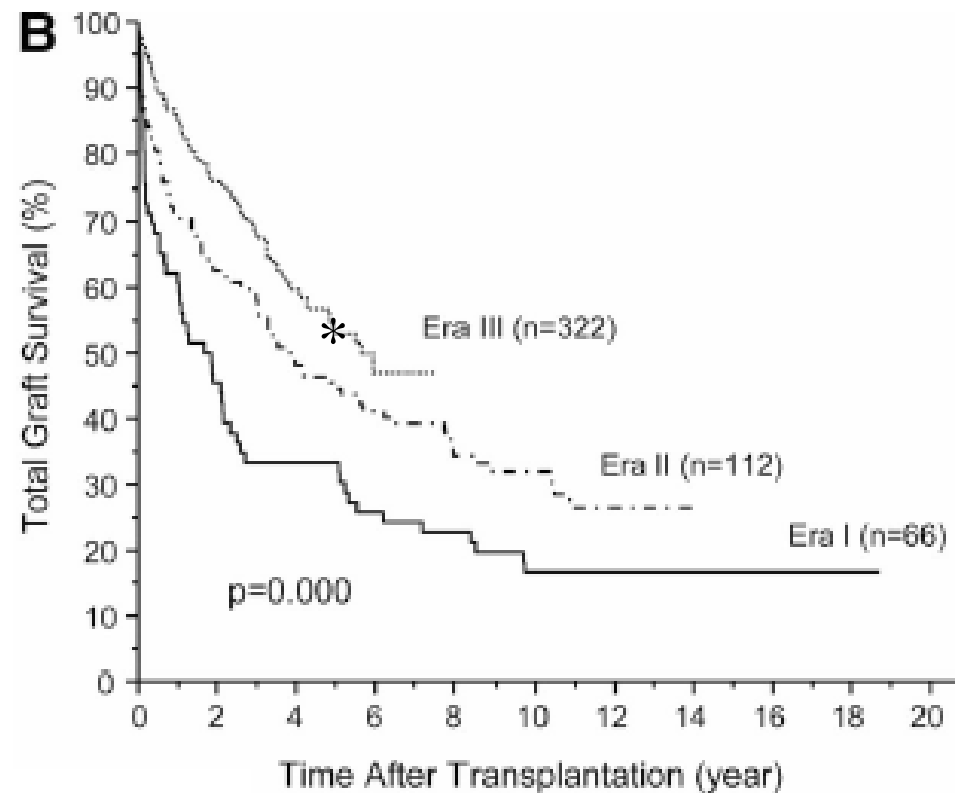
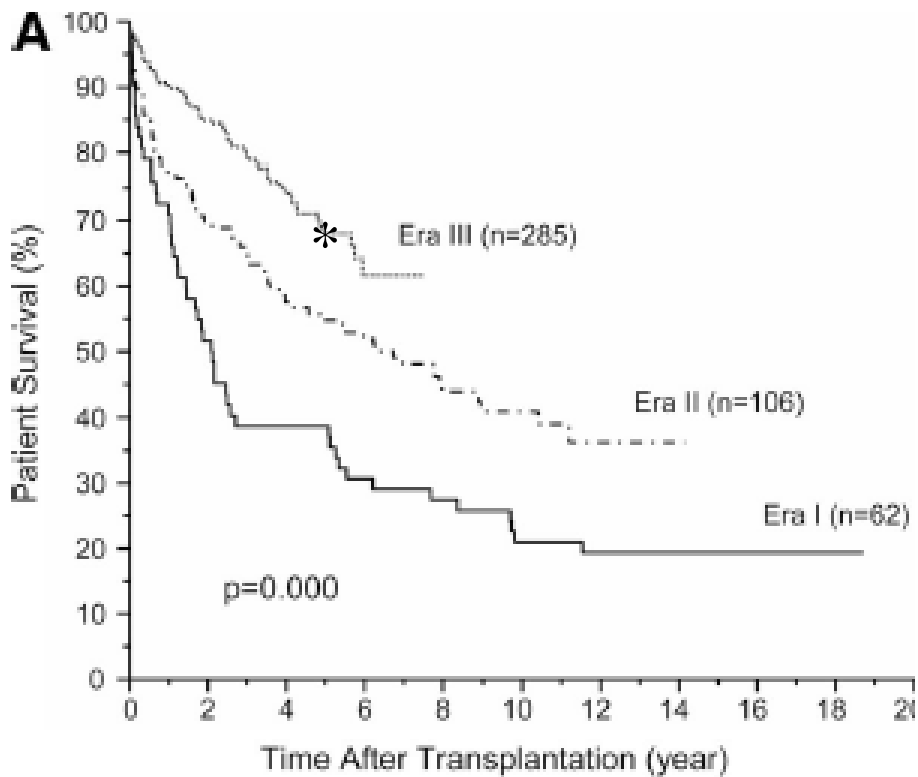
**30%**



