Surgical Management of Cholangiocarcinoma

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Proposed Questions

1. How do we identify unresectable tumors?
2. What is the management of surgically unresectable tumors?
3. How should we manage suspected cholangiocarcinomas without definitive tissue diagnosis?
Cholangiocarcinoma

EPIDEMIOLOGY

Relatively uncommon malignancy
More common outside the United States, particularly in South America and Eastern/Central Europe

Less common than gallbladder cancer

Incidence per 100,000 in U.S.:   
   1.0 in females
   1.5 in males

Increasing incidence with age
   70% of cases in over 65 years

Hilar location most common
Cholangiocarcinoma

Location

Peripheral
- 7-20%
- Intrahepatic mass
- Cirrhosis uncommon
- Etiology unknown

Hilar
- 40-60%
- Biliary confluence
- Most common

Distal
- 20-30%
- 10-15% of peripancreatic tumors
Cholangiocarcinoma
Johns Hopkins Experience (1973-2004)

- Distal: 42%
- Intrahepatic: 8%
- Perihilar: 50%

## Cholangiocarcinoma: Johns Hopkins Series (All Sites)

### Overall Survival

<table>
<thead>
<tr>
<th></th>
<th>Resected Margin neg (n = 259)</th>
<th>Resected Margin pos (n = 172)</th>
<th>Palliated (n = 133)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year Survival</td>
<td>30 %</td>
<td>10 %</td>
<td>2 %</td>
</tr>
<tr>
<td>Median Survival</td>
<td>28 mo</td>
<td>16 mo</td>
<td>8 mo</td>
</tr>
</tbody>
</table>

**Graph Notes:**
- Resected margin neg (n=259)
- Resected margin pos (n=172)
- Palliated (n=133)
- Median survival in months:
  - Resected Margin neg: 28 mo
  - Resected Margin pos: 16 mo
  - Palliated: 8 mo
- 5-year survival percentages:
  - Resected Margin neg: 30%
  - Resected Margin pos: 10%
  - Palliated: 2%
- Statistical significance: p < .001
Hilar Cholangiocarcinoma

**Treatment**

- Complete resection is the only effective therapy.
- Outcomes after R0 resection:
  - 5-year overall survival of 25-40%
  - DFS of 15-25%
- Few patients are resectable.
- R1/2 resections are not uncommon.
- Palliating the effects of biliary obstruction is often the primary treatment objective.
Defining Resectability for Hilar Cholangiocarcinoma

Questions to Ask When Considering Surgery?

1. Is complete (R0) resection possible?

2. Can it be done with enough remaining liver, adequate blood supply and good biliary drainage?

- Extent of disease
- Vascular involvement
- Lobar atrophy
- Metastatic disease
- Underlying liver disease
- Other comorbidities
Hilar Cholangiocarcinoma

CRITERIA OF UNRESECTABILITY

Patient-Related Factors
- Medical contraindication to major abdominal surgery
- Cirrhosis or insufficient remnant hepatic volume

Metastatic Disease
- N2 lymphadenopathy
- Distant metastases
Hilar Cholangiocarcinoma

CRITERIA OF UNRESECTABILITY

Local Tumor-Related Factors

- Tumor extension to secondary biliary radicles bilaterally
- Encasement or occlusion of the main portal vein proximal to its bifurcation
- Unilateral tumor extension to secondary bile ducts with contralateral vascular encasement or occlusion
- Atrophy of one hepatic lobe with contralateral portal vein encasement or secondary biliary extension
Bismuth-Corlette Classification of Biliary Extent of Hilar Cholangiocarcinoma
Hilar Cholangiocarcinoma

Goal of Resection:
Complete Tumor Excision with Negative Margins

**ESTABLISHED:**
- Excision of supraduodenal bile duct
- Cholecystectomy
- Restore biloenteric continuity

**LESS CONTROVERSIAL:**
- Routine hepatectomy/caudate (left resections)
- Portal lymphadenectomy
- Selected major vascular reconstruction

**MORE CONTROVERSIAL:**
- Routine PV resection (Neuhaus)
Hilar Cholangiocarcinoma

Anatomical Considerations

- Frequent submucosal tumor extension beyond gross margin (5 – 20 mm)
- Often unilateral extension to 2\textdegree{} biliary radicles and beyond
- Hepatic resection required

### Results Of Resection for Hilar Cholangiocarcinoma

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>N</th>
<th>Concomitant Liver Resection (%)</th>
<th>% R0 Resection</th>
<th>5-Year Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameron (1990)</td>
<td>39</td>
<td>20</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>Gerhards (2000)</td>
<td>112</td>
<td>29</td>
<td>14</td>
<td>-</td>
</tr>
<tr>
<td>Su (1996)</td>
<td>49</td>
<td>57</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>Hadjis (1990)</td>
<td>27</td>
<td>60</td>
<td>56</td>
<td>22</td>
</tr>
<tr>
<td>Jarnagin (2001)</td>
<td>80</td>
<td>78</td>
<td>78</td>
<td>27</td>
</tr>
<tr>
<td>Klempnauer (1997)</td>
<td>147</td>
<td>79</td>
<td>79</td>
<td>28</td>
</tr>
<tr>
<td>Neuhaus (1999)</td>
<td>95</td>
<td>85</td>
<td>61</td>
<td>22</td>
</tr>
<tr>
<td>Kosuge (1999)</td>
<td>65</td>
<td>88</td>
<td>88</td>
<td>33</td>
</tr>
<tr>
<td>Nimura (1990)</td>
<td>55</td>
<td>98</td>
<td>83</td>
<td>40</td>
</tr>
</tbody>
</table>

