IMPACT OF FIBROSCAN (VCTE) IN ASSESSMENT AND THERAPY OF CHRONIC LIVER DISEASES

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Liver fibrosis is a common manifestation of chronic liver diseases.

The most severe form of liver fibrosis, cirrhosis, is associated with increased morbidity and mortality.
LIVER BIOPSY

- Best available method for assessing liver fibrosis
- Not a «gold standard»
- Represents only 1/50 000 of hepatic parenchyma
- Sampling error
- Intra-and inter-observer variability
- Risk of bleeding, pneumothorax, haemobilia
- Mortality rate ~ 0.01%
- Cost, one day hospitalization
Non-invasive methods for the assessment of liver fibrosis

- "Biological approach"
  - Serum biomarkers
    - Fibro test
    - Fibro meter
    - APRI
    - F4
    - ELF
    - NAFLD fibrosis score

- "Physical approach"
  - Measuring liver stiffness
  - Sono-elastography
    - Vibration-controlled transient elastography (Fibroscan)
    - ARFI (acoustic radiation force impulse)
  - Magnetic elastography
TRANSIENT ELASTOGRAPHY
FIBROSCAN

FIBROSCAN, Echosens, Paris, France
Vibration-Controlled Transient Elastography (VCTE™) FIBROSCAN

- Fibroscan® is the only device based on VCTE™
- Echosens®, December 2003
- It is the first device clinically validated for the assessment of liver fibrosis
- 1-dimensional ultrasound transient elastography
- A vibrator generates a low frequency elastic shear wave (50 Hz) that propagates through liver tissue
- The velocity is directly related to tissue stiffness
The tip of the probe acts both as:
- a shear wave generator
- and an ultrasonic transducer.

The transducer emits and receives ultrasounds.

The vibrator generates the shear elastic wave.

Position of probe & explored volume

Cylinder of 1 cm wide & 4 cm long
From 25 mm to 65 mm below skin surface
This volume is at least 100 times bigger than a biopsy sample.
The results are expressed in kilopascals (kPa). They represent the median of 10 measurements and have a range from 2.5 to 75 kPa. Normal values of 3-6 kPa.
FIBROSCAN IN CLINICAL PRACTICE

- Painless
- Rapid (5 min)
- Bedside/Outpatient
- Immediate results
- Short training (100 exam.)
CONTRAINDICATIONS

- Ascites
- Pacemaker
- Pregnancy

LIMITATIONS

- Obesity
- Increased CVP
- Increases in ALT
  - acute hepatitis
  - HBV flares
MANUFACTURER’S QUALITATIVE CRITERIA

- Success rate > 60%
- IQR (interquartile range) < 30% of median
- Applicability 80%
- Failure rate 3%, unreliable results 16%
  - Western countries: obesity, fatty thoracic pad
  - Eastern countries: narrow intercostal spaces
- Reproducibility, accuracy
- Intra-operator, inter-operator standardized coefficient of variation 3.2% and 3.3% respectively
Area Under the ROC Curve, AUROC

- Area of 1 represents a perfect test
- Area of .5 represents a worthless test
- A rough guide for classifying the accuracy of a diagnostic test:
  - .90-1 = excellent (A)
  - .80-.90 = good (B)
  - .70-.80 = fair (C)
  - .60-.70 = poor (D)
  - .50-.60 = fail (F)
NON INVASIVE SURROGATE FOR LB
CHRONIC HEPATITIS C

First prospective studies in patients with CHC

- 183 patients
- threshold of significant fibrosis 7.1
- AUROC 0.83
- sensitivity 67%, specificity 89%

Castera et al. Gastroenterology 2005

- 251 patients
- threshold of significant fibrosis 8.8
- AUROC 0.79
- sensitivity 56%, specificity 91%