Multivisceral Tx  
Disease related

**25%**

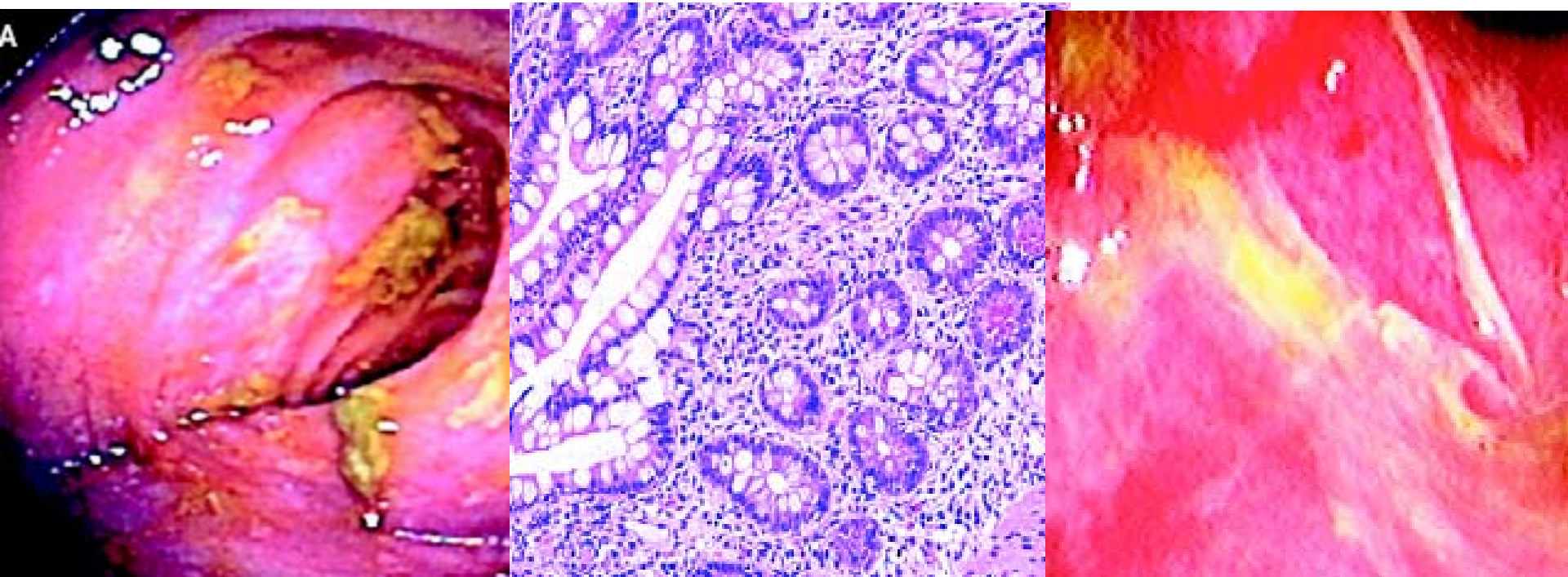
From [internationaltransplant.org](http://internationaltransplant.org)



