Cirrhosis Management for the Family Physician

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Objectives

• Assessment of significant hepatic fibrosis in patients with chronic liver diseases
• Understand the natural history of cirrhosis and complication development
• Develop a management routine for your patients with cirrhosis
Natural History of Chronic Liver Disease

- Chronic injury
- Fibrosis progression
- Cirrhosis
  - Portal hypertension and HCC
- Complications from portal hypertension
- Liver failure

Can be asymptomatic and difficult to identify

Natural History of Chronic liver Diseases

HCC

Normal Liver → Cirrhosis → Liver Failure

<table>
<thead>
<tr>
<th>Abnormalities</th>
<th>Normal 1</th>
<th>Normal 2</th>
<th>Normal 3</th>
<th>Normal 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>41-40 KPa</td>
<td>Soft</td>
<td>Hard</td>
<td>Rock</td>
<td></td>
</tr>
<tr>
<td>Point of no return</td>
<td></td>
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</tbody>
</table>

Improvement  ↔  Progression

Clinical Assessment of Fibrosis/Cirrhosis

<table>
<thead>
<tr>
<th>Biopsy</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>Decompensation</th>
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<tbody>
<tr>
<td>Non invasive tests</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Clinical symptoms</td>
<td>None/Min.</td>
<td>Fatigue</td>
<td>Varicose</td>
<td>EVH/Ascites/HE</td>
<td></td>
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<tr>
<td>Blood tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imaging studies</td>
<td>Abnormal</td>
<td>Cirrhosis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MELD</td>
<td></td>
<td></td>
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</table>
Liver Biopsy

Confirming diagnosis
Staging of liver
Assessing for coexisting liver diseases

Liver Biopsy

• Invasive procedure with a small risk of morbidity and mortality (1/500 to 1/1000)
  – Hemorrhage
• Sampling error
  – Examine 1/50,000 portion of liver
  – Variable levels of fibrosis throughout the liver (discordance rate ~30%)
  – Inadequate sample can be misleading

Indirect Methods to Assess Liver Fibrosis

• Blood tests
  – Panel of blood tests (routine and special blood tests)
  – A special calculator to determine the fibrosis score
  – Variable sensitivity, specificity, positive predictive value and negative predictive value
• Transient elastography
  – Measuring liver stiffness
Indirect Tests for Liver Fibrosis

- AST/ALT ratio greater than 1
- AST to Platelet ratio index (APRI)
- Fibrotest (alpha 2 macroglobulin, haptoglobin, gamma globulin, apolipoprotein A1, GGT and bilirubin)
- PGA Index (PT, GGT and apolipoprotein A1)
- Fibroindex (AST, PLT, GGT)
- FIB-4 Index (PLT, ALT, AST)
- Fibrometer (PLT, PT, AST, alpha-2 macroglobulin, hyaluronate, urea and age)
- Hepascore (bilirubin, GGT, hyaluronic acid, alpha 2 macroglobulin, age, gender)
- ActiTest (Fibrotest, ALT)

The AST-to-Platelet Ratio Index (APRI)

- \( \frac{\text{AST/ULN}}{\text{platelets}} \times 100 \)
  - 0.5 or less - no fibrosis or just a little
  - 1.5 or above - probably have cirrhosis
- APRI scores between 0.5 and 1.5 are related to progressive fibrosis (Metavir F1-to-F4)

Fibrotest

- Alpha 2 Macroglobulin
- Haptoglobin
- GGT
- Age
- Bilirubin
- Apo A1
- Gender
Fibrotest

<table>
<thead>
<tr>
<th>FibroTest</th>
<th>METAVIR</th>
<th>Knodell</th>
<th>Ishak</th>
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<tbody>
<tr>
<td>0.75-1.00</td>
<td>F4</td>
<td>F4</td>
<td>F6</td>
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<td>F3-F4</td>
<td>F3-F4</td>
<td>F5</td>
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<tr>
<td>0.69-0.72</td>
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<td>F3</td>
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<tr>
<td>0.49-0.58</td>
<td>F2</td>
<td>F1-F3</td>
<td>F3</td>
</tr>
<tr>
<td>0.32-0.48</td>
<td>F1-F2</td>
<td>F1-F3</td>
<td>F2-F3</td>
</tr>
<tr>
<td>0.28-0.31</td>
<td>F1</td>
<td>F1</td>
<td>F2</td>
</tr>
<tr>
<td>0.22-0.27</td>
<td>F0-F1</td>
<td>F0-F1</td>
<td>F1</td>
</tr>
<tr>
<td>0.00-0.21</td>
<td>F0</td>
<td>F0</td>
<td>F0</td>
</tr>
</tbody>
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Transient Elastography

- Fibroscan
- MR Elastography

- No risk
- Reducing sampling error by examining a larger mass of liver tissue
- Can be repeated as frequently as one wishes

Cirrhosis

- AST tends to be higher than ALT
- Ferritin is elevated, iron saturation index continues to rise
- Patients would have high IgG and MCV
- More severe portal hypertension – WBC and Platelet count will be low.
Assessment of Fibrosis

- Liver biopsy
- Non-invasive tests
- Transient Elastography

Complications of Cirrhosis

- Ascites
- Variceal Hemorrhage
- Hepatorenal Syndrome
- Hepatic Encephalopathy
- Nutrition deficiency
- Hepatoma
- Cardiopulmonary complications

Management of Ascites

- Dietary Na restriction (<88mmol/day)
- Diuretic therapy (always use combination – furosemide and spironolactone)
- Avoid renal dysfunction
- Large volume paracentesis
- Watch out for SBP
- TIPS
- Liver transplantation
Varices

- Gastroscopy is recommended when the diagnosis of cirrhosis is made
- Nonselective β-blockers should be used for the prevention of first variceal hemorrhage (primary prophylaxis)
- Patients with cirrhosis who survive an episode of active variceal hemorrhage should receive therapy to prevent recurrence of variceal hemorrhage (secondary prophylaxis)
- Combination of nonselective β-blockers plus EVL is the best option for secondary prophylaxis of variceal hemorrhage
Treatment of Encephalopathy

- Look for cause(s)
- Avoid precipitants
- Lactulose
- Antibiotics
- Rifaximin
- probiotics

Precipitants of Encephalopathy

- Excess protein
- Alcohol
- GI bleeding
- Sedatives/Hypnotics
- Surgery
- TIPS
- HCC
- Diuretics
- Low serum K+
- Plasma volume
- Azotemia

AGA
HCC

- It tends to be asymptomatic until the tumor is in an advanced stage.
- Early detection of HCC is essential in improving the prognosis.
- 80% of patients with HCC have underlying cirrhosis
- Surveillance = repeated application of screening tests (imaging study every 6 months – US/MRI)
- The goal of surveillance is to decrease the HCC mortality.

Approach for Patients with Cirrhosis

- Identify liver disease and cirrhosis early
- Treat the underlying liver disease to reverse cirrhosis or prevent progression if possible
- If disease cannot be controlled, monitor and treat cirrhotic complications
- Survey for liver cancer every 6 months
- Identify patients for liver transplantation early (Child-Pugh B and MELD > 15)