Surgical Therapy for HCC

Charles Cha, MD
Director of Minimally Invasive Hepatobiliary Surgery
Surgical Oncology
Yale HCC Symposium
3/1/19
Disclosures

• None
Incidence of HCC is increasing

Liver cancer death rate in US surged 43% in 16 years

By Maddie Bender, CNN

Updated 6:26 AM ET, Tue July 17, 2018
Treatment/Management of HCC

- Surgical resection
- Liver transplantation
- Microwave/Radiofrequency ablation
- Transarterial chemoembolization
- Stereotactic Radiotherapy
- Biologics/Chemotherapy
- Best Supportive Care
Surgical Therapy for HCC

Tumors without cirrhosis → Resect

Tumors with early cirrhosis → Resect if possible, Transplant if not

Tumors with late cirrhosis and CS PH → Transplant or Palliate
Is it Resectable?

- Oncologic Benefit
- Location of tumor
- Extent of resection
- Quality of liver

Resection?
Child’s-Pugh Score

<table>
<thead>
<tr>
<th>Measure</th>
<th>1 point</th>
<th>2 points</th>
<th>3 points</th>
<th>units</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bilirubin</strong> (total)</td>
<td>&lt;34 (&lt;2)</td>
<td>34-50 (2-3)</td>
<td>&gt;50 (&gt;3)</td>
<td>μmol/l (mg/dl)</td>
</tr>
<tr>
<td><strong>Serum albumin</strong></td>
<td>&gt;35</td>
<td>28-35</td>
<td>&lt;28</td>
<td>g/l</td>
</tr>
<tr>
<td><strong>INR</strong></td>
<td>&lt;1.7</td>
<td>1.71-2.20</td>
<td>&gt; 2.20</td>
<td>no unit</td>
</tr>
<tr>
<td><strong>Ascites</strong></td>
<td>None</td>
<td>Mild</td>
<td>Severe</td>
<td>no unit</td>
</tr>
<tr>
<td><strong>Hepatic encephalopathy</strong></td>
<td>None</td>
<td>Grade I-II (or suppressed with medication)</td>
<td>Grade III-IV (or refractory)</td>
<td>no unit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Points</th>
<th>Class</th>
<th>One year survival</th>
<th>Two year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6</td>
<td>A</td>
<td>100%</td>
<td>85%</td>
</tr>
<tr>
<td>7-9</td>
<td>B</td>
<td>81%</td>
<td>57%</td>
</tr>
<tr>
<td>10-15</td>
<td>C</td>
<td>45%</td>
<td>35%</td>
</tr>
</tbody>
</table>
Barcelona Clinic for Liver Cancer (BCLC) Algorithm

**BCLC**
- **Stage 0 Very Early**: 1 (≤2cm)
- **Stage A Early**: 1 (≤5cm) or 3 (≤3cm)
- **Stage B Intermediate**: > Milan Criteria
- **Stage C Advanced**: PVI, N1, M1
- **Stage D End Stage**: A / B

**Tumour**
- **Portal HT and / or Bilirubin?**
  - **No**
  - **Yes**

**Child Pugh Class**
- **Class A**
- **Class B**
- **Class C**

**Clinical Questions**
- **LT Candidate?**
  - **No**
  - **Yes**

**Treatment**
- **Resection**
- **RFA**
- **LT**
- **TACE**
- **Sorafenib**
- **Best Supportive Care**

**Curative Options**
- **5 Year Survival ~ 50-70%**
- **~ 20 mo**
- **~ 11 mo**
- **~ 3 mo**
Unos Liver Transplant Criteria

Policy 9: Allocation of Livers and Liver-Intestines

Effective Date: 1/17/2019

1. An evaluation of the number and size of lesions before local-regional therapy that meet Class 5 criteria using a dynamic contrast enhanced computed tomography (CT) or magnetic resonance imaging (MRI)
2. A CT of the chest to rule out metastatic disease
3. A CT or MRI to rule out any other sites of extrahepatic spread or macrovascular involvement
4. **An indication that the candidate is not eligible for resection**
5. An indication whether the candidate has undergone local-regional therapy
6. The candidate’s alpha-fetoprotein (AFP) level
Resection for HCC

Fraction surviving

Months

Resection
If it is Resectable, Resect!