Abu-Elmagd K et al Ann Surg 2009;250: 567-581

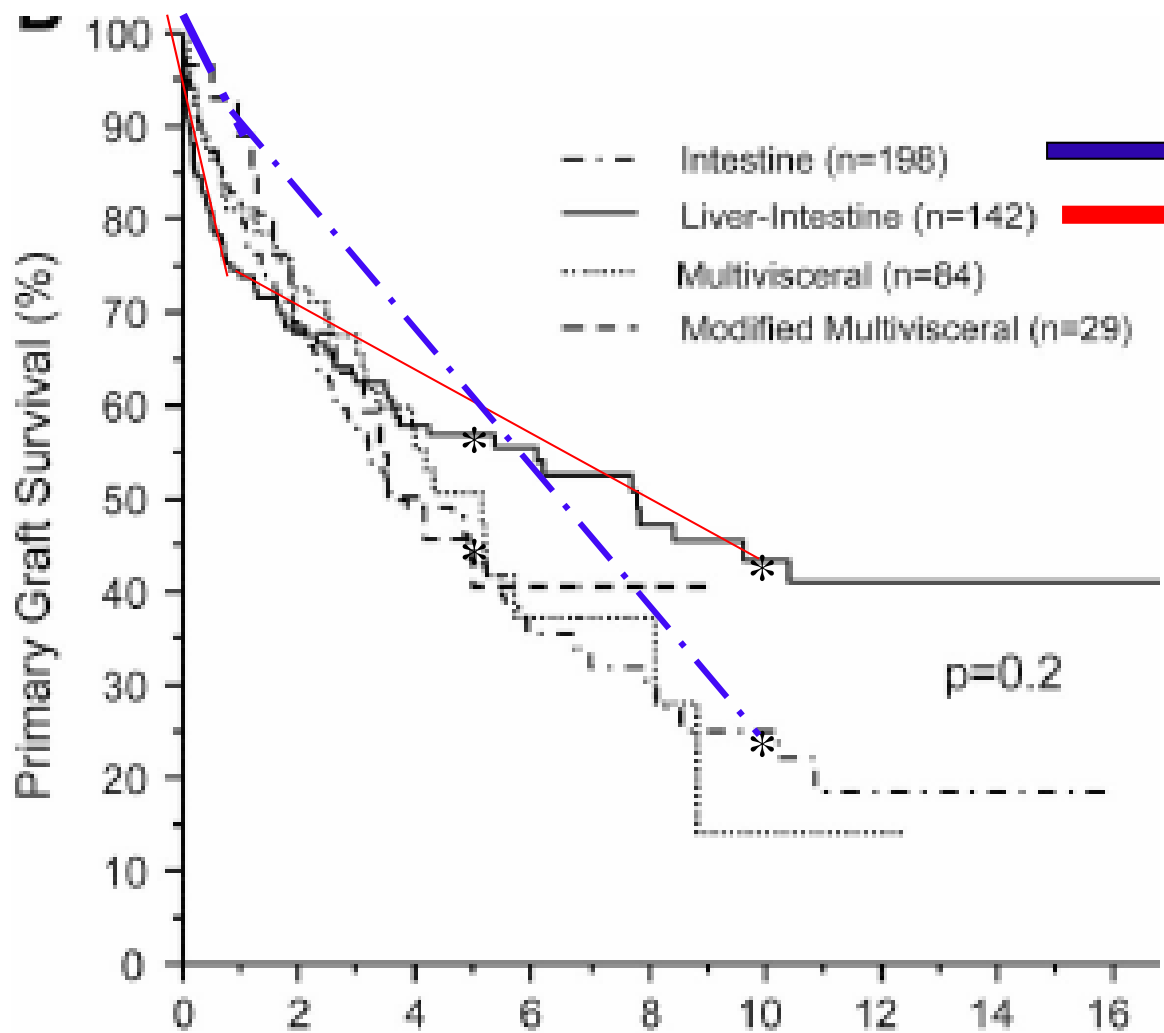
International registry (2009):  
 Hospital stay 40-60 d  
 Survival at 3 yr : 66%  
 Full functioning graft : 66%

# An example of moderate evolving to severe rejection (Needs early intervention even asymptomatic)



\*Acute cellular rejection occurred in the first 3-month in :  
90% vs. 50% of cases  
Phase 2 (1990-2000) vs. Phase 3 (post 2000)

T Fishbein NEJMed 2009, 361(10):998-1008



Abu-Elmagd K et al Ann Surg 2009;250: 567-581

## *Prognosis of Intestinal transplantation & home parenteral nutrition in adults.*

<b>Event</b>	<b>Intestinal Tx (% of patients)</b>	<b>long term HPN (% of patients)</b>
Survival at 1 yr	90%	> 90%
Survival patients at 5 yrs	50% to 60%	70% to 80%
Survival of graft at 5 yrs	40% to 50%	
Rejections (n ≥ 1)	70% of patients	
Renal Fonction	at 2 yrs : decreased GFR < to 50%	in SBS type I : Tubular Necrosis : 1%
Liver Fonction	---	at 5 yrs, cirrhosis : < 20%
Rehospitalisations :		
- Bacterial Infections	90%	66 %
- Fungal Infections	9%	3%
- Viral Infections	25%	< to 1%
- Thromboses	visceral 5%	catheter-related : 25%
Quality of life		
- Karnofsky score	80 in 85%	80 in 70%
- HPN dependency	15-20%	100%

# Prognosis of ITx\*

- Better overall Prognosis related to :
  - N° of Cases > 10 vs few cases per year
  - Home vs. Hospitalized patient
- In One-yr survivors, better 5-Yr prognosis :
  - no rejection in the 3-mo after grafting
  - Liver/intestine vs. Intestine alone

