The Risks of Surgery in Patients with Liver Disease

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Disclosures

- I have no relevant disclosures relevant to the content of this presentation
Objectives

- Define the scope of the problem of surgeries performed in patients with liver disease
- Review basic principles of preoperative assessment of patients with liver disease
- Outline approaches to estimate surgical mortality in patients with liver disease
- Discuss strategies to optimize preoperative management of liver disease

Defining the Problem

- Prevalence of liver cirrhosis rising and expected to increase over next 20-30 years
- Surgery in cirrhotic patients is common – 10% of cirrhotic patients require surgery other than liver transplantation in their final two years of life
- Surgery is associated with increased morbidity and mortality in patients with cirrhosis
- Limited data available to guide evidence-based preoperative care and risk assessment

Projected Prevalence of Chronic HCV, Cirrhosis, and Complications Over 4 Decades

<table>
<thead>
<tr>
<th></th>
<th>2000</th>
<th>2010</th>
<th>2020</th>
<th>2030</th>
<th>2040</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV infection</td>
<td>2,940,678</td>
<td>2,870,391</td>
<td>2,681,556</td>
<td>2,433,709</td>
<td>2,177,089</td>
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<tr>
<td>Cirrhosis</td>
<td>472,103</td>
<td>720,807</td>
<td>858,788</td>
<td>879,747</td>
<td>826,134</td>
</tr>
<tr>
<td>Decompensated cirrhosis</td>
<td>65,294</td>
<td>103,117</td>
<td>134,743</td>
<td>146,408</td>
<td>142,732</td>
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<tr>
<td>Hepatocellular carcinoma</td>
<td>7,271</td>
<td>11,185</td>
<td>13,183</td>
<td>13,390</td>
<td>12,528</td>
</tr>
<tr>
<td>Liver-related death</td>
<td>13,000</td>
<td>27,732</td>
<td>36,483</td>
<td>39,875</td>
<td>39,064</td>
</tr>
</tbody>
</table>


Cirrhosis has risen from the 14th to the 8th leading cause of death in U.S. in 2010
- 49,500 deaths
- 1.23 million years of life lost

### The State of US Health, 1990-2010: Burden of Diseases, Injuries, and Risk Factors

<table>
<thead>
<tr>
<th>Disease and Injuries</th>
<th>YLL Rank</th>
<th>1990</th>
<th>2000</th>
<th>2010</th>
<th>Median Change, %</th>
<th>Age Standardized YLL Rank</th>
<th>1990</th>
<th>2000</th>
<th>2010</th>
<th>Median Change, %</th>
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</thead>
<tbody>
<tr>
<td>Liver cancer</td>
<td>35</td>
<td>28 (10)</td>
<td>24 (12)</td>
<td>20 (14)</td>
<td>5.2</td>
<td>30 (10)</td>
<td>25(10)</td>
<td>22 (9)</td>
<td>19 (11)</td>
<td>-5.2</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>22</td>
<td>20 (12)</td>
<td>20 (12)</td>
<td>20 (12)</td>
<td>5.3</td>
<td>28 (10)</td>
<td>22 (10)</td>
<td>20 (10)</td>
<td>20 (10)</td>
<td>0.3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>21</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>5.3</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>0.3</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>23</td>
<td>23 (12)</td>
<td>23 (12)</td>
<td>23 (12)</td>
<td>5.3</td>
<td>23 (12)</td>
<td>23 (12)</td>
<td>23 (12)</td>
<td>23 (12)</td>
<td>0.3</td>
</tr>
<tr>
<td>Brain cancer</td>
<td>19</td>
<td>18 (12)</td>
<td>18 (12)</td>
<td>16 (12)</td>
<td>5.3</td>
<td>20 (12)</td>
<td>20 (12)</td>
<td>18 (12)</td>
<td>16 (12)</td>
<td>-2.7</td>
</tr>
<tr>
<td>Falls</td>
<td>24</td>
<td>24 (12)</td>
<td>24 (12)</td>
<td>24 (12)</td>
<td>5.3</td>
<td>24 (12)</td>
<td>24 (12)</td>
<td>24 (12)</td>
<td>24 (12)</td>
<td>0.3</td>
</tr>
<tr>
<td>Overdose</td>
<td>22</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>5.3</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>22 (12)</td>
<td>0.3</td>
</tr>
</tbody>
</table>

**Preoperative Screening for Liver Disease**

- **Primary objectives:**
  - To identify undiagnosed liver disease in asymptomatic individuals
  - To identify cirrhosis in patients with known chronic liver disease
  - Is cirrhotic, is the patient compensated or decompensated?
  - If compensated cirrhotic, does the patient have portal hypertension?