Ziol et al. Hepatology 2005
CHRONIC HEPATITIS C

PPV: 77-78%
NPV: 95-97%

7.1 / 8.8 9.5 12.5 / 14.6

3  F2  F3  F4

75 KPa

Ziol et al. Hepatology 2005; 41: 48-54
CHRONIC HEPATITIS C

N = 251 CHC patients

N = 183 CHC patients

Ziol et al. Hepatology 2005; 41: 48-54
Perform LSM

≤ 6 kPa
- No significant fibrosis
- F0
- No biopsy

≥ 12 kPa
- Advanced fibrosis
- F3
- F4
- No biopsy

Intermediate values
- Grey area
- F2
- Biopsy if results influence management
- Implementation of other NI tests
The effect of using non-invasive markers of fibrosis in the frequency of liver biopsy in chronic hepatitis C in France

Castera et al. J Hepatol 2007; 46: 528-9
“Cost and time savings from a rapid access model of care using transient elastography to screen and triage patients with chronic hepatitis C infection”

- “Rapid access to assessment and treatment “ (RAAT) model of care
- TE as part of RAAT for assessment of patients with chronic HCV in comparison to conventional management with LB
- RAAT had lower costs, shorter time to Rx
  - AU$ 2716, 194 days vs $ 5005, median= 420 days (p < 0.01)
- Based on real world audit data, TE as part of a new model of care, is cost saving to the health system and reduces waiting times.

Whitty LA et al. J Med Econ 2014
Chronic hepatitis C
EASL Clinical Practice Guidelines

- **Liver biopsy** still regarded as reference method to assess grade of inflammation & stage of fibrosis (A2)
- **TE** can be used to assess liver fibrosis in CHC (A2)
- Non-invasive **serum makers** can be recommended for detection of significant fibrosis (METAVIR F2 – F4) (A2)
- **Combination of blood tests or TE & blood test**
  Improve accuracy & reduce necessity of liver biopsy (C2)

EASL Clinical Practice Guidelines: Management of hepatitis C virus infection.
CIRRHOSIS

12.5 / 14.6

3

F4

75 KPa

Ziol et al. Hepatology 2005; 41: 48-54
COMPLICATIONS OF CIRRHOSIS

- 711 patients with liver diseases
- F3F4 144

Cumulative incidence of HCC based on LSM

866 CHC – Mean follow-up 3 years

LSM > 25 kPa   HR 45.5 (p < 0.001)
20 < LSM ≤ 25 kPa  HR 25.6 (p < 0.001)
15 < LSM ≤ 20 kPa  HR 20.9 (p < 0.001)
10 < LSM ≤ 15 kPa  HR 16.7 (p < 0.001)
LSM ≤ 10 kPa    HR 0

LSM: Liver Stiffness Measurement – HR: Hazard Ratio
CHRONIC HEPATITIS B

- Many clinical studies for CHB
- No difference in diagnostic accuracy between CHC, CHB
- More accurately detects cirrhosis than significant fibrosis
  - AUROC 0.85-0.97 vs 0.65-0.97
- Data confirmed in several meta-analyses
CHRONIC HEPATITIS B
Meta-analysis

