Liver Transplantation for Cholangiocarcinoma

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Primary Liver Cancer

• Hepatocellular carcinoma
• Hepatoblastoma
• Cholangiocarcinoma
Transplantation for Primary Liver Cancer

- Hepatocellular carcinoma ✓
- Hepatoblastoma ✓
- Cholangiocarcinoma ?
Cholangiocarcinoma

- **Position**
  - Peripheral, hilar, distal

- **Pathology**
  - Papillary, nodular, infiltrating

- **Predisposing factors**
  - PSC, choledochal cyst, parasites
Transplantation for Cholangiocarcinoma

- **Position**
  - Peripheral, *hilar*, distal

- **Pathology**
  - Nodular, papillary, *infiltrating*

- **Predisposing factors**
  - *PSC*, choledochal cyst, parasites
Surgical Treatment of Cholangiocarcinoma

• Liver transplantation no longer performed for CC in most transplant centres (including ANZ)
  - ‘Poor’ long term outcome
  - Competing demands for donor organs

• Results of resection for hilar CC improved
  - Extended resection (PVE plus drainage of FLR)
  - Excision/reconstruction portal vein
Transplantation for Cholangiocarcinoma

• Historical data
• Neoadjuvant chemo-radiation
• Unanswered questions
• Is there a role for transplantation?
# Transplantation for Cholangiocarcinoma - Registry and Multi-centre

<table>
<thead>
<tr>
<th>Registry</th>
<th>Year</th>
<th>Number</th>
<th>3yr surv (%)</th>
<th>5yr surv (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Transplant Registry</td>
<td>1988</td>
<td>80</td>
<td>9 (IH) 16 (EH)</td>
<td>2 (IH) 0 (EH)</td>
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<tr>
<td>Cincinnati Transplant Tumour Registry</td>
<td>2000</td>
<td>207</td>
<td>-</td>
<td>23</td>
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<tr>
<td>Spanish multi-centre</td>
<td>2004</td>
<td>36</td>
<td>65 (IH) 53 (EH)</td>
<td>42 (IH) 30 (EH)</td>
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<tr>
<td>Canadian multi-centre (incidental tumours)</td>
<td>2005</td>
<td>10</td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td>UNOS</td>
<td>2008</td>
<td>280</td>
<td>-</td>
<td>38</td>
</tr>
<tr>
<td>German Survey</td>
<td>2008</td>
<td>47</td>
<td>31 (57*)</td>
<td>22 (48*)</td>
</tr>
<tr>
<td>ANZ LT Registry</td>
<td>2009</td>
<td>29</td>
<td>-</td>
<td>34</td>
</tr>
</tbody>
</table>

*(n=689)*

* 15 patients since 1998
# Transplantation for Cholangiocarcinoma - Single centres

<table>
<thead>
<tr>
<th>Single Centre</th>
<th>Year</th>
<th>Number</th>
<th>3yr surv (%)</th>
<th>5yr surv (%)</th>
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<tbody>
<tr>
<td>Kings, London</td>
<td>1987</td>
<td>26</td>
<td>10</td>
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</tr>
<tr>
<td>Niguarda, Milan</td>
<td>1994</td>
<td>11</td>
<td>53</td>
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</tr>
<tr>
<td>Hochschule, Hannover</td>
<td>1996</td>
<td>25</td>
<td>21</td>
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</tr>
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<td>Pittsburgh</td>
<td>1998</td>
<td>38</td>
<td>32</td>
<td>25</td>
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<td>Baylor, Dallas</td>
<td>1998</td>
<td>14</td>
<td>41</td>
<td>-</td>
</tr>
<tr>
<td>UCLA</td>
<td>2000</td>
<td>25</td>
<td>35</td>
<td>-</td>
</tr>
<tr>
<td>Humboldt, Berlin</td>
<td>1999</td>
<td>15</td>
<td>-</td>
<td>38</td>
</tr>
<tr>
<td>Goteborg, Sweden</td>
<td>2003</td>
<td>15</td>
<td>33</td>
<td>-</td>
</tr>
<tr>
<td>Omaha, Nebraska (CRT)</td>
<td>2002</td>
<td>11</td>
<td>-</td>
<td>45</td>
</tr>
<tr>
<td>Mayo, Rochester (CRT)</td>
<td>2009</td>
<td>111</td>
<td>83</td>
<td>72</td>
</tr>
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\[ n=291 \]
Transplantation for Cholangiocarcinoma
- Incidental versus non-incidental

- 3 studies, 232 patients
  - no difference in outcome
# Transplantation for Cholangiocarcinoma - Single centres

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“Liver transplantation with neoadjuvant chemo-radiation is more effective than resection for hilar cholangiocarcinoma”