*Increasing inclusion of liver resection*
*Increasing R0 resection rate*
*Improving survival*
Hilar Cholangiocarcinoma

PREOPERATIVE EVALUATION

1. Cholangiography
   • Assessment of extent of biliary ductal involvement
   • ERCP vs MRCP vs PTC

2. Cross-sectional imaging
   • Soft tissue extent, lobar atrophy, vascular involvement, remnant volume, metastases
   • CT vs MRI

Controversies:
   • Role of preoperative stenting
   • FDG-PET
   • Staging laparoscopy
Non-Invasive Imaging: MRI/MRCP

- High quality images of the biliary tree - as good as cholangioscopy for assessing biliary tumor extent*.
- Provides additional data regarding metastases, vascular involvement, lobar atrophy.

*Lee et al. Gastrointest Endosc 2002;56:25
Intrabiliary MRI

Arepally et al. (JHH)
Hilar Cholangiocarcinoma

LAPAROSCOPIC STAGING

- Most useful to rule out metastatic disease.
- Less helpful for cholangiocarcinoma than GB cancer.
- Consider in locally advanced cases.
Hilar Cholangiocarcinoma and Gallbladder Cancer

STAGING LAPAROSCOPY

100 patients with potentially resectable biliary cancer
   hilar cholangioca = 56
   gallbladder ca = 44
All underwent staging laparoscopy prior to surgical exploration

RESULTS:
Overall 69% were unresectable (HC = 59%, GB = 82%)
Laparoscopy yield: 48% in patients with gallbladder cancer
   (56% in those w/o previous cholecystectomy)
   25% in patients with hilar cholangiocarcinoma
Most useful at detecting peritoneal or liver metastases.

Hilar Cholangiocarcinoma

Role of FDG-PET

- Not useful for infiltrating cholangiocarcinoma
- False negatives due to low volume metastases
- False positives due to stents or recent cholecystectomy

<table>
<thead>
<tr>
<th></th>
<th>GC</th>
<th>Nodular CC (Mass 1 cm)</th>
<th>Infiltrating CC (No mass)</th>
<th>Total CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>14</td>
<td>22</td>
<td>14</td>
<td>36</td>
</tr>
<tr>
<td>True positive</td>
<td>7</td>
<td>17</td>
<td>2</td>
<td>19</td>
</tr>
<tr>
<td>False negative</td>
<td>2</td>
<td>3</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>True negative</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>False positive</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>78% (7/9)</td>
<td>85% (17/20)</td>
<td>18% (2/11)</td>
<td>61% (19/31)</td>
</tr>
<tr>
<td>Specificity</td>
<td>80% (4/5)</td>
<td>50% (1/2)</td>
<td>100% (3/3)</td>
<td>80% (4/5)</td>
</tr>
<tr>
<td>PPV</td>
<td>88% (7/8)</td>
<td>94% (17/18)</td>
<td>100% (2/2)</td>
<td>95% (19/20)</td>
</tr>
<tr>
<td>NPV</td>
<td>67% (4/6)</td>
<td>25% (1/4)</td>
<td>25% (3/12)</td>
<td>25% (4/16)</td>
</tr>
</tbody>
</table>

Biliary Stents for the Management of Surgically Unresectable Cholangiocarcinoma
Management of Surgically Unresectable Cholangiocarcinoma

Percutaneous vs. Endoscopic Stenting?

- RCT (n=75)
  - Superior technical and clinical success with endo
  - Better control of bilirubin levels
  - Significantly fewer complications
  - Lower 30-day mortality rate

Speer et al. Lancet (Jul 1987)
Percutaneous vs. Endoscopic Stenting for Palliating Hilar Cholangiocarcinoma?

- RCT comparing metallic percutaneous stent vs. endoscopic stent
- 54 patients
- Success rate = 75% (p) vs 58% (e)
- Complication rate 61% (p) vs 35% (e)
- No difference in freedom from recurrent obstruction
- Median survival better in percutaneous group (3.7 vs 2.0 mo, p=0.02)

Pinol et al, Radiology 2002
Selective Unilateral Stent Drainage for Unresectable Hilar Cholangiocarcinoma

- MRCP & CT: guide selective guidewire access
- Goal: drain only largest intercommunicating segmental ducts with 1 uncovered metal stent
- 35 patients, success rate = 71%
- Percutaneous stenting required in 3 patients
- 30-day morbidity = 0
- Median patency of metal stent = 8.9 months

Freeman, Gastrointest Endosc 2003
Single versus Double Endo Stents

- Prospective RCT of 157 hilar CA (Bismuth I-III)
  - Unilateral drainage adequate
    - Fewer technical failures
    - Less instrumentation
    - Few early complications
  - Attempts to place 2nd biliary stent: early complications (cholangitis) w/o survival benefit

De Palma, Gastrointest Endosc 2001
1. Achieving complete margin negative resection remains the goal in selected patients with hilar cholangiocarcinoma, requiring hepatic resection in nearly all cases.

2. Advances in non-invasive imaging have allowed better identification of unresectable cases.

3. The role of PET, laparoscopic staging remain controversial.

4. The choice of stent palliation approach (endo vs perc) should individualized.