INDICATIONS FOR INTESTINAL TRANSPLANTATION

Loris Pironi
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Loris Pironi
Chronic Intestinal Failure Centre
Dpt. of Internal Medicine & Gastroenterology
St. Orsola-Malpighi H. – University of Bologna
Italy
Irreversible Benign Intestinal Failure
Treatment Options

- Home Parenteral Nutrition (HPN)
- Intestinal Transplantation (ITx)
Types of ITx

**Isolated small bowel**
no liver failure + normal gastro-duodenal tract

**Combined small bowel + liver**
progressive liver failure, some hypercoagulability syndromes

**Multivisceral (small bowel + stomach ± pancreas) ± liver**
CIPO, Gardner S, extensive FAP, some malignancy, total occlusion of splanchnic circulation
Survival after ITx

International ITx Registry ≥ 1998
Children 61%, Adults 39%

Intestinal Transplant Registry (Grant, ’05)
Efficacy of ITx

Graft Function
(N=406 survived > 6 mo)

Modified Karnofsky Performance Score
(N=406 survived > 6 mo)

Intestinal Transplant Registry (Grant, '05)
Survival
HPN vs ITx

International ITx Registry ≥ 1999
Children 61%, Adults 39%

% Survival

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
0 1 2 3 4 5
Years Post Tx

- Multivisceral
  - Intestine + Liver
  - Intestine

HPN - Children (Paris, '80-00 - Colomb,Goulet, 2004)
HPN - Adults (Bologna, '86-01 - Pironi, 2003)
HPN - Adults (France, '80-89 - Messing, 1995)
# Safety

## HPN vs ITx

<table>
<thead>
<tr>
<th></th>
<th>HPN (% of total deaths)</th>
<th>ITx (% of total deaths)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deaths</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-related</td>
<td>Ad: 3 – 20 %</td>
<td>80 – 100 %</td>
</tr>
<tr>
<td></td>
<td>Ch: 23 – 42 %</td>
<td>(Ch = Ad)</td>
</tr>
</tbody>
</table>

**HPN:** CVC-sepsis, CVC-vein thrombosis, liver failure

**ITx:** sepsis-MOF, rejection, lymphomas, technical reasons

**HPN-Ad:** Messing, ’95; Jeppesen, ’98; Pironi, ’03;

**HPN-Ch:** Vargas, ’87; Gambarara, ‘02; Guarino, ‘03; Colomb & Goulet, ’04

**ITx:** Intestinal Transplant Registry (Grant, ’05)
HPN vs ITx

- **Survival**: HPN > ITx
- **Safety**: HPN > ITx
Indications for ITX

CURRENT DOCUMENTS

2000: USA Medicare Coverage Policy Decision

2001: American Society of Transplantation Position Paper on Pediatric ITx
<table>
<thead>
<tr>
<th>HPN-Failure</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver failure</td>
<td>• patients destined to die on HPN</td>
</tr>
<tr>
<td>(impending or overt)</td>
<td></td>
</tr>
<tr>
<td>CVC-related thrombosis</td>
<td>• complete loss of venous access is rare</td>
</tr>
<tr>
<td>(≥ 2 central veins)</td>
<td></td>
</tr>
<tr>
<td>Frequent CVC-sepsis</td>
<td>• low mortality rate</td>
</tr>
<tr>
<td>(2 / yr; fungemia, Shock, ARDS)</td>
<td>• often due to poor CVC care</td>
</tr>
<tr>
<td>Frequent severe dehydration</td>
<td>• frequent infections in ITx</td>
</tr>
<tr>
<td>(despite optimal HPN)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• risk of renal failure on HPN</td>
</tr>
<tr>
<td></td>
<td>• risk of crf after ITx &gt; after any Tx</td>
</tr>
</tbody>
</table>

(AGA technical review and position statement, Gastroenterology 2003)
### Indications for ITx
American Society of Transplantation

