Living related liver transplantation - extended indications?

Christoph E. Broelsch

Falk Symposium 150

Klinik für Allgemein- und Transplantationschirurgie
Universitätsklinikum Essen
## Mortality on the waitinglist

<table>
<thead>
<tr>
<th></th>
<th>1998</th>
<th>1999</th>
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<th>2002</th>
<th>2003</th>
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<tbody>
<tr>
<td><strong>WL January</strong></td>
<td>24</td>
<td>22</td>
<td>29</td>
<td>61</td>
<td>86</td>
<td>97</td>
<td>137</td>
</tr>
<tr>
<td><strong>Died on list</strong></td>
<td>10</td>
<td>15</td>
<td>22</td>
<td>30</td>
<td>26</td>
<td>49</td>
<td>41</td>
</tr>
<tr>
<td><strong>Tx</strong></td>
<td>74</td>
<td>97</td>
<td>81</td>
<td>100</td>
<td>112</td>
<td>119</td>
<td>122</td>
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<tr>
<td><strong>Removed</strong></td>
<td>4</td>
<td>7</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td><strong>WL December</strong></td>
<td>22</td>
<td>29</td>
<td>61</td>
<td>86</td>
<td>97</td>
<td>137</td>
<td>140</td>
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<tr>
<td><strong>Rate of mortality:</strong></td>
<td>11.11%</td>
<td>13.39%</td>
<td>29.33%</td>
<td>27.52%</td>
<td>20.00%</td>
<td>17.19%</td>
<td>26.85%</td>
</tr>
</tbody>
</table>
Extended Indications for ALDLT

The basic question is not “who can we transplant” but

1) **Who benefits from a transplant?**

2) **How “important” is the benefit?**

3) **Who judges?**

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SPECIAL REPORT

Ethical Considerations and Rationale of Adult-to-Adult Living Donor Liver Transplantation

*Massimo Malagò,* *Giuliano Testa,* *Amadeo Marcos,* ‡*John J. Fung,* ‡*Mark Siegler,* ‡

David C. Cronin,* ‡*and Christoph E. Broelsch*
Potential LDLT-Candidates

All LTx Candidates in Essen...in particular:

• End stage disease without chance on the waiting list
  • Late referral, non-residents
• Acute on chronic cirrhosis
• HCCs without extra hepatic disease
• Other (Resistant HBV, tumors post-chemotherapy... etc.)
The principle of equipoise
Liver transplantation in Essen

- LDLTx right
- LDLTx left/left lateral
- Split ltx
- Standard ltx

Year: 1996 to 2004 until Febr 2005

#
Living Donor Tx

n = 144

- Left lateral: 24
- Left: 9
- Right: 111

LTX ESSEN April 1998 – February 2005

Klinik für Allgemein- und Transplantationschirurgie, Universitätsklinikum Essen
Extended Indications for LDLT:

**Basic concept:** time shortage and/or poor prognosis without LT

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
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<tbody>
<tr>
<td>,,Advanced“ Tumors</td>
<td>24</td>
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<tr>
<td>HCC</td>
<td>18</td>
</tr>
<tr>
<td>non HCC</td>
<td>6</td>
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<tr>
<td>Chronic decompensated cirrhosis (DESLD)</td>
<td>16</td>
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<tr>
<td>Tumors + decompensated cirrhosis</td>
<td>9</td>
</tr>
<tr>
<td>Procedure</td>
<td>Count</td>
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<td>---------------------------------</td>
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<tr>
<td>Med. treatment</td>
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<tr>
<td>Chemoembolisation</td>
<td>110</td>
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<tr>
<td>RITA</td>
<td>125</td>
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<tr>
<td>Exploration- Biopsy</td>
<td>92</td>
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<tr>
<td>Liver resection</td>
<td>148</td>
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<tr>
<td>LTx</td>
<td>88</td>
</tr>
</tbody>
</table>
HCC and LTx - State of The Art: The Milan Criteria

- \( \leq 3 \) nodules
- \( \leq 3 \text{ cm} \)
- no vascular invasion

HCC and LDLT Strategy in Essen

Cadaveric Organs LT
Conservative policy
(Milan Criteria - 5cm)

Living Donor
Opening to selected "advanced" tumors

Standard Indications vs Extended Indications
HCC and Liver transplantation in adults

Essen 1998 - 2002 NEW

Right Living donor Tx n=93
HCC 34%

Cadaveric LTx n=349
HCC 5,1%

Mean F-up 37 mo.
The Pittsburgh staging system for HCC Pre-transplantation
HCC diagnostic failures

Pre Transplantation diagnostics are far from being exact!!

