CURRENT STRATEGIES FOR TREATMENT OF HEPATOCELLULAR CARCINOMA

David J. Reich, MD, FACS
Professor and Chief, Division of Multiorgan Transplantation and Hepatobiliary Surgery
Vice Chairman, Department of Surgery
Drexel University College Of Medicine
Epidemiology

- >500,000 new HCC / year
- Risk factors: cirrhosis, hepatitis, Asian, age > 50, male > female
- May cause decompensation of ESLD
- Asymptomatic until large so need screening:
  - patients with cirrhosis / hepatitis B
  - at least twice / yr
  - AFP & US (CT or MRI better)
  - HCC doubles in size every 4 months!
Evaluation

- Hx/Px (age, comorbidities, hepatitis/cirrhosis)
- Labs: LFTs, AFP, hepatitis screen
- Ultrasound:
  - single vs. multiple, steatosis, cirrhosis, PVT
- MRI with gad / 3 phase CT
  - non-enhanced, arterial enhancement, portal washout
  - chest CT, bone scan
- Not usually indicated: Bx, PET
- Laparoscopy…
Therapeutic Challenges

- Chemotherapy generally ineffective
- Resection / RFA typically limited by cirrhosis, portal hypertension, coagulopathy, ESLD
- Multifocallity frequent with HCC (entire liver subject to carcinogenic influence)
- Transplantation generally only cure (stage 1-2) (? resection / RFA for small HCC in Child’s A)

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Surgical Biology Of HCC

• Dysplastic nodule
• HCC
• Intrahepatic metastasis
  – microscopic portal-portal spread
  – does not imply systemic spread
  – impact on postsurgical recurrence
• Resection - LARGE
• Transplant - small
“size matters!”
## Child Pugh Classification

<table>
<thead>
<tr>
<th>Albumin</th>
<th>Ascites</th>
<th>Bilirubin</th>
<th>Encephalopathy</th>
<th>PT Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3.5</td>
<td>None</td>
<td>&lt;2</td>
<td>None</td>
<td>1-3</td>
</tr>
<tr>
<td>2.8-3.5</td>
<td>Controlled</td>
<td>2-3</td>
<td>I</td>
<td>4-6</td>
</tr>
<tr>
<td>&lt;2.8</td>
<td>Uncontrolled</td>
<td>&gt;3</td>
<td>II</td>
<td>&gt;6</td>
</tr>
</tbody>
</table>

- **5-6 points:** 10% mortality
- **7-9 points:** 30% mortality
- **10-15 points:** 75% mortality
Discussion Topics

- Hepatic resection
- Liver transplantation (LTX)
- Radiofrequency ablation (RFA)
- Transarterial chemoembolization (TACE)
- Chemotherapy
Treatment

• Surgery only cure
  – resect non-cirrhotics, (Child’s A with small HCC?)
  – transplant cirrhotics with stage 1-2 HCC

• RFA
  – RFA superior to ethanol injection and to TACE
  – curative for small HCC in Child’s A?
  – contraindicated in cirrhotics with HCC >5cm or advanced Child’s C ESLD
  – palliative for unresectable / nontransplantable HCC
  – bridge to transplant for Child’s A-B with HCC 2-4 cm

• TACE
  – palliative for large HCC (> 5 cm)
  – bridge to transplant for Child’s C or large HCC
Liver Resection

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Suitability For Resection

- No cirrhosis or Child’s class A
- Absence of portal hypertension
  - platelet count > 100K, no varices
  - hepatic venous pressure gradient < 10 mm Hg
- Size
  - no fixed limit
  - low likelihood of cure if macroscopic vascular invasion
- Survival: 85% @1yr; 40% @5yr
Improved Outcomes After Liver Resection

- Hepatobiliary surgeons
  - growing number, HPB and LTX surgical teams
  - global collaboration
- Better understanding of physiology (hepatology, coagulation)
- Improved ancillary support (anesthesia, critical care, radiology)
- Better understanding of anatomy
  - Couinad, lessons from reduced size transplants
- Improved preoperative evaluation
  - comorbidities, liver function, tumor imaging
- More effective technology
  - US dissectors, precoagulators, staplers, hemostasis
Complications of Hepatobiliary Surgery