#### Further Indications

<table>
<thead>
<tr>
<th>Condition</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locally invasive tumors (desmoids in FAP,..)</td>
<td>• frequent cause of death</td>
</tr>
<tr>
<td>Ultra short bowel (&lt; 10 cm jejunum C; &lt; 50 cm in A)</td>
<td>• greater risk for HPN-failure</td>
</tr>
<tr>
<td>Congenital intractable mucosal d. (microvillus inclusion, tufting enteropathy,..)</td>
<td>• death may occurs in few yrs</td>
</tr>
<tr>
<td>IF with high morbidity / poor QoL (severe CIPO, high output stoma,..)</td>
<td>• not clearly demonstrated&lt;br&gt;• risk of Munchausen S.</td>
</tr>
</tbody>
</table>

(Kaufman et al, Pediatr Transplantation, 2001)
Irreversible Benign Intestinal Failure

Indications for ITx

Criteria
- HPN Failure
- Primary disease related risk of death
- IF with high morbidity poor QoL

Role of ITx
- Life saving
- Preemptive
- Rehabilitation

Candidates
- Liver failure > other causes
- Some carefully selected cases
- ? A few very particular cases
Candidates for ITx
A EUROPEAN SURVEY in 2004
(ESPEN HAN-Working Group, 2004)*

HPN centres 41 - European Countries 9

Patients on HPN

USA Medicare
Am. Transplantation Soc.
Indications for ITx

Candidates for ITx

Adults 688

Pediatr. (≤ 18 y) 166

16 %

34 %

Candidates for ITx “A European survey”

Indication criteria subgroups

- HPN failure
- High risk primary disease
- Poor QoL

(ESPEN HAN-Working Group, 2004)
### Indications in candidates for ITx

<table>
<thead>
<tr>
<th>Indication</th>
<th>Adults</th>
<th>Pediatrics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver failure</td>
<td>0%</td>
<td>20%</td>
</tr>
<tr>
<td>Vein Thrombosis</td>
<td>20%</td>
<td>0%</td>
</tr>
<tr>
<td>CVC-Sepsis</td>
<td>40%</td>
<td>60%</td>
</tr>
<tr>
<td>Dehydration</td>
<td>60%</td>
<td>40%</td>
</tr>
<tr>
<td>Desmoids</td>
<td>80%</td>
<td>20%</td>
</tr>
<tr>
<td>Congenital disorder</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Ultra short bowel</td>
<td>80%</td>
<td>20%</td>
</tr>
<tr>
<td>Poor quality of life</td>
<td>60%</td>
<td>40%</td>
</tr>
</tbody>
</table>

(ESPEN HAN-Working Group, 2004)
From HPN to ITx

Prognosis on HPN without HPN-failure

Prognosis on HPN with HPN-failure

Timing for referral-listing

Prognosis after ITx

Prognosis on waiting list
### Negative prognostic factors on HPN

#### Without HPN-failure
- Age < 1 yr (C)
- Age > 40 yr (A)
- SBS with jejunum < 50 cm (A)
- SBS with jejunum < 10 cm (C)
- Arterial mesenteric infarction (A)
- Chronic intestinal obstruction (A,C)
- Primary non digestive disease (C)
- Intractable diarrhea (C)
- Congenital mucosa diseases (C)
- Centre low experience (A,C)

#### With HPN-failure
- Liver failure
- Other causes of HPN-failure

**HPN-Ad:** Messing, ’95; Jeppesen, ’98; Scolapio, ’99; Pironi, ’03;  
**HPN-Ch:** Vargas, ’87; Gambarara, ‘02; Guarino, ‘03; Colomb & Goulet, ‘04
Issues with liver failure on HPN

| Histology                  | not always predictive of liver recovery  
|                           | irreversibility point of is not clear |
| Liver recovery            | possible after autologus intestinal function recovery |
| Isolated liver Tx         | some SBS, very likely to be weaned from HPN after Tx |
| Isolated ITx              | not recommended (few cases of stage 3 fibrosis and cholestasis reversal, after isolated ITx) |

(AGA technical review, Gastroenterology 2003)  
(Fishbein, Gastroenterology 2003)  
(Goulet, JPGN 2004)
# Prognosis on waiting list

<table>
<thead>
<tr>
<th>Type of ITx</th>
<th>Factors elongating time on WL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ITx</td>
<td>Donor / recipient</td>
</tr>
<tr>
<td></td>
<td>- matching size (children &gt; ad.)</td>
</tr>
<tr>
<td></td>
<td>- CMV status</td>
</tr>
<tr>
<td></td>
<td>- ABO blood group</td>
</tr>
<tr>
<td>Liver + SB ITx</td>
<td>Liver UNOS status</td>
</tr>
</tbody>
</table>