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<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Cytology/histology or CA199&gt;100 and/or FISH polysomy plus radiology (stricture or mass)</td>
<td>Cytology/histology</td>
</tr>
<tr>
<td><strong>Exclusions</strong></td>
<td>Resectable or mass &gt;3cm</td>
<td>Resectable or mass &gt;2cm</td>
</tr>
<tr>
<td><strong>Chemotherapy</strong></td>
<td>5FU → CTB until OLT</td>
<td>5FU until OLT</td>
</tr>
<tr>
<td><strong>Brachytherapy</strong></td>
<td>Iridium 192: 2-3,000 cGy</td>
<td>Iridium 192: 6,000 cGy</td>
</tr>
<tr>
<td><strong>External Beam Radiation</strong></td>
<td>4,500 cGy</td>
<td>no</td>
</tr>
<tr>
<td><strong>Staging laparotomy</strong></td>
<td>Yes (-ve EUS/FNA)</td>
<td>Yes</td>
</tr>
</tbody>
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Diagnosis *(n=167)*

↓

External Beam Radiation

↓

Intrabiliary Brachytherapy

↓

Chemotherapy (5FU/CTB)

↓

EUS and Operative Staging *(n=143, 86%)*

↓

Liver Transplantation *(n=111, 66%)*

- 35 LDLT
- 75 DDLT
- 1 domino

65% PSC (2006)

Transplantation for Cholangiocarcinoma
Mayo & Omaha Results

- Omaha (n=11)
  45% overall survival (2.8-14.5 years follow-up)
- Mayo (n=111)
  - 72% 5yr survival from time of diagnosis (2006)
  - Factors associated with recurrence (14%)
    - Age, CA199>100, prior cholecystectomy, mass, PNI
    - (PSC not associated with recurrence)

Transplantation for Cholangiocarcinoma
- Questions about CRT
Transplantation for Cholangiocarcinoma - Questions about CRT

- Diagnostic accuracy
Transplantation for Cholangiocarcinoma
- Questions about CRT

• Diagnostic accuracy

~ 40% no residual cancer in explant (2006)
Transplantation for Cholangiocarcinoma
- Questions about CRT

- Diagnostic accuracy
  - ~ 40% no residual cancer in explant
  - ? complete pathological response
  - ? incorrect diagnosis

*Bangarulingam et al, Hepatology 2010, 51: 174-80*
Transplantation for Cholangiocarcinoma
- Questions about CRT

• Diagnostic accuracy
• Survival data
Transplantation for Cholangiocarcinoma
- Questions about CRT

- Diagnostic accuracy
- Survival data
- Determining unresectability
Transplantation for Cholangiocarcinoma - Questions about CRT

• Diagnostic accuracy
• Survival data
• Determining unresectability
• What is the optimal CRT regimen?
Hazard ratio for death, 0.64 (95\% CI, 0.52–0.80)
P<0.001

no. at Risk
- Gemcitabine: 206, 151, 97, 53, 28, 15, 4, 3, 2
- Cisplatin–gemcitabine: 204, 167, 120, 76, 51, 28, 17, 8, 2

Valle et al, NEJM, 2010, 362;1273-81 (ABC-02 trial)
Transplantation for Cholangiocarcinoma
- Questions about CRT

• Diagnostic accuracy
• Survival data
• Determining unresectability
• What is the optimal CRT regimen?
• Reproducibility & generalisability?
Transplantation for Cholangiocarcinoma - Questions about CRT

- Diagnostic accuracy
- Survival data
- How do you rule out resectability?
- What is the optimal CRT regimen?
- Reproducibility & generalisability?
- Vascular complications
  ~ 20% arterial and venous

Mantel et al, Liver Transplantation 2007, 13, 1372-81
Is liver transplantation for cholangiocarcinoma justified on the basis of current knowledge?
Transplantation for Cholangiocarcinoma
- Organ shortage

- Waiting list mortality ~ 15%
Transplantation for Cholangiocarcinoma
- Organ shortage

- Waiting list mortality ~ 15%
- Other ‘marginal’ indications
  - Re-OLT for recurrent hepatitis C
  - Extended criteria for HCC
  - Morbidly obese recipients
Transplantation for Cholangiocarcinoma

Live Donor Liver Transplantation
Transplantation for Cholangiocarcinoma

- Standardised multi-centre protocols
  - Meaningful outcome data available sooner
  - Provide external validity
  - Equitable
Transplantation for Cholangiocarcinoma
Conclusions

• Historical results do not justify liver transplantation alone (including ‘cluster’ operation)

• Neoadjuvant chemo-radiation appears to improve outcome – important questions remain

• Prospective multicentre protocols needed to confirm and clarify the role of neoadjuvant chemo-radiation plus OLT