Table 1. Characteristics of studies evaluating the performance of transient elastography for staging liver fibrosis.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Patients (n)</th>
<th>Final sample size (n)</th>
<th>Failure LSM (reason)</th>
<th>LB (reason)</th>
<th>Male (%)</th>
<th>Mean BMI (kg/m²)</th>
<th>Etiology of disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan</td>
<td>2009</td>
<td>China</td>
<td>186</td>
<td>161</td>
<td>1 (SR &lt; 60%, &lt; 10VM)</td>
<td>22 (&lt; 15mm, &lt; 6pt)</td>
<td>76.0</td>
<td>240</td>
<td>HBV</td>
</tr>
<tr>
<td>Marcellin</td>
<td>2009</td>
<td>France</td>
<td>203</td>
<td>173</td>
<td>14 (SR &lt; 50%, &lt; 7VM)</td>
<td>15 (&lt; 10pt)</td>
<td>66.5</td>
<td>245</td>
<td>HBV</td>
</tr>
<tr>
<td>Wong</td>
<td>2008</td>
<td>China</td>
<td>182</td>
<td>133</td>
<td>10 (SR &lt; 60%, &lt; 10VM, IQR/M &lt; 0.3)</td>
<td>37 (&lt; 15mm, &lt; 6pt)</td>
<td>70.0</td>
<td>250</td>
<td>HBV, HCV, NAFLD, AIH, PBC</td>
</tr>
<tr>
<td>Kim</td>
<td>2010</td>
<td>Korea</td>
<td>235</td>
<td>200</td>
<td>5 (SR &lt; 60%, &lt; 10VM)</td>
<td>10 (&lt; 15mm)</td>
<td>71.5</td>
<td>234</td>
<td>HBV</td>
</tr>
<tr>
<td>Wang</td>
<td>2009</td>
<td>China</td>
<td>364</td>
<td>320</td>
<td>8 (SR &lt; 65%, &lt; 10VM)</td>
<td>36 (&lt; 10mm)</td>
<td>62.2</td>
<td>244</td>
<td>HBV, HCV</td>
</tr>
<tr>
<td>Kim</td>
<td>2009</td>
<td>Korea</td>
<td>194</td>
<td>91</td>
<td>0 (SR &lt; 60%, &lt; 8VM)</td>
<td>4 (&lt; 10mm, &lt; 10pt)</td>
<td>80.2</td>
<td>238</td>
<td>HBV</td>
</tr>
<tr>
<td>Kim</td>
<td>2009</td>
<td>Korea</td>
<td>130</td>
<td>130</td>
<td>0 (SR &lt; 60%, &lt; 10VM)</td>
<td>0 (&lt; 10mm, &lt; 6pt)</td>
<td>79.2</td>
<td>253</td>
<td>HBV</td>
</tr>
<tr>
<td>Sporea</td>
<td>2010</td>
<td>Italy</td>
<td>140</td>
<td>140</td>
<td>0 (SR &lt; 60%, &lt; 10VM, IQR/M &lt; 0.3)</td>
<td>0 (N/A)</td>
<td>77.9</td>
<td>N/A</td>
<td>HBV, HCV</td>
</tr>
<tr>
<td>Jeon</td>
<td>2007</td>
<td>Korea</td>
<td>45</td>
<td>45</td>
<td>0 (N/A)</td>
<td>0 (N/A)</td>
<td>N/A</td>
<td>N/A</td>
<td>HBV, HCV</td>
</tr>
<tr>
<td>Chang</td>
<td>2007</td>
<td>Singapore</td>
<td>35</td>
<td>33</td>
<td>2 (obesity, narrow ICS)</td>
<td>0</td>
<td>N/A</td>
<td>256</td>
<td>HBV</td>
</tr>
<tr>
<td>Tawande</td>
<td>2008</td>
<td>Thailand</td>
<td>104</td>
<td>104</td>
<td>0 (N/A)</td>
<td>0 (N/A)</td>
<td>63.0</td>
<td>236</td>
<td>HBV</td>
</tr>
<tr>
<td>Choi</td>
<td>2008</td>
<td>Korea</td>
<td>48</td>
<td>48</td>
<td>0 (N/A)</td>
<td>0 (N/A)</td>
<td>58.3</td>
<td>233</td>
<td>HBV</td>
</tr>
<tr>
<td>Castera</td>
<td>2009</td>
<td>France</td>
<td>60</td>
<td>60</td>
<td>0 (N/A)</td>
<td>0 (N/A)</td>
<td>N/A</td>
<td>N/A</td>
<td>HBV</td>
</tr>
<tr>
<td>Chang</td>
<td>2009</td>
<td>Singapore</td>
<td>88</td>
<td>84</td>
<td>3 (N/A)</td>
<td>1 (N/A)</td>
<td>71.6</td>
<td>N/A</td>
<td>HBV</td>
</tr>
<tr>
<td>Jia</td>
<td>2010</td>
<td>China</td>
<td>486</td>
<td>486</td>
<td>0 (N/A)</td>
<td>0 (N/A)</td>
<td>N/A</td>
<td>220</td>
<td>HBV</td>
</tr>
<tr>
<td>Lesmana</td>
<td>2010</td>
<td>Indonesia</td>
<td>62</td>
<td>62</td>
<td>0 (N/A)</td>
<td>0 (N/A)</td>
<td>N/A</td>
<td>228</td>
<td>HBV</td>
</tr>
<tr>
<td>Chen</td>
<td>2011</td>
<td>China</td>
<td>389</td>
<td>315</td>
<td>0 (N/A)</td>
<td>0 (N/A)</td>
<td>N/A</td>
<td>N/A</td>
<td>HBV</td>
</tr>
<tr>
<td>Zhu</td>
<td>2011</td>
<td>China</td>
<td>178</td>
<td>175</td>
<td>0 (N/A)</td>
<td>0 (N/A)</td>
<td>N/A</td>
<td>N/A</td>
<td>HBV</td>
</tr>
</tbody>
</table>

