Why to biopsy? Indications for liver biopsy in common medical liver diseases- how are they changing?

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What are we currently using liver biopsy for?

- Assessing severity of Clinically/serologically diagnosed disease
- Providing a diagnosis (and prognosis) for undiagnosed liver disease
- Adding additional diagnoses
Deaths from Chronic Liver Disease in 1993 & 2009

Rates per 100,000 population

Bhala, Aithal & Ferguson, BMJ, 2013
Alcohol Consumption in the UK

Williams et al, Lancet, 2014
BALLETTS study

• 8 practices in Birmingham
• 2006-2008
• Abnormal test in liver panel
• No symptoms of liver disease
• No history of liver disease/alcohol/ivdu

Cause of Abnormal LFTs

- 54.9% had a cause identified

**Graph:**
- NAFLD
- ALD
- Screen +
- Unexplained
Biopsy in diagnosed disease

- AMA
- Anti-HCV
- HBsAg
- C282Y Haemochromatosis
- Alcohol
- NAFLD

Mixed aetiology

Additional information

Fibrosis stage
Typical Algorithm Performance:

ELF

Rosenberg et al Gastroenterology 2004
ELF markers Performance
F0,1,2 vs F3,4
Fibroscan
Performance of Transient Elastography for the Staging of Liver Fibrosis: A Meta-Analysis
M FRIEDRICH–RUST
GASTROENTEROLOGY 2008;134:960–974

• Meta analysis of 50 studies
• Differing aetiologies
• Different populations
1.1.3 Offer transient elastography to diagnose cirrhosis for:
• people with hepatitis C virus infection
• men who drink >50 u/wk and women >35 units of alcohol per week

1.1.4 Offer either transient elastography or ARFIE to diagnose cirrhosis for people with NAFLD and advanced liver fibrosis (ELF score of 10.51+).
Non-alcoholic fatty liver disease: NICE guideline

1.1.5 Consider the diagnosis of fatty liver in people with type 2 diabetes and metabolic syndrome

1.1.11 Use the ELF test for advanced liver fibrosis if NAFLD has been diagnosed
1.1.12 Diagnose people with advanced liver fibrosis and refer them to a relevant specialist in hepatology, if they have:
- an ELF score of 10.51 or above and
- NAFLD.

Colloredo J Hepatol 2003;39:275
161 biopsies

<table>
<thead>
<tr>
<th>Length</th>
<th>Grade</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3cm</td>
<td>50%</td>
<td>59%</td>
</tr>
<tr>
<td>1.5</td>
<td>60%</td>
<td>68%</td>
</tr>
<tr>
<td>1cm</td>
<td>87%</td>
<td>80%</td>
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</tbody>
</table>

% mild disease
Clinician and Pathologist interaction

• Adequacy of core
  – Size
  – Number of portal tracts
• Stage of disease
• Grade of inflammation
• Narrative comment
Staging of disease

Hepatitis C: factors affecting response

- genotype
- viral load
- ALT
- BMI
- Age
- Gender
- IL28B (ethnicity)

Stage of liver disease
Abbvie in G1 cirrhosis

Hepatitis B

- More biopsies undertaken
  - More HBV in the UK
  - Greater understanding of natural history and the potential for active disease despite serology
  - Lifelong therapy
  - Disease activity important as well as fibrosis stage
Key features in HBV

EASL guidelines on treatment:

**Were based on histology**
F2 fibrosis or above
“significant” necro-inflammation

HBV DNA and ALT trigger liver biopsy

NICE less histology based
Fibroscan increasingly used
Cholestatic liver disease

• Few clinicians using biopsy for PBC
  – Variability well established
  – Key prognostic marker remains Bilirubin
  – Main reason for biopsy is potential for overlap with AIH
  – Response to therapy and new drugs in trials may have impact

• PSC: diagnosis in unsuspected cases

Garrido and Hubscher JClin Pathol 1996;49:556
Overlap PBC/AIH

• In reality rare and clinically difficult
• Signposted by bloods, despite AMA+
  – ALT>200
  – IgG elevated
  – Interface hepatitis relatively common in “pure PBC”
Liver biopsy in alcohol related liver disease

- Cirrhosis
- Alcoholic hepatitis
- Other diagnoses
Liver biopsy in suspected ALD

- STOPAH study (steroids in acute alcoholic hepatitis)
- Clinical diagnosis of AH
- Biopsy in subset
- Confirmed clinical diagnosis in 92%
Liver biopsy in ALD

- Cirrhosis: 85%
- Alcoholic hepatitis: 92%
- Other diagnoses: 8%

Thursz M et al NEJM 2015
Liver biopsy in NAFLD

- Fibrosis markers will screen most out
- Biopsy still important in those with high marker scores
- CRN score (ballooning) useful clinically in terms of progression risk
- End point in trials is histological
<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Cryptogenic hepatitis</td>
<td>9%</td>
</tr>
<tr>
<td>Drug reactions</td>
<td>8%</td>
</tr>
<tr>
<td>Normal liver</td>
<td>6%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>3%</td>
</tr>
<tr>
<td>PBC/PSC</td>
<td>2.5%</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>1.9%</td>
</tr>
<tr>
<td>Granulomas/sarcoid</td>
<td>1.7%</td>
</tr>
<tr>
<td>Others</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

Conclusions

- Liver biopsy still an essential test
- Fibrosis markers now validated and in use
- Population having biopsy likely to be “enriched” for more fibrotic disease
- Use in HCV pretty much gone
- Mixed aetiology much more common
- Clinical interaction with reporting pathologist will make best use of biopsy