Increased risk:
- large resection
- proximity to major vasculature
- extended duration of vascular occlusion
- cirrhosis/portal hypertension/coagulopathy
- steatosis
- hepatitis
- obstructive jaundice
- blood loss/transfusion

Decreased risk:
- skilled/experienced surgeon
- preoperative imaging
- maximal exposure
- full mobilization of the liver
- control of inflow/outflow vessels
- intraoperative ultrasonography
- low CVP
- appropriate use of Pringle and TVI maneuvers
- availability of hemostatic resection equipment (CUSA, Harmonic scalpel, vascular staplers...)

(Chart shows a vertical arrow indicating increased risk as it moves up, and decreased risk as it moves down.)
Liver Transplantation
Transplantation For HCC

• Transplant cirrhotics with stage 1-2 HCC
• LTX addresses HCC and ESLD
• Unresectable stage 2 HCC gets allocation priority because size does correlate with vascular invasion and metastases
  – Milan criteria:
    • single tumor ≤ 5 cm or
    • up to 3 tumors - largest ≤ 3 cm
• Excellent survival: 90% @1yr; 75% @5yr
• LTXs for HCC on the rise (2% in 1995; 20% in 2004)
• Options for those beyond Milan
Waitlist and Transplant Activity for Liver, 1999-2008

- Waiting List at Year End
- Total Liver Transplants
- Deaths on Waiting List

Source: OPTN/SRTR Annual Report Tables 1.3, 1.6, 1.7
MELD Score

Enter values to calculate MELD and press Calculate.

Creatinine: mg/dl
Total Bilirubin: mg/dl
INR:

Calculate MELD

MELD score: 
Expedite Transplantation:

- Early referral/listing!!!
- Safe, aggressive use of livers from the extended donor pool is imperative:
  - older donors - steatotic livers
  - HBcAb+ donors - injured livers
  - HCV+ donors - reduced size livers
  - DCD - living donors
Indications

Compared to historic controls, current liver recipients are:

• Sicker
  (IDDM, low GFR, obesity, CAD, pulmonary HTN, other comorbidities)
• Older
• More complex technically
Liver Transplantation for HCC

Strategies to decrease drop-out rate

cirrhotic patients with HCC waiting for liver transplantation

Increase pool of donors

Extended criteria donors

Adjuvant treatment during waiting time

TACE

RFA

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Adjusted Liver Recipient 1-Year Survival by Year of Transplant (SRTR)

Year

Survival, %

Liver Transplant Survival (SRTR, 2007)

1-year survival (2007):
- Patient: 89%
- Graft: 84%

Survival, %

Months

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Ablative Therapies

• RFA:
  – percutaneous, laparoscopic, or open
  – safe
  – RFA superior to ethanol injection and to TACE
  – curative for small HCC in Child’s A
  – bridge to tx for Child’s A-B with HCC <5cm
  – palliative for unresectable / untransplantable HCC
    (too large, too many, vascular involvement, liver disease, comorbidities)
  – contraindicated in cirrhotics with HCC >5cm or advanced Child’s C ESLD
  – survival: 95% @1yr; 40% @5yr

• TACE:
  – palliative
  – bridge to transplant for Child’s C or large HCC
  – survival: 80% @1yr; 30% @5yr
Before and After RFA:
Summary

1. HCC surveillance for cirrhotics and HBV
2. Triple phase CT or MRI
3. Avoid biopsy
4. Early referral key (size matters)
5. Treatment limited by extent of liver disease
6. Resect non-cirrhotics and Child’s A cirrhotics without PHTN
7. Transplant unresectable HCC that meets Milan Criteria
8. Even with allocation priority need to limit progression on waitlist (bridge RFA or TACE, extended criteria donors)
9. Patients with HCC > 5cm can be downstaged
10. Future:
   - role of sorafenib; better agents
   - molecular screening and staging

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Team Work

- hepatology
- liver surgery
- radiology
- oncology
Ubuntu: Zulu word for

“I am who I am because of those around me.”
HUH Outcomes

Liver Recipient Survival

Outcomes at 1 Year, %

7/08 – 9/10 (actual)
Expected (SRTR)

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