Better understanding of the anatomy

Segmental based resection techniques

Newer techniques to preserve more liver
   Non-anatomic resections
   Portal and hepatic vein embolization
   Staged bilobar resection

Newer techniques to minimize impact to patient
   Laparoscopic and minimally invasive techniques
How much can we take out?

Gross Anatomy

Eight Segments

75-80% of liver in non-cirrhotic
Up to 60% in early cirrhotic
Resection of segment II (left).
Posterior Sectorectomy
Anatomically Based Segmental Resections

Greater technical flexibility

- Less extensive resections in patients with limited disease
- Bilateral resections in patients with multiple tumors
Portal Vein Embolization

Normal Portal Vein

Post Embolization

Anticipated liver remnant
PVE prior to hepatectomy

• Increase remnant liver volume ~15%

• Meta-analysis, 37 studies 1,088 patients
  • morbidity 2.2%
    • Liver abscess 3; cholangitis 2; left or main portal vein thrombus 2; subcapsular hematoma 2; portal hypertension 1

• 6 weeks wait for maximum hypertrophy
If it is Resectable, Resect!

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  Laparoscopic and minimally invasive techniques
Laparoscopic Hepatectomy
Laparoscopic Hepatectomy:
More than cosmesis
Meta-analysis: Lap vs open resection for HCC

Chen, K et al, Can J Gastroenterol Hepatol. 2018

Postop Complications and Liver Failure Favors Lap Resection

5 yr OS favors Lap Resection
Liver Resections 2007-2018 n=538

Total livers

Laparoscopic livers
538 Liver Procedures

272 Major Resections

59 (22%) Extended Hepatectomy

2007-2018
Extended Hepatectomies n=59

<table>
<thead>
<tr>
<th></th>
<th>LOS</th>
<th>SICU days</th>
<th>Peak bili</th>
<th>Peak INR</th>
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<tr>
<td>Open</td>
<td>17.6</td>
<td>6.6</td>
<td>8.0</td>
<td>1.4</td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>7.2</td>
<td>1.8</td>
<td>1.7</td>
<td>1.1</td>
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## Cost Analysis

<table>
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<tr>
<th></th>
<th>Procedure done in association with extended hepatectomy</th>
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<tbody>
<tr>
<td></td>
<td>PVE</td>
</tr>
<tr>
<td>Average Days Saved</td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>2.9</td>
</tr>
<tr>
<td>Hospital</td>
<td>4.9</td>
</tr>
<tr>
<td>Upfront Costs</td>
<td>-$3,000</td>
</tr>
<tr>
<td>Average Cost Savings per Patient</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$13,050-$18,850</td>
</tr>
<tr>
<td>Complication Rate Decrease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21%</td>
</tr>
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</table>
Survival by Treatment

- **Resection**: N=154
- **Ablation**: N=143
- **Supportive**: N=115

Significance: p < 0.001
Overall Survival After Resection (n=180)

Cha et al., Ann Surg 2003
90 patients (55%) recurred at a median followup of 2 years
5yr recurrence free survival 25%

Cha et al., JACS, 2003
Overall Survival of Transplant Eligible Resected Patients

No recurrence
N=15

Recurrence
N=20

Survival

93%

57%

p=.01

Cha et al., Ann Surg 2003
Resection vs Ablative procedures

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total</th>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>M-H. Fixed, 95% CI</th>
<th>Year</th>
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<tbody>
<tr>
<td>Huang</td>
<td>52</td>
<td>115</td>
<td>28</td>
<td>115</td>
<td>96.3%</td>
<td>1.86 [1.27, 2.72]</td>
<td>2010</td>
<td></td>
</tr>
<tr>
<td>Lee</td>
<td>4</td>
<td>34</td>
<td>1</td>
<td>29</td>
<td>3.7%</td>
<td>3.41 [0.40, 28.84]</td>
<td>2014</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>149</td>
<td>144</td>
<td>100.0%</td>
<td></td>
<td></td>
<td><strong>1.91 [1.32, 2.79]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>56</td>
<td>29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 0.31, df = 1 (P = 0.58); I² = 0%
Test for overall effect: Z = 3.39 (P = 0.0007)
Are we underutilizing resection in HCC?
Patients with intermediate cirrhosis/
Clinically evident portal hypertension

