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

Evaluation of treatments
- Antiviral and antifibrotic drugs
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$^3$
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**

**Legend**
- **maximum**
- **median**
- **IQR**
- **minimum**

**Stiffness (kPa) (logarithmic scale)**

**Elasticity (kPa)**

**Fibrosis stage (METAVIR)**

- F01
- F2
- F3
- F4
ROC CURVES

AUROC
( CONFIDENCE INTERVALS 95%)

- F≥2 : 0.79 (0.73-0.84)
- F≥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><strong>Stiffness</strong></td>
<td>$r$</td>
<td>0.55</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>$p$</td>
<td>&lt;0.0001</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>Fibrosis</strong></td>
<td>$r$</td>
<td>-</td>
<td>0.36</td>
</tr>
<tr>
<td></td>
<td>$p$</td>
<td>-</td>
<td>&lt;0.0001</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

Univariate Spearman correlation
METAVIR F: 0.70 (p << 0.001)
METAVIR A: 0.45 (p << 0.001)
Steatosis: 0.35 (p << 0.001)

Univariate Spearman correlation
METAVIR F: 0.70 (p << 0.001)
METAVIR A: 0.45 (p << 0.001)
Steatosis: 0.35 (p << 0.001)

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)
- **103 Patients**

**Causes:**
- 71 VHC
- 14 VHB
- 15 VHC+HIV
- 2 VHB+HIV
- 1 VHC+VHB

**Results**

- **Fibrosis Score:**

<table>
<thead>
<tr>
<th></th>
<th>F0</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>9</td>
<td>58</td>
<td>14</td>
<td>7</td>
<td>15</td>
</tr>
</tbody>
</table>

- **AUROC:**

<table>
<thead>
<tr>
<th>≥ F2</th>
<th>≥ F3</th>
<th>= F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.94</td>
<td>0.95</td>
<td>0.93</td>
</tr>
</tbody>
</table>
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>$F \geq 2$</td>
<td>8.7</td>
<td>0.55</td>
<td>0.84</td>
</tr>
<tr>
<td>$F \geq 3$</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.
FIBROSIS AREA (morphometry)

- **Patients**

69 patients with chronic hepatitis C
without ascites, and previous anti-viral treatment

<table>
<thead>
<tr>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>21</td>
<td>5</td>
<td>23</td>
</tr>
</tbody>
</table>

- **Results**

Spearman correlation test

\[ r < 0.001 \]

<table>
<thead>
<tr>
<th>Parameters</th>
<th>( r )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis area METAVIR score</td>
<td>0.66</td>
</tr>
<tr>
<td>Elasticity METAVIR score</td>
<td>0.65</td>
</tr>
<tr>
<td>Elasticity fibrosis area</td>
<td>0.74</td>
</tr>
</tbody>
</table>

\( \Rightarrow \) Liver elasticity is closely correlated to fibrosis area.
FIBROSCAN VERSUS BLOOD TESTS

FibroScan

FibroTest

APRI

Castera Al. Gastroenterology 2005
## 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>
</tbody>
</table>
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)
FIBROSCAN PROS AND CONS

**PROS**
- easy, quick, not too costly
- very specific for extensive fibrosis or cirrhosis
- Allows to split patients between 3 groups
  . Without significant fibrosis
  . With extensive fibrosis or cirrhosis
  . Intermediate
- closely related to the area of fibrosis in patients with chronic hepatitis

**CONS**
- high rate of failure in obese patients
SCREENING IN HIGH RISK PATIENTS

227 patients in alcoholic abstinence program

Blood tests

LSM

LSM > 13 kPa

yes

Suspected cirrhosis

41

no

Absence of cirrhosis

LB

Confirmation of cirrhosis

34

33
**FOLLOW-UP OF LSM IN TREATED PATIENTS WITH CHRONIC HEPATITIS C**

<table>
<thead>
<tr>
<th></th>
<th>BEFORE TREATMENT</th>
<th>END OF TREATMENT</th>
<th>6 MONTHS AFTER</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=85)</td>
<td>14.1 ± 7.2</td>
<td>10.9 ± 6.5</td>
<td>11.2 ± 8.6</td>
</tr>
<tr>
<td>SVR</td>
<td>12.0 ± 6.7</td>
<td>9.1 ± 3.7</td>
<td>7.5 ± 2.4</td>
</tr>
<tr>
<td>RR</td>
<td>14.6 ± 5.6</td>
<td>11.5 ± 5.0</td>
<td>12.8 ± 7.2</td>
</tr>
<tr>
<td>NR</td>
<td>16.9 ± 8.1</td>
<td>13.3 ± 9.1</td>
<td>16.1 ± 12.2</td>
</tr>
</tbody>
</table>

**6 MONTHS AFTER TREATMENT**

**END OF TREATMENT**

**BEFORE TREATMENT**
CONCLUSION

1) In patients with chronic liver diseases LSM by fibroscan reflects fibrosis stage.

2) Fibroscan is a reliable screening tool for extensive fibrosis or cirrhosis in high risk groups.

3) Fibroscan might allow to assess the influence of treatments on liver fibrosis.