XI ISBTransplant symposium september 2009;

\* From the International transplant registry 2009 (unpublished data) :  
Multivariate analysis

# HPN for (non malignant) permanent IF vs. Preemptive ITx

- **My first choice will be**
  - Tailored, Specific HPN disease track
  - Integrated « IF care » in a tertiary care centre
- **ITx before irreversible HPN failure**
  - in a Home patient,
  - in a high volume-case centre

HPN for (non malignant) irreversible IF  
and ITx for HPN failure : Yes

ITx for deemed irreversible IF  
and HPN for ITx failure : No



# Long term Home Parenteral Nutrition vs Intestinal Transplantation for (non malignant) severe Intestinal Failure

**We have to drive the boat  
and be prepared to confront the tempest**

**Safe Line & Host**

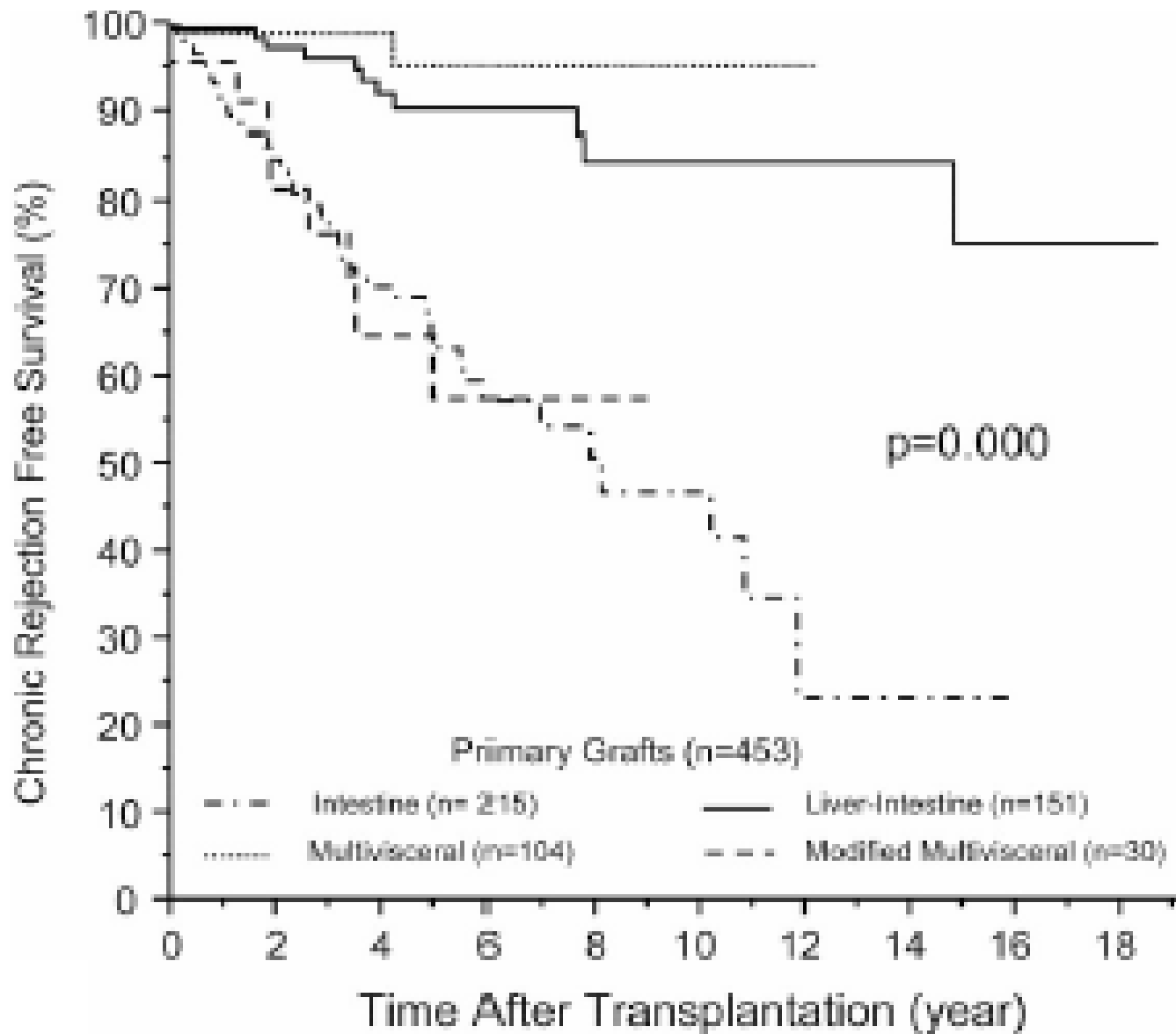
The goal is to  
avoid / postpone  
HPN failure