<table>
<thead>
<tr>
<th>Modality</th>
<th>HCC Sensitivity</th>
<th>Dysplastic Nodule Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>40%</td>
<td>0%</td>
</tr>
<tr>
<td>CT</td>
<td>50%</td>
<td>20%</td>
</tr>
<tr>
<td>NMR</td>
<td>70%</td>
<td>27%</td>
</tr>
</tbody>
</table>

Libbrecht L Liver Transplantation 2002:8,749-761
HCC diagnostic failures
Intention-to-treat vs. pathologic stage
Essen n= 55
CT-NMR presenting the same Pre/post TX diagnosis

- UICC (6) 57,9%
- TNM (6) 31,0%
- Milano 31,6%
- Pittsburgh 39,5%
- UCSF 36,1%

Sotiropulos, Malagó, Paul: Transplantation in press
Extended Indications for LDLT: Results

- DESLD
- Tumor DESLD
- Tumor extended
- non extended

Surviving patient follow up (months)

p=0.0025

n=18
n=8
n=18
n=67
LDLT for HCC
Modified criteria

HCC confined to the liver, no PVT

However

Observation time ≥ 3 months
Age < 60 y.
Tumor < 50% total volume
AFP < 5000
No DESLD
LDLT for HCC
Modified criteria - Results

p=0.078
LDLT for HCC  
04/1998- 12/2004

Tumor recurrence  n=4/32 all
4/18 ext.

6 mo post-LDLT: multifocal (liver, lungs), no therapy, death in 10 mo

23 mo post-LDLT: R adrenalectomy + V. Cava Resection, death in 63 mo

35 mo post-LDLT: lung resection-RITA, RTx of the Orbita, alive 62 mo

56 mo post-LDLT: pelvic soft tissue and bone, alive 58 mo
Decompensated End-Stage Liver Disease

T2 definition - adults

chronic liver disease with acute deterioration

- recipient has to be hospitalized
- life expectancy < 29 days
- Child-Turcotte-Pugh (CTP) score > 9
- one or more of defined complications
- no sepsis/MOF/high dose vasopressors

T2: time to LT 5 months
T2: mean MELD in Essen 23

- September 17, 2003
  - T2 priority in all ET countries
  - New T2 criteria:
    - CTP ≥ 11 + ≥ 1 defined complication
LD Patient Survival - MELD
n=111

Surviving patient follow up (months)

11-17
18-27
<10
>=28

p=0.2079
Indications for living donor liver transplantation

Extended Criteria

Conclusion

Extended indications present response to Organ Shortage with regional differences

HCC: confined to liver, no PVT, low AFP, age <60y., MELD <23
observation > 3 mos

DESLD: age <60y., recompensation (DESLD) -> MELD <23

Combination of DESLD and advanced tumors:
unsatisfactory, cirrhosis mainly responsible

LDLT for extended indications is justified because it meets the special regional needs
Zur Anzeige wird der QuickTime™ Dekompressor "Foto - JPEG" benötigt.
Extended Indications for LDLT:

Basic concept: time shortage and/or poor prognosis without LT

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| Chronic decompensated cirrhosis(DESLD) | 18 |

| Tumors + decompensated cirrhosis     | 8  |
The HCC patient on the transplant list: Dropout risks

Dropout probability

7.3%, 25.3%, 43.6% at 6, 12, 24 months
23% at 12 months
50%

Yao Liver Transplantation 2002
Llovet Hepatology 1999
Schwartz Ann Surg 2002
The UCSF staging system for HCC Pre-transplantation

- 1 nodule max 6.5 cm
- 2 or 3 nodules ≤ 4.5 cm
- Total diameter of tumors ≤ 8 cm.

LT for HCC: expansion of the tumor size limits does not adversely impact survival

Yao F Y, Liver Transplantation 2002: 8, 765-74
LD Patient Survival - Age >60 yr.

DESLD

Tumor und Zirrhose

p=0.045

p=0.268