LSM, liver stiffness measurement; LB, liver biopsy; BMI, body mass index; SR, success rate; VM, valid fibroscan measurement; IQR, interquartile range; M, median; ICS, intercostal space; HBV, hepatitis B virus; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease; AIH, autoimmune hepatitis; PBC, primary biliary cirrhosis.
doi:10.1371/journal.pone.0044930.t001

Chon et al. PLOS ONE 2012
## Table 3. Meta-analysis results of LSM cutoff values for staging liver fibrosis.

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Weighted Mean LSM value (kPa)</th>
<th>Range (kPa)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F ≥ 2</td>
<td>7.9</td>
<td>6.1–11.8</td>
<td>74.3</td>
<td>78.3</td>
</tr>
<tr>
<td>F ≥ 3</td>
<td>8.8</td>
<td>8.1–9.7</td>
<td>74.0</td>
<td>63.8</td>
</tr>
<tr>
<td>F = 4</td>
<td>11.7</td>
<td>7.3–17.5</td>
<td>84.6</td>
<td>81.5</td>
</tr>
</tbody>
</table>

LSM, liver stiffness measurement; kPa, kilopascal.
doi:10.1371/journal.pone.0044930.t003

## Table 4. Characteristics of previous reported meta-analyses versus current study.

<table>
<thead>
<tr>
<th>Number of included studies</th>
<th>Number of included subjects for analysis</th>
<th>AUROC</th>
<th>Sensitivity/Specificity (%)</th>
<th>Cutoff values (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>≥ F2</td>
<td>≥ F3</td>
<td>F4</td>
</tr>
<tr>
<td>Chon et al</td>
<td>18</td>
<td>0.859</td>
<td>0.887</td>
<td>0.929</td>
</tr>
</tbody>
</table>

AUROC, area under the receiver operating characteristic curve; kPa, kilopascal.
doi:10.1371/journal.pone.0044930.t004
“Long-term changes of liver stiffness values assessed using transient elastography in patients with chronic hepatitis B receiving entecavir”

- N=121, CHB, 3-year ETV treatment
- LSM values baseline vs completion of 3-year treatment
- Median baseline LSM was **14.3 kPa**
- Median value after 3-year ETV treatment was **7.3 kPa** (P < 0.001)
- Higher baseline LSM value was the single independent predictor of a significant decline in LS value on multivariate analysis (P<0.001)

Kim MN et al. Liver Int 2013
“Liver stiffness-based optimization of hepatocellular carcinoma risk score in patients with chronic hepatitis B”

- LSM-HCC score, prognostic model using TE to predict HCC
- N=1555, CHB referred for TE
- N=1035 training cohort and N=520 validation cohort
- 38 patients (3.7%) in the training cohort and 17 patients (3.4%) in the validation cohort developed HCC
- **LSM-HCC score**: LSM, age, serum albumin and HBV DNA
  - Range **0 to 30**
  - AUROC curves of LSM-HCC score 0.83–0.89
  - By applying the **cutoff value of 11**, the score excluded future HCC with **high negative predictive value** (99.4%–100%) at 5 years.

