Evaluation and Staging of Liver Fibrosis

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Recorded on April 29, 2013
Dr Peters has reported the following financial relationships with commercial firms:

- Consultant: Merck & Co, Inc, Theravance, and Roche
- Data safety monitoring board: Biotron
- Scientific advisor: Clinical Care Options
- Her spouse is employed by Genentech (Roche)
Outline

① Indications for liver biopsy
② Interpreting liver biopsy findings
③ Indirect and direct biomarkers
④ Imaging
Indications for Liver Biopsy
## Indications for Liver Biopsy

<table>
<thead>
<tr>
<th><strong>YES</strong></th>
<th><strong>NO</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Patient would only accept treatment if significant fibrosis</td>
<td>- Patient wants treatment even if no fibrosis</td>
</tr>
<tr>
<td>- Treatment different for patients with cirrhosis and labs and radiographic studies do not suggest cirrhosis</td>
<td>- Patient does not want treatment</td>
</tr>
<tr>
<td>- Patient fails to achieve SVR and no recent biopsy available</td>
<td>- Treatment contraindicated</td>
</tr>
<tr>
<td>- Chance of SVR low</td>
<td>- Cirrhosis on imaging or clinically</td>
</tr>
<tr>
<td></td>
<td>- New drugs results in high SVR for all</td>
</tr>
</tbody>
</table>
Interpreting Liver Biopsy Findings
Fibrosis Progression: F0–F4

F-0 is normal

F1
Central Vein
Portal Tract Fibrosis
Numerous

F2
Few Septa

F3

F4
Cirrhosis
Sampling Error of Liver Biopsy
Sampling Error of Liver Biopsy

Fibrosis area: 65%
Sampling Error of Liver Biopsy

Fibrosis area: 65%

Fibrosis area: 15%

Courtesy of M. Pinzani, Florence
Sampling Error of Liver Biopsy

Fibrosis area: 65%

Incorrect allocation of 20%-30% of patients

Fibrosis area: 15%

Courtesy of M. Pinzani, Florence
Liver Biopsy Size in 355 Samples: The Smaller the Piece the Milder the Disease

<table>
<thead>
<tr>
<th>Length of specimen</th>
<th>&gt; 3 cm</th>
<th>1.5 cm</th>
<th>1 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Portal Tracts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>complete</td>
<td>22.4 ± 4.9</td>
<td>10.3 ± 2.2</td>
<td>6.4 ± 1.2</td>
</tr>
<tr>
<td>Grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>49.7%</td>
<td>60.2%</td>
<td>86.6%</td>
</tr>
<tr>
<td>Moderate</td>
<td>38.5%</td>
<td>39.1%</td>
<td>17.4%</td>
</tr>
<tr>
<td>Severe</td>
<td>11.8%</td>
<td>0.6%</td>
<td>0</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (F0-1)</td>
<td>59%</td>
<td>68.3%</td>
<td>80.1%</td>
</tr>
<tr>
<td>Moderate (F2)</td>
<td>29.8%</td>
<td>24.2%</td>
<td>14.9%</td>
</tr>
<tr>
<td>Severe (F3-4)</td>
<td>11.2%</td>
<td>7.4%</td>
<td>4.9%</td>
</tr>
</tbody>
</table>

Colloredo, *J Hep*, 2003
Liver Biopsy Value

- Still the best test to assess fibrosis in an individual patient in United States
- Only as good as the adequacy of the specimen
- More expensive than serum markers or elastography
- Requires expert for acquisition and pathology
- Less needed in viral hepatitis over time
- If therapy uncertain, biopsy is the best test to learn stage of disease
Pros and Cons of Liver Biopsy

- Invasive, requires expertise, US guidance
- Risky: bleeding in 1 in 1000; pain
- Requires expert pathology assessment
  - > 2 cm, > 6 portal tracts for diagnosis
  - > 2 cm, >11 portal tracts for staging
- But assesses more than fibrosis
  - Fat that can impact response to therapy
  - Inflammation and location (eg, nonalcoholic fatty liver disease in hepatitis B virus)
  - Other liver disease (autoimmune hepatitis, alcohol use)
Fibrosis Is a Dynamic Process Not Reflected in Static Biopsy Sample
Indirect and Direct Biomarkers
Fibrosis Is a Dynamic Process Not Reflected in Static Biopsy Sample
Noninvasive Tests of Fibrosis Likely to Be an Alternative in the Future

**Blood tests**
- Fibrotest
- AST-to-platelet ratio index
- Enhanced liver fibrosis
- Forns index
- FIBROSpect
- Fibrometer
- Hepascore
- FIB-4 (coinfected patients)

**Liver Imaging**
- Transient elastography
- Diffuse-weighted magnetic resonance imaging (MRI)
- MRI elastography
- MR spectroscopy

Fibrosis Tests

Indirect
- Markers of liver injury ALT/AST
- Markers of hepatic function-indirect
  - Prothrombin time, albumin, alfa 2 macroglobulin, haptoglobin, platelets

Direct
- Markers of matrix production or degradation
  - Procollagen, hyaluronic acid, tissue inhibitors of metalloproteininases, matrix metalloproteininases, YKL-40
Imaging
Hepatic Elastography
Elastography: Fibroscan

Affected by weight, access of probe (2 cm), steatosis
Summary

Staging of Liver Disease

- Less important prior to hepatitis C virus (HCV) treatment as treatment success increases
- Noninvasive markers improving
- Transient elastography now approved in United States
- Ultrasound, computed tomography (CT), MRI useful in cirrhosis but not useful to stage disease