Surgery in Patients with Cirrhosis

Cirrhosis

- Pathological Finding
- Diffuse bridging fibrosis surrounding abnormal regenerative nodules of hepatocytes
- Reduced hepatocyte mass, altered hepatic blood flow
- Irreversible, progressive
- **NOT** a measure of hepatic function or clinical compensation
Cirrhosis IS NOT Comorbid Condition!
Surgery in Patients with Cirrhosis

Elective Surgery and Mortality

Nationwide Volume and Mortality after Elective Surgery in Cirrhotic Patients

Nicholas G Csikesz, BS, Louis N Nguyen, MD, MBA, MPH, Jennifer F Tseng, MD, MPH, FACS, Shimul A Shah, MD

22,569 Cirrhosis & Portal Hypertension

Csikesz et al JACS 2009; 208:96
Surgery in Patients with Cirrhosis

Aims

• Overview ‘natural history’ of cirrhosis

• Identify predictors of operative morbidity, mortality and survival, thus, selection

• Provide information for counseling patients regarding their operative risk

• Algorithm for operative management
  - Any non-transplant operation
  - Hepatic Resection
### Surgery in Patients with Cirrhosis

#### Does my patient have cirrhosis?

<table>
<thead>
<tr>
<th>Finding</th>
<th>Total Patients</th>
<th>Cirrhosis</th>
<th>Positive LR (95% CI)</th>
<th>P Value</th>
<th>Negative LR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distended abd veins</td>
<td>1208</td>
<td>215</td>
<td>11</td>
<td>.003</td>
<td>0.72</td>
<td>.001</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>622</td>
<td>160</td>
<td>10</td>
<td>.004</td>
<td>0.86</td>
<td>.09</td>
</tr>
<tr>
<td>Ascites</td>
<td>1198</td>
<td>450</td>
<td>7.2</td>
<td>.05</td>
<td>0.69</td>
<td>.001</td>
</tr>
<tr>
<td>Palmar erythema</td>
<td>1795</td>
<td>536</td>
<td>5.0</td>
<td>&lt;.001</td>
<td>0.59</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Spider nevi</td>
<td>1821</td>
<td>694</td>
<td>4.3</td>
<td>&lt;.001</td>
<td>0.61</td>
<td>.14</td>
</tr>
<tr>
<td>Jaundice</td>
<td>1425</td>
<td>312</td>
<td>3.8</td>
<td>.005</td>
<td>0.82</td>
<td>.53</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>1707</td>
<td>819</td>
<td>3.5</td>
<td>&lt;.001</td>
<td>0.74</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Firm liver</td>
<td>849</td>
<td>461</td>
<td>3.3</td>
<td>.07</td>
<td>0.37</td>
<td>.46</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>1558</td>
<td>674</td>
<td>2.4</td>
<td>&lt;.001</td>
<td>0.37</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Udell et al, JAMA 307:832-842, 2012
**Surgery in Patients with Cirrhosis**

*Does my patient have cirrhosis?*

<table>
<thead>
<tr>
<th>AST:platelet ratio index (APRI)(^\text{71})</th>
</tr>
</thead>
<tbody>
<tr>
<td>[(\text{AST/upper limit of normal AST}) \times (100/\text{platelet count [x} \times 10^3/\text{μL}]) ]</td>
</tr>
<tr>
<td>Higher values of the APRI increase the likelihood of cirrhosis and lower values decrease the likelihood of cirrhosis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bonacini cirrhosis discriminant score (CDS)(^\text{94})</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Score</strong></td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
</tbody>
</table>

The modified Bonacini CDS has a range of possible values from 0 to 11; higher scores identify patients with higher likelihood of cirrhosis and lower scores identify patients with lower likelihood of cirrhosis.

<table>
<thead>
<tr>
<th>Lok index(^\text{114})</th>
</tr>
</thead>
<tbody>
<tr>
<td>[\exp(\text{logodds}) / \left[1 + \exp(\text{logodds})\right]]</td>
</tr>
<tr>
<td>logodds = [-5.56 - (0.0089 \times \text{Platelet count [x} \times 10^3/\text{μL}]) + (1.26 \times \text{AST:ALT ratio}) + (5.27 \times \text{INR})]</td>
</tr>
</tbody>
</table>

The Lok index is an odds ratio normalized to possible values between 0 and 1; a higher fraction (i.e., probability) increases the likelihood of cirrhosis, while a lower fraction reduces the likelihood of cirrhosis. (See also http://www.haltctrial.org/cirrhosis.html.)