- **Careful history and physical exam**
  - Scleral icterus, jaundice, palmar erythema, spider nevi
  - Gynecomastia, temporal wasting, ascites, splenomegaly

- **Investigation of risk factors for liver disease**

- **Review of medications, alcohol, and supplements**

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HCC has risen from the 39th to 30th leading cause of death in U.S.

-19,500 deaths

-398,900 years of life lost (YLL)

Liver mortality from cirrhosis and HCC combined would be 5th leading cause of death
Preoperative Screening for Liver Disease

• Focused laboratory screening
  – Liver serologic investigation (viral, autoimmune, iron, etc.)
  – LFTs, Albumin, PT/INR, platelet count
• Consideration for HBV and HCV screening based on CDC and USPSTF recommendations
  – HCV: birth age cohort (1945-1965) or if other risk factors
  – HBV: born in endemic region or if other risk factors
• Abdominal imaging
  – Ultrasound, CT, MRI
  – Liver spleen scan
  – Liver elastography (Fibroscan, ARFI)

Physiology of Cirrhosis in Patients Undergoing Surgery

• Portal hypertension
  – Ascites
  – Encephalopathy
  – Variceal bleeding
• Impaired Coagulation
• Infections
• Impaired wound healing
• Malnutrition
• Poor hepatic reserve
• Increased mortality
How to Estimate Risk of Surgery in Patients with Liver Disease

Child-Pugh Turcotte

<table>
<thead>
<tr>
<th>Clinical and Lab Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>1</td>
</tr>
<tr>
<td>Ascites</td>
<td>1</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>1</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>1</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>1</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>1</td>
</tr>
</tbody>
</table>

Class A: 5 to 6 points (mild liver disease)  
Class B: 7 to 9 points (moderate liver disease)  
Class C: 10 to 15 points (severe liver disease)  
Class D: 16 to 19 points (end stage liver disease)

MELD

MELD = 3.78 \times \log_{10} \text{serum bilirubin (mg/dL)} + 
11.20 \times \log_{10} \text{INR} + 
9.57 \times \log_{10} \text{serum creatinine (mg/dL)} + 
6.43 \text{ (constant for liver disease etiology)}

Notes:
If the patient has been dialyzed twice within the last 7 days, then the value for serum creatinine used should be 4.0
Any value less than one is given a value of 1.0 (e.g., if bilirubin is 0.8, a value of 1.0 is used) to prevent the occurrence of scores below 0 (the natural logarithm of 1 is 0, and any value below 1 would yield a negative result)

How to Estimate Risk of Surgery in Patients with Liver Disease

Post-operative Mortality Risk in Patients with Cirrhosis

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

What is the age? [ ]
What is the cirrhosis? [ ]
What is the bilirubin? [ ]
What is the creatinine? [ ]
What is the BMI? [ ]
What is the etiology of cirrhosis? [ ]

Compute [ ]
Probability of Mortality

Risk of Mortality in Patients with Cirrhosis Undergoing Surgery

- 92 patients undergoing abdominal surgery over 12 year period at a single institution
- Surgeries performed: cholecystectomy (17), hernia (9), GI tract (54), other surgeries (12)
- Mortality rate:
  - Child A: 10%
  - Child B: 30%
  - Child C: 82%
- Higher mortality in emergent operations (50%) vs. elective operations (18%), \( p=0.001 \)
- Predictors: ascites \( (p=0.006) \), PSE \( (p=0.002) \), elevated PT \( (p=0.021) \)


MELD: Risk of Abdominal Surgery in Patients with Cirrhosis

- 772 patients with cirrhosis undergoing abdominal, orthopedic and cardiovascular operations.
- MELD, ASA and age used to quantify mortality risk in cirrhotic patients postoperatively.
- Increased risk of mortality up to 90 days postoperatively
- Mortality rates
  - MELD <7: 5.7%
  - MELD 8-11: 10.3%
  - MELD 12-15: 25.4%
- Increased risk for ASA class IV (+5.5 MELD) and V (100% mortality)

MELD: Outcomes of Abdominal Operations in Patients with Cirrhosis in Transplant Center

• 100 patients at major liver transplant center (Child A=50, Child B=33, Child C=17) between 2002-2008
• Factors predicting surgical outcome evaluated in multivariate logistic regression model
• Overall 30 day mortality was 7% (CTP A=2%, CTP=B 12%, CTP C=12%)
• MELD score ≥ 15 = 29% mortality
  – Albumin <2.5 = 60%
  – Albumin ≥2.5 = 14% (p<0.01)
• Predictors of mortality: ASA>3, emergency surgery, intraoperative blood loss >150 mL, ascites, Tbili >1.5, albumin <3