## Clinical status deteriorates with time on list

( liver + SB ITx > isolated SB ITx)

(AGA technical review, Gastroenterology 2003)
(Goulet, JPGN 2004)
Mortality on waiting list

- Any ITx > any other solid organ Tx list
- Liver + SB ITx > isolated SB ITx (95% vs 5%)
- Liver + SB ITx > liver Tx only (all UNOS and ages)
- ITx children < 6 yrs > ITx older children and adults

(AGA technical review, Gastroenterology 2003)
(Goulet, JPGN 2004)
Positive prognostic factors after ITx

ITx ≥ 1998

- Patient at home before ITx
- Younger age
- 1st transplant
- Induction antibody therapy
- Centre experience > 10 ITx

Intestinal Transplant Registry (Grant, ’05)
Late referral for ITx

Risk of higher mortality rates

• on waiting list
• after ITx
Candidates for ITx “A European survey”

Time of candidacy

Adult candidates

108

Immediate 14.8 %
Potential 85.2 %

Pediatric candidates

57

Immediate 15.8 %
Potential 84.2 %

“Time of candidacy”
Clinical judgment by HPN physician

(ESPEN HAN-Working Group, 2004)
Candidates for ITx “A European survey”
Immediate candidacy by indication

<table>
<thead>
<tr>
<th>Condition</th>
<th>Immediate Candidacy (%) of Candidates for Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver failure</td>
<td>Adults: 0%  Pediatrics: 40%</td>
</tr>
<tr>
<td>Vein Thrombosis</td>
<td>Adults: 20%  Pediatrics: 20%</td>
</tr>
<tr>
<td>CVC-Sepsis</td>
<td>Adults: 0%  Pediatrics: 80%</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Adults: 0%  Pediatrics: 0%</td>
</tr>
<tr>
<td>Desmoids</td>
<td>Adults: 0%  Pediatrics: 0%</td>
</tr>
<tr>
<td>Congenital disorder</td>
<td>Adults: 20%  Pediatrics: 0%</td>
</tr>
<tr>
<td>Ultra short bowel</td>
<td>Adults: 0%  Pediatrics: 0%</td>
</tr>
<tr>
<td>Poor quality of life</td>
<td>Adults: 0%  Pediatrics: 0%</td>
</tr>
</tbody>
</table>

(ESPEN HAN-Working Group, 2004)
Candidates for ITx “A European survey”

1 year outcome of candidates for ITx

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dead on HPN</td>
<td>5</td>
</tr>
<tr>
<td>Dead on list</td>
<td>1</td>
</tr>
<tr>
<td>Isolated-SB</td>
<td>9</td>
</tr>
<tr>
<td>Liver+SB</td>
<td>2</td>
</tr>
<tr>
<td>Multivisc.</td>
<td>1</td>
</tr>
</tbody>
</table>

(ESPEN HAN-Working Group, 2005)
Candidates for ITx “A European survey”

1 year outcome of candidates for ITx

Potential and Immediate

- Not referred: 47%
- Referred/Listed: 35%
- Transplanted: 18%
- Immediate: 7%

Adults and Pediatrics

- Not referred: 54%
- Referred/Listed: 33%
- Transplanted: 12%
- Pediatrics: 5%

(ESPEN HAN-Working Group, 2005)
Candidates for ITx “A European survey”

1 year outcome of candidates for ITx

Indications in “referred-listed-ITx” patients

- HPN-failure: 62%
- Underlying disease: 46%
- QoL: 6%
- Pediatrics: 46%
- Adults: 32%

(ESPEN HAN-Working Group, 2005)
Irreversible Benign Intestinal Failure

A pathway from HPN to ITx

Irreversible benign intestinal failure

Prevention of HPN-failure

• HPN-failure
• Disorders with poor prognosis
• ? Very poor QoL

Referral for evaluation of candidacy for ITx

IF center + ITx center

Prognostic evaluation

Continue HPN or list for ITx