AST indicates aspartate transaminase; ALT, alanine aminotransferase; INR, international normalized prothrombin ratio.
Surgery in Patients with Cirrhosis

Clinical Course of Cirrhosis

Decompensated

Stage 1
Compensated
Stage 2
Stage 3
Decompensated
Stage 4

- NO VARICES
- NO ASCITES

1%

7%

4.4%

3.4%

4%

20%

7.6%

57%

VARICES
- NO ASCITES

ASCITES
- BLEEDING

BLEEDING + ASCITES

D’Amico et al, J Hepatol 44:217, 2006
Surgery in Patients with Cirrhosis

‘Natural History’ of Cirrhosis

<table>
<thead>
<tr>
<th>Yrs</th>
<th>Pts at risk</th>
<th>MedSurv Comp Cirrhosis</th>
<th>MedSurv Decomp Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>806</td>
<td>12 years</td>
<td>2 years</td>
</tr>
<tr>
<td>2</td>
<td>600</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>450</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>335</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>275</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>248</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

D'Amico et al J Hepatol 44:217, 2006
Surgery in Patients with Cirrhosis

‘Natural History’ by CTP Class

D’Amico et al, J Hepatol 44:217, 2006
Surgery in Patients with Cirrhosis
Significant Predictors of Decompensation
and Death in Cirrhosis

• CTP Class – *most robust and consistent*

• CTP Component (each)

• Age

• Gender

• Platelets

• MELD ?

D’Amico J Hepatol 2006;44:217
Surgery in Patients with Cirrhosis

Probability of Decompensation

D’Amico et al, J Hepatol 44:217, 2006
Surgery in Patients with Cirrhosis
Predictors of Decompensation

- **HVPG**
  - N = 79
  - N = 134

- **MELD**
  - N = 154
  - N = 54

- **Serum Albumin**
  - N = 98
  - N = 114

**Survival (%)**

- ≥ 10 mmHg
- < 10 mmHg

- ≥ 10
- < 10

- < 4 g/dL
- ≥ 4 g/dL

< 10 mm Hg = 90% compensation

Surgery in Patients with Cirrhosis
Predictors of Decompensation

Summary

• CPT score accurately stratifies overall mortality for patients with cirrhosis but not decompensation.

• Currently no metrics accurately identify or predict the frequency and rate of decompensation in patients with compensated cirrhosis.
Surgery in Patients with Cirrhosis
Non-invasive Operative Risk Assessment

Liver Focused
‘Cirrhosis Only’

- Scoring Systems
  - Liver
  - HCC

- Quantitation of Hepatic Reserve
Surgery in Patients with Cirrhosis

Quantitation of Hepatic Reserve

- Indocyanine green clearance
- Galactose elimination capacity
- Aminopyrine breath test
- Drug or amino acid clearance
- 99m Tc-galactosyl albumin imaging

None reliably predictive of outcome

## Surgery in Patients with Cirrhosis

### Child-Turcotte-Pugh Class

<table>
<thead>
<tr>
<th>Points</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Moderate</td>
<td>Advanced</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Controlled</td>
<td>Refractory</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>&lt; 2</td>
<td>2 – 3</td>
<td>&gt; 3</td>
</tr>
<tr>
<td>Albumin (Gm/dl)</td>
<td>&gt; 3.5</td>
<td>2.8 – 3.5</td>
<td>&lt; 2.8</td>
</tr>
<tr>
<td>INR</td>
<td>&lt; 1.7</td>
<td>1.7 – 2.3</td>
<td>&gt; 2.3</td>
</tr>
</tbody>
</table>

### CTP Class

<table>
<thead>
<tr>
<th>Class</th>
<th>Points</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>5 – 6</td>
</tr>
<tr>
<td>B</td>
<td>7 – 9</td>
</tr>
<tr>
<td>C</td>
<td>10 - 15</td>
</tr>
</tbody>
</table>
Surgery in Patients with Cirrhosis

**MELD Score**

**Model for End-stage Liver Disease**

\[
\text{MELD} = 9.57 \times \ln (\text{creatinine}) + 3.78 \times \ln (\text{total bilirubin}) + 11.20 \times \ln (\text{INR}) + 6.43
\]

