Defining the Role of Liver Transplantation in Hepatobiliary Cancers

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Defining the Role of Liver Transplant in Hepatobiliary Cancers

- Hepatocellular cancer
- Cholangiocarcinoma
  - Intrahepatic CCA
  - Extrahepatic CCA
Hepatocellular Carcinoma

- Most common primary malignancy of the liver
- Number 1 cause of death in cirrhosis
Observed and projected HCC incidence
HCC: Risk Factor Overview

• 70% - 90% occurs within an established background of chronic liver disease and cirrhosis

• Major etiologies of HCC:
  • Hepatitis C
  • Hepatitis B
  • Alcoholic liver disease
  • Nonalcoholic steatohepatitis
Management of HCC
Treatment options

• Surgical resection

• Local therapies (Interventional Radiology)
  • Radiofrequency ablation (RFA)
  • Ethanol or Acetic acid injection
  • Chemoembolization (TACE or DebTACE)
  • 90 Yttrium spheres

• Chemotherapy

• Liver Transplant
Defining the Role of Liver Transplantation in Hepatocellular Cancer
Liver Transplantation (LT)

- Curative Treatment for chronic disease and HCC
- MELD exception points for HCC

### Survival

<table>
<thead>
<tr>
<th>Year</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>91%</td>
</tr>
<tr>
<td>2 year</td>
<td>75%</td>
</tr>
<tr>
<td>5 year</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>Milan Criteria</td>
<td>~50%</td>
</tr>
<tr>
<td>Extended criteria</td>
<td>~50%</td>
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</tbody>
</table>

Surgical Resection

- Choice of therapy for patients without cirrhosis
- 5-15% HCC patients eligible

### Survival

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<td>1 year</td>
<td>97%</td>
</tr>
<tr>
<td>3 year</td>
<td>84%</td>
</tr>
<tr>
<td>5 year</td>
<td>26-57%</td>
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</tbody>
</table>
Selection of surgical candidates is key

- Patients with no portal HTN and TB <1mg/dL
- Patients with clinically irrelevant portal HTN and TB <1mg/dL
- Patients with portal HTN and TB >1mg/dL

- Llovet et al, Hepatology 1999
Liver transplant

- Milan criteria
  - Solitary HCC 2 cm to 5 cm
  - 3 nodules each ≤ 3 cm
  - No evidence of vascular invasion
  - No evidence of extrahepatic disease

- Most centers treat lesions upon listing for liver transplant
  - RFA
  - TACE or DebTACE
Expanding transplant selection criteria

- UCSF criteria
  - Single tumor ≤ 6.5 cm
  - ≤ 3 tumors ≤ 4.5 cm with total ≤ 8 cm

- Patients are treated with local therapy

- Waiting time of 3 months

- If disease activity now within Milan criteria and no new lesions develop, patients are eligible for MELD exception
Expanding Milan: Up to 7 criteria

1: 6cm tumor = $1 + 6 = 7$

4 tumors: $1cm + 1cm + 2cm + 3 cm = 7$
Use of extended selection criteria in liver transplant for HCC

- Milan criteria (1)
- Extended criteria (2)
- Beyond (3)

Recurrence-free survival

- At risk
  - Baseline (1): 143
  - 1 year: 109
  - 2 years: 74
  - 3 years: 51
  - 4 years: 37
  - 5 years: 26
  - Baseline (2): 41
  - 1 year: 29
  - 2 years: 23
  - 3 years: 17
  - 4 years: 12
  - 5 years: 9
  - Baseline (3): 56
  - 1 year: 32
  - 2 years: 22
  - 3 years: 18
  - 4 years: 11
  - 5 years: 5

- p < 0.001
- 1 vs 2: p = 0.350
- 1 vs 3: p < 0.001
- 2 vs 3: p = 0.004
Immunosuppression: The impact of sirolimus post LT for HCC

- There was no difference in those patients receiving or not receiving sirolimus post LT
- There was a trend to survival improvement in older recipients
- Yanik et al. Hepatology May 2016
Defining the Role of Liver Transplant in Hepatobiliary Cancers

- Cholangiocarcinoma
  - Intrahepatic CCA
  - Mass in the liver
  - Peripheral intraductal
- Extrahepatic CCA
  - Distal and perihilar
Increasing incidence of *intrahepatic* cholangiocarcinoma in the US

165% increase

Pathogenesis of intrahepatic cholangiocarcinoma
Traditionally outcomes for LT for intrahepatic CCA were poor

- Surgical resection for intrahepatic CCA

<table>
<thead>
<tr>
<th>Author</th>
<th>Study period</th>
<th>Resected patients (n)</th>
<th>Rate of R0 resections (%)</th>
<th>Mortality rate (%)</th>
<th>3-year survival rate (%)</th>
<th>5-year survival rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weimann et al. [31]</td>
<td>1978–1996</td>
<td>95</td>
<td>–</td>
<td>5.0</td>
<td>31</td>
<td>21</td>
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<tr>
<td>Paik et al. [33]</td>
<td>1994–2005</td>
<td>97</td>
<td>93</td>
<td>–</td>
<td>52</td>
<td>31</td>
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<tr>
<td>Tamandl et al. [34]</td>
<td>1994–2007</td>
<td>74</td>
<td>72</td>
<td>9.5</td>
<td>45</td>
<td>28</td>
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<tr>
<td>Endo et al. [30]</td>
<td>1990–2006</td>
<td>82</td>
<td>85</td>
<td>1.2</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Lang et al. [4]</td>
<td>1998–2006</td>
<td>83</td>
<td>64</td>
<td>7.1</td>
<td>38</td>
<td>21</td>
</tr>
</tbody>
</table>
Liver transplant may have superior results to surgical resection for early intrahepatic CCA but there is much more research needed.
UCLA protocol may challenge role of liver transplant for intrahepatic CCA

Treatment protocol

% Disease free survival
Survival is reasonable in very early (single \( \leq 2 \text{ cm} \)) iCCA with HCC

Early: single lesion \(< 2\text{cm} \)   Advanced: anything beyond
Extrahepatic cholangiocarcinoma

Incidence 1.2 per 100,000 males
Incidence 0.8 per 100,000 females
Liver transplant for hilar cholangiocarcinoma
Establishing the diagnosis of CCA

- Routine cytology (RC) 15% to 30% sensitivity
- Improves with directed biopsy 50% sensitivity
- FISH improves accuracy of diagnosis
  - Sensitivity from 15% in RC to 34% FISH
  - Specificity equivalent 97%
- Patients considered for transplant can NEVER have EUS or percutaneous biopsy
- Remember to exclude IgG4 cholangiopathy
Mayo Transplant Protocol

1. Continuous 5-FU infusion + EBRT for 4 weeks
2. Brachytherapy - 4 sessions over 2 days
3. Exploratory surgery (proximity to OLT)
4. Oral Capecitabine-3 week cycles
5. No extrahepatic or nodal involvement
6. Listing for OLT
Survival after liver transplant for CCA

- Transplantation (n=38)
  - 92% at 0 years
  - 82% at 1 year
  - 82% at 2 years
  - 82% at 3 years
  - 48% at 4 years
  - 21% at 5 years

- Resection (n=26)
  - 82% at 0 years
  - 82% at 1 year
  - 82% at 2 years
  - 82% at 3 years
  - 21% at 5 years
Liver transplant criteria for hilar CCA

- Established diagnosis of CCA
- Intrahepatic tumor volume $\leq 3$ cm
- No evidence of extrahepatic disease
- Lymph node negative (EUS and later surgical exploration)
The protocol can be done successfully outside Mayo Clinic.
This is a precise protocol…
Thank you

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