Screening for alcoholic liver disease

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Portsmouth Hospitals NHS Trust
Alcohol related hospital admissions in the South East region, 2007-08
age standardised rate per 100,000 population, UA and CC

<table>
<thead>
<tr>
<th>Area</th>
<th>Rate per 100,000 pop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isle of Wight UA</td>
<td>640</td>
</tr>
<tr>
<td>Wokingham UA</td>
<td>840</td>
</tr>
<tr>
<td>West Berkshire UA</td>
<td>888</td>
</tr>
<tr>
<td>Buckinghamshire CC</td>
<td>896</td>
</tr>
<tr>
<td>Oxfordshire CC</td>
<td>934</td>
</tr>
<tr>
<td>Windsor &amp; Maidenhead UA</td>
<td>1031</td>
</tr>
<tr>
<td>Hampshire CC</td>
<td>1044</td>
</tr>
<tr>
<td>Southampton UA</td>
<td>1055</td>
</tr>
<tr>
<td>Bracknell Forest UA</td>
<td>1108</td>
</tr>
<tr>
<td>Surrey CC</td>
<td>1123</td>
</tr>
<tr>
<td>Kent CC</td>
<td>1209</td>
</tr>
<tr>
<td>Reading UA</td>
<td>1231</td>
</tr>
<tr>
<td>West Sussex CC</td>
<td>1272</td>
</tr>
<tr>
<td>Medway UA</td>
<td>1378</td>
</tr>
<tr>
<td>East Sussex CC</td>
<td>1454</td>
</tr>
<tr>
<td>Milton Keynes UA</td>
<td>1478</td>
</tr>
<tr>
<td>Slough UA</td>
<td>1512</td>
</tr>
<tr>
<td>Brighton &amp; Hove UA</td>
<td>1709</td>
</tr>
<tr>
<td>Portsmouth UA</td>
<td>1794</td>
</tr>
</tbody>
</table>

South East (1161)
England (1473)

Source: DH / Association of Public Health Observatories, Local Alcohol Profiles for England.
The majority of our alcohol-related admissions are for chronic complications such as cirrhosis.
Liver deaths in Portsmouth 1993-2008

Mortality rate for chronic liver disease including cirrhosis (ICD10 K70, K73-K74) for persons Portsmouth, England and South East England, 1993 to 2008
Source: NCHOD. Compendium of Clinical and Health Indicators

Linear trend equation: $y = 0.4344x + 7.3905$
Alcoholic Liver Disease (ALD)

Healthy Liver → Alcohol → Alcoholic Fatty Liver Fibrosis / Hepatitis → Alcohol → Liver Cirrhosis → Alcohol → HCC

90-100% of alcoholics reveal steatosis
10-35% show signs of alcoholic fibrosis / hepatitis
10% develop cirrhosis

Only a minority of heavy drinkers develop severe liver disease!
Pathogenesis of alcoholic liver injury
Clustering of risk factors for liver cirrhosis

- Poor socio-economic status
- Alcohol misuse
- Obesity
- Chronic viral hepatitis – esp HCV
Determinants of health

Public health: The social gradient

Influence of obesity and alcohol intake on deaths from liver disease in Scotland

Hart CL et al. BMJ 2010

Alcohol > 15 units / week    BMI > 30
Scottish Midspan cohort study of 9559 men from 1965-1987

Hart CL et al. BMJ 2010
Alcohol + Hepatitis C = More cirrhosis
Liver fibrosis: Alcohol is different to other aetiologies

- Fibrosis in alcoholic liver disease is more *dynamic* than in other liver disorders
- Fibrosis in ALD is more affected by individual factors
  - Age, gender, type / quantity of drinking
  - Genetic variation
- Alcohol withdrawal usually leads to rapid clinical improvement but not to rapid fibrosis regression
Options for Liver fibrosis assessment

- Liver Biopsy
- Serum Biomarkers
- FibroScan
What does a liver biopsy add?

- Diagnosis – but cannot distinguish ALD from NAFLD/NASH
- Staging – eg acute alcoholic steatohepatitis versus decompensated cirrhosis
- Prognostic information
  - But functional tests are better – Child’s-Pugh, MELD, HVPG, etc
- Diagnosis of cirrhosis to implement screening for HCC, varices, etc
  - Probably the major indication in 2012
Clinical suspicion for advanced fibrosis

Low
- Preserved synthetic function
- Normal physical exam
- Short duration of disease
- Normal imaging

Intermediate
- Increased INR, low platelets
- Stigmata of liver disease
- Long disease duration
- Splenomegaly/irregular liver

High
- Non-invasive
  - Serum assay of hepatic fibrosis/Fibroscan/combo
- No biopsy
  - Confirm with either serum assay of hepatic fibrosis/Fibroscan/combo

Indeterminate
- Early disease
  - Serial testing every 6-12 months
- Liver biopsy

Cirrhosis apparent
- Screen for varices and hepatocellular carcinoma

Figure 3: Use of biomarkers for staging of liver fibrosis and diagnosis of cirrhosis

Schuppan, Afdhal
Lancet 2009
# Accuracy of non-invasive fibrosis markers in 541 NAFLD patients

<table>
<thead>
<tr>
<th>Test</th>
<th>AUROC</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fib-4</td>
<td>0.802</td>
<td>0.75-0.84</td>
</tr>
<tr>
<td>Angulo</td>
<td>0.768</td>
<td>0.72-0.82</td>
</tr>
<tr>
<td>AST:ALT</td>
<td>0.742</td>
<td>0.69-0.79</td>
</tr>
<tr>
<td>APRI</td>
<td>0.730</td>
<td>0.68-0.77</td>
</tr>
<tr>
<td>AST:Plts</td>
<td>0.720</td>
<td>0.67-0.77</td>
</tr>
</tbody>
</table>

FIB4 $\geq 2.67$ gives 80% positive predictive value
FIB4 $\leq 1.30$ gives 90% negative predictive value

Non-invasive serum markers

- Can be cheap
- Acceptable to patients
- Most accurate at predicting no or minimal fibrosis
- Less accurate in intermediate range
- Less accurate in ALD versus other dis
- Influenced by active inflammation
Transient elastography (TE) - Fibroscan

Transient elastography: principles

Normal liver (soft)  Cirrhosis (stiff)

Factors affecting liver stiffness

- fibrosis
- inflammation
- cholestasis
- Venous pressure
- else

Liver stiffness

F4 cut-off values are higher in ALD as compared to viral hepatitis

<table>
<thead>
<tr>
<th>disease</th>
<th>n</th>
<th>AUROC F4</th>
<th>Cut-off F4</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>193</td>
<td>0.95</td>
<td>12.5</td>
<td>Castera et al, 2005</td>
</tr>
<tr>
<td>HBV</td>
<td>202</td>
<td>0.93</td>
<td>11.0</td>
<td>Marcellin P et al, 2009</td>
</tr>
<tr>
<td>ALD</td>
<td>103</td>
<td>0.92</td>
<td>19.5</td>
<td>Nguyen-Khac E et al, 2008</td>
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<tr>
<td>ALD</td>
<td>45</td>
<td>0.97</td>
<td>25.8</td>
<td>Kim SG et al, 2009</td>
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<tr>
<td>ALD</td>
<td>101</td>
<td>0.92</td>
<td>11.5</td>
<td>Mueller S et al, 2010</td>
</tr>
</tbody>
</table>

LS rapidly decreases during alcohol detoxification

Screening for alcoholic liver disease - summary

• Higher risk groups
  – Drinking patterns
  – Obesity
  – Comorbidities eg HCV

• Clues from blood tests

• FibroScan potentially useful – *after detox*