**Score:** 5 - 40

**Exclusion:** CRF, BD Obstruction,

**Calculation** [www.mayoclinic.org/girst/mayomodel15.htm](http://www.mayoclinic.org/girst/mayomodel15.htm)

Malinchoc et al, Hepatology 2000;31:864
<table>
<thead>
<tr>
<th></th>
<th>CTP</th>
<th>MELD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of variables</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Quantitative variables</td>
<td>3/5</td>
<td>3/3</td>
</tr>
<tr>
<td>Derivation of variables</td>
<td>Empirical</td>
<td>Statistical</td>
</tr>
<tr>
<td>Variables weighted to</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>their influence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Ceiling” effect of</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>quantitative variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logarithmic transformation of</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Needs computation</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Variables influenced by</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>clinical judgment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Score</td>
<td>Discrete</td>
<td>Continuous</td>
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</table>
# Cirrhosis

## Comparison of Clinical Scoring

<table>
<thead>
<tr>
<th>Scores</th>
<th>Objective Parameter</th>
<th>Subjective Parameter</th>
<th>Parameter Readily Available</th>
<th>Prospectively Designed</th>
<th>Validated Internally/Externally</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDEAL</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes/Yes</td>
</tr>
<tr>
<td>CTP *</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>MELD</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes/Yes</td>
</tr>
</tbody>
</table>

* Ceiling effect: No discrimination between bilirubin of 3 mg and 30 mg/dL
* Floor effect: No discrimination between albumin 1.5 g/dL and 2.8 g/dL

Kamath and Kim, Hepatology 2007;45:797
Surgery in Patients with Cirrhosis
Nontransplant Operative Mortality by CTP Class

Mansour et al, Surgery 1997; 122:730
Surgery in Patients with Cirrhosis
MELD and Non-transplant (30 Day) Mortality


Risk = 1 % / MELD pt for MELD < 20, and 2 % / MELD pt for MELD > 20
Risk Factors for Mortality after Surgery in Patients with Cirrhosis

Teh SH, Nagorney DM, Stevens S, Offord K, Therneau T, Plevak D, Talwalkar J, Kim WR, Kamath PS

Division of General Surgery, Biostatistics, Anesthesia and Gastroenterology & Hepatology, Mayo Clinic College of Medicine, Rochester, USA

Gastroenterology 2007;132:1261-1269
Surgery in Patients with Cirrhosis

MELD Distribution – Non-transplant Ops.

Teh et al, Gastroenterology 2007;132:1261
Surgery in Patients with Cirrhosis

MELD and Postoperative Survival

30-Day

90-Day

Long Term

Survival (%)

Days Following Surgery

Years Following Surgery

P < 0.001

P < 0.001

P < 0.001

6-10 (n=432)

11-15 (n=243)

16-20 (n=68)

21-25 (n=15)

26-39 (n=10)

7-day = ASA Score

Teh et al Gastroenterology 2007;132:1261
Surgery in Patients with Cirrhosis
Era and Postoperative Survival

30-Day

90-Day

Long Term

Teh et al, Gastroenterology 2007;132:1261
Surgery in Patients with Cirrhosis
Operative Category, Postoperative Mortality

Teh et al. Gastroenterology 2007;132;1261
Surgery in Patients with Cirrhosis
Operative Category, Postoperative Mortality

Long Term

Graph showing survival rates over years following surgery for different categories:
- Dig A (n=373)
- Dig B (n=214)
- Ortho (n=107)
- Cardio (n=79)

Survival (%) against Years Following Surgery.

P = 0.691

Teh et al Gastroenterology 2007;132;1261
Surgery in Patients with Cirrhosis
MELD and Postoperative Mortality

Teh et al, Gastroenterology 2007;132:1261
Surgery in Patients with Cirrhosis
Predictive Modeling for Risk of Death

MELD – most powerful predictor

• Relative risk of death increases by 15% / MELD point from 30 days to 1 yr and by 6% / yr subsequently

• Clinical adage:
  For each MELD point ≥ 8, mortality risk increases 2%
Surgery in Patients with Cirrhosis

Post-operative Mortality Risk in Patients with Cirrhosis

To determine the risk of post-operative mortality for all types of major surgery, especially gastro-intestinal, orthopedic and cardiac surgery (includes open-heart procedures), please enter the following variables:

- What is the age? □
- What is the ASA score? □ (use 1-5)
- What is the bilirubin? □ (mg/dl)
- What is the creatinine? □ (mg/dl)
- What is the INR? □
- What is the etiology of cirrhosis? ○ Alcoholic or Cholestatic  ○ Viral/Other

Mortality Risk Models
- The MELD Model
- The MELD-Na Model
- The MELD Model, UNOS modification
- MELD score and 90-day mortality rate for alcoholic hepatitis
- Post-operative Mortality Risk in Patients with Cirrhosis
- Other mathematical models for liver disease patients