Neither Multiple Tumors Nor Portal Hypertension Are Surgical Contraindications for Hepatocellular Carcinoma

TAKEKI ISHIZAWA, KIYOSHI HASEGAWA, TAKU AOKI, MICHIRO TAKAHASHI, YOSUKE INOUE, KEIJI SANO, HIROSHI IMAMURA, YASUHIKO SUGAWARA, NORIHIRO KOKUDO, and MASATOSHI MAKUUCHI

Hepato-Biliary-Pancreatic Surgery Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, Tokyo, Japan

GASTROENTEROLOGY 2008;134:1908-1916
Roayaie et al makes argument that resection is underutilized:

- Multi-institutional study of 8656 BRIDGE study patients:
  - 1700 “non-ideal” HCC patients with portal hypertension were resected without significant difference in outcome or survival compared to non-cirrhotic patients

- Suggests with expansion of resection criteria, the pool of liver resection candidates could increase by 60%

- Retrospective, selected population that underwent resection
Excellent oncologic outcomes achievable
5 yr survivals of 20-50% for tumors > 10cm
No other options other than palliative therapy
Risk of recurrence higher in these patients
If it is Resectable, Resect!

Better understanding of the anatomy

Segmental based resection techniques

Newer techniques to preserve more liver
  Portal and hepatic vein embolization
  Staged bilobar resection

Newer techniques to minimize impact to patient
  Laparoscopic and minimally invasive techniques

Expanding criteria for resection in solitary large tumors and patients with intermediate PH
Assess tumor size, location, extrahepatic metastases

- Potentially resectable
  - Assess severity of liver disease
    - Child-Pugh A/B*:
      - Optimize medical therapy, consider PVE
      - Intraoperative evaluation
        - Resect
        - Unresectable
          - Consider intraoperative ETOH injection, RFA, cryoablation
      - Child-Pugh C
    - Unresectable
      - Liver transplant candidate?
        - No
          - Evaluate for transplant
            - Consider "bridging" therapy, e.g., TACE
        - Yes
          - No
            - Extrahepatic metastases
              - > 5 cm
                - Tumor size, number
                  - Single
                    - ≤ 5 cm
                      - RFA PEI/cryoablation, TACE, stereotactic radiotherapy, or radiotherapeutic microspheres may be alternatives depending on tumor characteristics, location, and local expertise
                  - Multiple
                    - ≤ 5 cm
                      - Sorafenib Clinical Trial
                        - > 4 lesions

Thomas M B et al. JCO 2010
Treatment/Management of HCC

- Surgical resection
- Liver transplantation
- Percutaneous ablation
  - Microwave/Radiofrequency ablation
- Transarterial chemoembolization
- Stereotactic Radiotherapy
- Biologics/Chemotherapy
- Best Supportive Care

Curative

Potentially Curative

Palliative
Summary

- Therapy of liver tumors in patients with cirrhosis remains challenging integrating a number of surgical and non-surgical modalities.

- Resection is the treatment of choice for HCC in non-cirrhotics and early cirrhotics (intermediate cirrhotics).
Yale Liver Cancer Program

• Multi-disciplinary treatment approach through Liver Tumor Boards and Clinic

• Integrative therapy including surgical resection, transplantation, radiofrequency ablation, chemotherapy, radiation, chemoembolization and radioembolization

• Minimally-invasive Hepatopancreatobiliary Surgery Program approaches for liver, pancreatic and upper GI surgery
Robotic resection?