Contraindications for elective surgery

• Acute hepatitis
• Alcoholic hepatitis
  – Abstinence from alcohol for at least 12 weeks improves hepatic inflammation and hyperbilirubinemia
  – Reassess after 12 weeks
• Acute liver failure
Risk of Mortality in Patients with Cirrhosis Undergoing Cholecystectomy

- Meta-analysis of 44 studies (n= 2005 patients) comparing open (OC) vs. laparoscopic cholecystectomy (LC)
- Total surgeries: OC (249) and LC (1756)
- All patients had Child A or B cirrhosis
- Overall mortality rate:
  - Laparoscopic: 0.74%
  - Open: 2.0%
- Laparoscopic approach was associated with shorter operative time, reduced surgical complication rates, and reduced hospitalization length of stay


Differential Risk by Surgery Type

- **LOW RISK**: HEENT, dental, pacemaker insertion, GI endoscopy, laparoscopy, GU procedures, lymph node biopsy or resection, bronchoscopy and laryngoscopy

- **MODERATE RISK**: back surgery (laminectomy/disk), thyroidectomy and other endocrine surgery, intracranial, head and neck, major vascular, rectal/anal surgery, hysterectomy, hand/foot/knee orthopedic, breast biopsy and mastectomy, peripheral artery or carotid artery surgery, prostate/bladder procedures

- **HIGH RISK**: esophagus/stomach, cardiac, AAA/aneurysm repair, hepatobiliary, small/large bowel, pancreas, hip surgery, lung resection, back fusion, laparotomy
Differential Risk by Surgery Type

- Cardiac surgery (n= 54): higher mortality with high CP score: 4.6% (CP <8), 70% (CP ≥8)
- Neurosurgery (n=144): overall mortality 24% (Child A 38%, Child B 60%, Child C 84%) * emergency brain trauma
- Head and neck surgery (n=61): higher mortality with MELD >9.73 (23.3% vs. 3.2%, p=0.026)
- General trauma surgery (n=37): higher mortality in cirrhotic (12%) vs. non-cirrhotic patients (6%) with OR 5.65
- Orthopedic hip surgery (n=29): higher mortality in cirrhotic (21%) vs. non-cirrhotic patients (3%) – highest mortality in emergency traumatic hip surgery (60%)


Preoperative Management

- Ascites
  - Na restriction, aldactone/lasix, therapeutic paracentesis
  - TIPS shunt
- Esophageal and Gastric Varices
  - EGD screening
  - Non-selective beta-blockers or pre-emptive band ligation
  - TIPS shunt
- Hepatic Encephalopathy
  - Lactulose, rifaximin
  - Avoid known precipitants
- Nutrition
  - Nutrition consult
  - Enteral feeding
Preoperative Management

• Coagulopathy
  – Correct to maintain INR <1.5 – vitamin K, FFP
  – Platelets > 50,000/uL – platelet transfusion
  – Fibrinogen > 200 – cryoglobulin
  – Potential role for thromboelastogram (TEG)

• Fluid Management
  – Avoid over-resuscitation (NS, D5W) → fluid overload
  – Prefer albumin or other colloid fluids
  – Monitor electrolytes and renal function

• Pulmonary
  – Hydrothorax: thoracentesis/tap before surgery
  – HPS: PaO2 <60 associated with hypoxia and difficult extubation
  – PPS: ok to proceed if 35-50 mm Hg, high risk if >50 mm Hg

Preoperative Management: Anesthesia

• Altered hemodynamics of cirrhosis
  – ICU monitoring
  – Arterial line, central venous pressure monitoring

• Induction agents
  – Halothane and enflurane to be avoided
  – Isoflurane, sevoflurane, desflurane appear to be safe
  – Caution with proprofol

• Muscle relaxants
  – Preference for cis-atracurium

• Avoid hypercarbia
  – Concern for decreased hepatic perfusion
Postoperative Management

• Ascites
  – Aldactone/lasix
  – May consider short-term drain to promote wound healing
• Pain control
  – Caution with narcotics
  – Use low-dose narcotics – dilaudid preferred due less hepatic clearance
• Sedatives
  – Lorazepam, oxazepam, temazepam preferred (less 1st pass elimination)
  – Midazolam OK in context of ICU monitoring
  – Avoid diazepam, chlordiazepoxide, clonazepam

Conclusions

• Increasing burden of liver cirrhosis in the U.S.
• Surgery is common in cirrhotic patients and is associated with increased morbidity and mortality
• Preoperative evaluation requires careful assessment for the presence of cirrhosis and portal hypertension
• CPT and MELD scores provide reasonable estimates of mortality risk in patients with liver disease undergoing surgery
• Cautious preoperative optimization of liver disease and postoperative care is essential to improve liver outcomes
• Future research needed to provide evidence-based guidelines