Probability of Mortality
### MELD Score

Predicts 3 month survival from INR, bilirubin, and creatinine

<table>
<thead>
<tr>
<th></th>
<th>PSC</th>
<th>HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INR</strong></td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td><strong>Bilirubin</strong></td>
<td>15</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>Creatinine</strong></td>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td><strong>MELD Score</strong></td>
<td>21</td>
<td>22</td>
</tr>
</tbody>
</table>

Days to Event (PSC)  
1.5  
1.5  
1.2  
1.2  
1.0  
1.0  
1.0  
1.0  
11  
10  
9  
8  
8
Hepatic Resection of Hepatocellular Carcinoma in Patients with Cirrhosis: MELD Score Predicts Perioperative Mortality


Division of General Surgery, Division of Gastroenterology & Hepatology¥, Biostatistics *
Mayo Clinic College of Medicine, Rochester

Teh et al, J Gastro Surg 2005;9:1207
Surgery in Patients with Cirrhosis

CTP vs MELD, Resection of HCC

CTP Class

<table>
<thead>
<tr>
<th>CTP A</th>
<th>CTP B</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>60</td>
<td>6</td>
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<tr>
<td>8</td>
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</tr>
<tr>
<td>10</td>
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<td>12</td>
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<tr>
<td>14</td>
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<td>16</td>
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</tr>
<tr>
<td>18</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
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</tbody>
</table>

Number of patients

MELD Score

<table>
<thead>
<tr>
<th>MELD Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>9</td>
</tr>
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<td>10</td>
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<td>11</td>
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<td>14</td>
</tr>
<tr>
<td>15</td>
</tr>
<tr>
<td>16</td>
</tr>
<tr>
<td>17</td>
</tr>
</tbody>
</table>

Number of patients

P = 0.18

Surgery in Patients with Cirrhosis
MELD, Survival after Resection of HCC

Teh et al, J Gastroint Surg 2005;9:1207
Surgery in Patients with Cirrhosis
MELD, HCC Size and Survival

MELD ≤ 8

\( p = 0.02 \)

MELD ≥ 9

\( p = 0.01 \)

\[ \text{Teh et al, J Gastro Surg 2005;9:1207} \]
Surgery in Patients with Cirrhosis
MELD Profiles After Hepatectomy

No Liver Failure

N=16

N=164

Surgery in Patients with Cirrhosis

MELD Profiles After Hepatectomy


 Liver failure

N=31
29%

N=169
3.6%
## Surgical Resection for HCC with Cirrhosis
### Risk Score for HCC Resection – NIS n=2834

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>1.26 (0.86-1.86)</td>
<td>.2413</td>
</tr>
<tr>
<td><strong>Age group, y</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤55</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>56-65</td>
<td>1.24 (0.77-2.00)</td>
<td>.3687</td>
</tr>
<tr>
<td>66-75</td>
<td>1.32 (0.84-2.07)</td>
<td>.2286</td>
</tr>
<tr>
<td>&gt;75</td>
<td>2.45 (1.45-4.10)</td>
<td>.0006</td>
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<tr>
<td><strong>Charlson comorbidity score</strong></td>
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<tr>
<td>0</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.94 (1.17-3.23)</td>
<td>.0102</td>
</tr>
<tr>
<td>2</td>
<td>2.87 (1.59-5.18)</td>
<td>.0005</td>
</tr>
<tr>
<td>≥3</td>
<td>7.55 (4.68-12.17)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Procedure type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RFA/enucleation</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Wedge resection</td>
<td>1.80 (1.03-3.15)</td>
<td>.0391</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>4.03 (2.52-6.46)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Nonteaching hospital</td>
<td>1.95 (1.28-2.98)</td>
<td>.0019</td>
</tr>
</tbody>
</table>

![Estimated Mortality (%)](simons_etal_cancer_2010_116_1733_38_bar_graph)

Simons et al, Cancer 2010;116:1733-38
Surgery in Patients with Cirrhosis
Operative Risk Assessment

**Summary**

- Increases in CTP class and MELD score correlate with operative morbidity and mortality in patients with cirrhosis.
- MELD stratifies operative risk more precisely than CTP class and provides a statistical model for counseling patients.
- MELD identifies patients with cirrhosis at risk of liver failure postoperatively.
Surgery in Patients with Cirrhosis
Surgery in Patients with Cirrhosis

References