*versus*

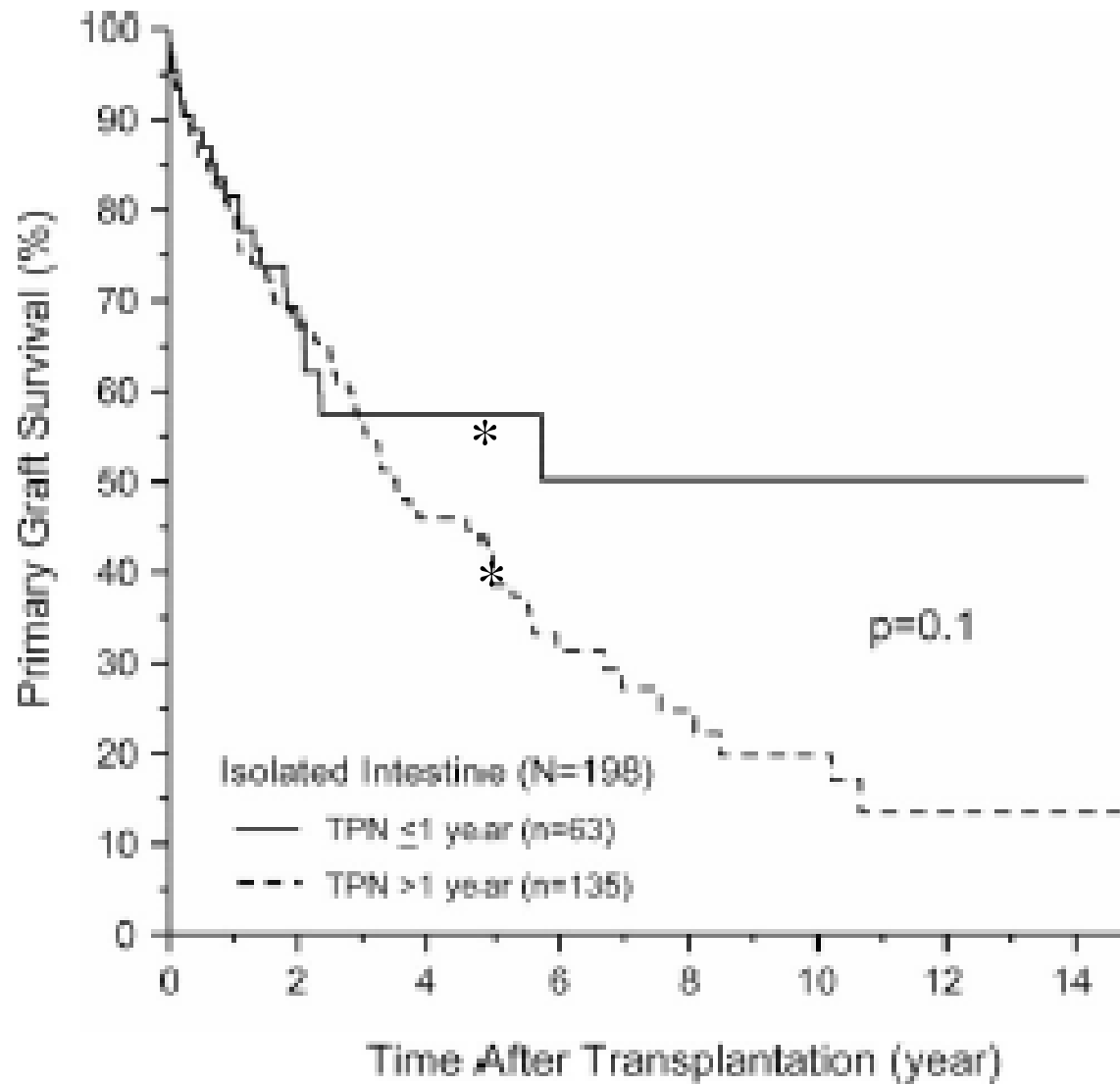
**Allograft & Host**

The goal is to  
reduce rejection  
& infection

**In all cases we have to do a « patient 's education »**



Abu-Elmagd K et al Ann Surg 2009;250: 567-581



Abu-Elmagd K et al Ann Surg 2009;250: 567-581