NON INVASIVE ASSESSMENT OF LIVER FIBROSIS : FIBROSCAN

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ASSESSMENT OF FIBROSIS: WHY?

Management of individual patients
- Significant fibrosis → Treatment
- Cirrhosis → Screening for varices and HCC

Screening for cirrhosis or extensive fibrosis
- In high risk patients
- In the general population

Evaluation of treatments
- Antiviral and antifibrotic drugs
ELASTOMETRY (FIBROSCAN)

HOW TO MEASURE ELASTICITY?

Generate an elastic
Shear wave
Measure its speed $V_s$
Elasticity
$E \propto V_s^2$
Volume of exploration > 3 cm$^3$
INTER OBSERVER REPRODUCTIBILITY OF LSM

Fraquelli et al, Gut 2007
PATIENTS WITH HCV CHRONIC HEPATITIS

327 HCV + patients with no ascites

23 patients excluded: unreliable stiffness measurement; success rate less than 60% upon 10 measurements

53 patients excluded: biopsy not suitable for fibrosis stage assessment; less than 10 portal tracts in the absence of cirrhosis

251 patients included

Small biopsy 126 patients

Large biopsy 125 patients
BOX PLOTS. N=251

Stiffness (kPa) (logarithmic scale)

Elasticity (kPa)

Fibrosis stage (METAVIR)

Legend

- maximum
- median
- IQR
- minimum
ROC CURVES

AUROC

( CONFIDENCE INTERVALS 95%)

- $F \geq 2 : 0.79 (0.73-0.84)$
- $F \geq 3 : 0.91 (0.87-0.96)$
- $F = 4 : 0.97 (0.93-1.00)$
### Univariate analysis (Kendall’s coefficient)

<table>
<thead>
<tr>
<th></th>
<th>Fibrosis</th>
<th>Activity</th>
<th>Steatosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stiffness</td>
<td>$r$ 0.55</td>
<td>0.21</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>$p$ &lt;0.0001</td>
<td>0.0003</td>
<td>0.0008</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>$r$ -</td>
<td>0.36</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>$p$ -</td>
<td>&lt;0.0001</td>
<td>0.008</td>
</tr>
</tbody>
</table>

### Multivariate analysis (multiple regression)

Only fibrosis was significantly correlated to liver stiffness measurement.
VALIDATION OF DIAGNOSIS ACCURACY IN AN INDEPENDENT HCV POPULATION

Total number of included patients: 639
Number of unreliable liver samples: 86 (13%)
Number of unreliable LSM: 59 (9%)
Patients kept for statistical analysis: 494

<table>
<thead>
<tr>
<th>METAVIR</th>
<th>F</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>6</td>
<td>39</td>
<td>31</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td></td>
<td>6</td>
<td>56</td>
<td>35</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Steatosis</td>
<td></td>
<td>4</td>
<td>27</td>
<td>15</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

Area under ROC curves (95% confidence interval)
- F01 versus F234 = 0.84 (0.80-0.87)
- F012 versus F34 = 0.93 (0.90-0.95)
- F0123 versus F4 = 0.96 (0.94-0.98)

Univariate Spearman correlation
- METAVIR F: 0.70 (p << 0.001)
- METAVIR A: 0.45 (p << 0.001)
- Steatosis: 0.35 (p << 0.001)
LIVER BIOPSIES > 30 mm

- 103 Patients

Causes:

71 VHC
14 VHB
15 VHC+HIV
2 VHB+HIV
1 VHC+VHB

- Results

<table>
<thead>
<tr>
<th>Fibrosis Score:</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
</tr>
<tr>
<td>-----</td>
</tr>
<tr>
<td>N</td>
</tr>
</tbody>
</table>

≥ F2 ≥ F3 = F4

AUROC 0.94 0.95 0.93
The optimum thresholds were chosen to maximize the sum of sensitivity and specificity.

<table>
<thead>
<tr>
<th>Threshold (kPa)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>F ≥ 2</td>
<td>8.7</td>
<td>0.55</td>
<td>0.84</td>
</tr>
<tr>
<td>F ≥ 3</td>
<td>9.6</td>
<td>0.84</td>
<td>0.85</td>
</tr>
<tr>
<td>F = 4</td>
<td>14.5</td>
<td>0.84</td>
<td>0.94</td>
</tr>
</tbody>
</table>

* Obtained by the jack-knife method.
FIBROSCAN IN HBV PATIENTS

202 patients
- 15 non interpretable biopsies
- 14 LSM considered as non reliable
Statistical analysis on 173 patients

AUROC
F01 versus F234: 0.81 (0.73-0.86)
F012 versus F34: 0.93 (0.88-0.96)
F0.123 versus F4: 0.93 (0.82-0.98)
### Concordance with Liver Biopsy

#### AUROC

<table>
<thead>
<tr>
<th></th>
<th>F01/F234</th>
<th>F012/F34</th>
<th>F0123/F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>APRI</td>
<td>0.78</td>
<td>0.84</td>
<td>0.83</td>
</tr>
<tr>
<td>FibroTest</td>
<td>0.85</td>
<td>0.90</td>
<td>0.87</td>
</tr>
<tr>
<td>FibroScan</td>
<td>0.83</td>
<td>0.90</td>
<td>0.95</td>
</tr>
<tr>
<td>Combinaison</td>
<td>0.88</td>
<td>0.95</td>
<td>0.95</td>
</tr>
<tr>
<td>FibroTest+FibroScan</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Percentage of concording results

<table>
<thead>
<tr>
<th></th>
<th>F01/F234</th>
<th>F0123/F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>FibroTest</td>
<td>80</td>
<td>81</td>
</tr>
<tr>
<td>FibroScan</td>
<td>73</td>
<td>83</td>
</tr>
<tr>
<td>Combinaison</td>
<td>84</td>
<td>95</td>
</tr>
<tr>
<td>FibroTest+FibroScan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIBROSCAN   /    BLOOD TESTS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical parameter</td>
<td>Many biological parameters</td>
<td></td>
</tr>
<tr>
<td>directly linked to fibrosis</td>
<td>not directly related to fibrosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>and prone to the influence of</td>
<td></td>
</tr>
<tr>
<td></td>
<td>extra hepatic conditions</td>
<td></td>
</tr>
<tr>
<td>One single device</td>
<td>Dozens of predictive tests</td>
<td></td>
</tr>
</tbody>
</table>
FIBROSIS ≠ FIBROSIS STAGE
Acute HDV hepatitis

Sarcoïdosis

Alcoholic cirrhosis

Normal liver
Chronic hepatitis $\rho=0.50; p<0.0001$

Cirrhosis $\rho=0.43; p=0.005$

Steatohepatitis $\rho=0.22; p=0.16$

All patients $\rho=0.60; p<0.0001$

Figure 2
SCREENING IN HIGH RISK PATIENTS

227 patients in alcoholic abstinence program

Blood tests

LSM

LSM > 13 kPa

Suspected cirrhosis

LB

Absence of cirrhosis

Confirmation of cirrhosis

41

34

33
CONCLUSION

1) In patients with chronic liver disease LSM reflects the amount of liver fibrosis.

2) It has particularly good performances for the diagnosis of cirrhosis.

3) Fibroscan might be a reliable screening tool for the diagnosis of cirrhosis in high risk groups or even in the general population.
**FUTURE**

**Improvements to come**
- Improvement in software
- New probes for obese patients and also for children (or patients with small intercostal spaces)

**Future developments**
- 1 D measurements
- 2 D imaging