Grace Lai-Hung Wong et al. J Hepatol 2014
"Liver stiffness-based optimization of hepatocellular carcinoma risk score in patients with chronic hepatitis B"

Table 2: Factors associated with hepatocellular carcinoma in the training cohort.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Univariate</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio (95% CI)</td>
<td>p value</td>
</tr>
<tr>
<td>Age &gt; 50 yr</td>
<td>4.9 (2.4-10.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin ≤35 g/L</td>
<td>4.9 (1.1-15.9)</td>
<td>0.008</td>
</tr>
<tr>
<td>Total bilirubin &gt;18 μmol/L</td>
<td>0.7 (0.3-1.7)</td>
<td>0.47</td>
</tr>
<tr>
<td>HBV DNA categories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2000 IU/ml</td>
<td>1</td>
<td>0.91</td>
</tr>
<tr>
<td>2000-200,000 IU/ml</td>
<td>0.9 (0.3-2.8)</td>
<td>0.91</td>
</tr>
<tr>
<td>&gt;200,000 IU/ml</td>
<td>3.2 (1.2-8.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>LSM categories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤8.0 kPa</td>
<td>1</td>
<td>0.001</td>
</tr>
<tr>
<td>8.1-12.0 kPa</td>
<td>5.6 (2.3-13.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;12.0 kPa</td>
<td>10.9 (4.7-25.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3: Components of LSM-HCC score.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Score*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 50 yr</td>
<td>+10</td>
</tr>
<tr>
<td>≤50 yr</td>
<td>0</td>
</tr>
<tr>
<td>Albumin ≤35 g/L</td>
<td>+1</td>
</tr>
<tr>
<td>&gt;35 g/L</td>
<td>0</td>
</tr>
<tr>
<td>HBV DNA categories ≥2000 IU/ml</td>
<td>+5</td>
</tr>
<tr>
<td>≤2000 IU/ml</td>
<td>0</td>
</tr>
<tr>
<td>Liver stiffness measurement ≤8.0 kPa</td>
<td>0</td>
</tr>
<tr>
<td>8.1-12.0 kPa</td>
<td>+8</td>
</tr>
<tr>
<td>&gt;12.0 kPa</td>
<td>+14</td>
</tr>
</tbody>
</table>

*Total score ranges from 0 to 30. Scores of 0-10 and 11-30 indicate low and high risk, respectively.

Fig. 2. The 3-year and 5-year incidences of HCC in different strata of LSM-HCC score. (A) Training cohort; (B) validation cohort.
NON ALCOHOLIC FATTY LIVER DISEASE

- Many clinical studies to evaluate TE in predicting fibrosis stage
- Applicability issues, failure or unreliable results due to obesity
- Possible underestimation of the histological fibrosis stage, as hepatic steatosis may attenuate the elastic shear wave
- TE can be useful to select patients for liver biopsy
“Diagnosis of Fibrosis and Cirrhosis Using Liver Stiffness Measurement in Nonalcoholic Fatty Liver Disease”

- N=246 patients
  - AUROC for F3 ≥ 0.93 and F4 0.95
  - 7.9 kPa
    - (SE, SPE, NPV, PPV for F3≥ 91%, 75%, 52%, and 97%)
    - LSM not affected by steatosis, necroinflammation, or BMI
    - Discordance of at least two stages between transient elastography and histology 33 (13.4%) due to liver biopsy length and F 0-2 disease

- Transient elastography is accurate in most NAFLD patients

HEPATOLOGY 2010;51:454-462
Diagnosis of Fibrosis and Cirrhosis Using Liver Stiffness Measurement in Nonalcoholic Fatty Liver Disease

- AUROC for F3 ≥ 0.93 and F4 0.95
- Because high NPV and modest PPV, TE is useful as a screening test to exclude advanced fibrosis
- Liver biopsy may be considered in NAFLD patients with liver stiffness of at least 7.9 kPa
PBC AND PSC

Diagnostic performance of TE in chronic cholestatic diseases

- Prospective study, TE and LB
- PBC=73, PSC=28
- LSM range from 2.8-69.1 kPa (median 7.8 kPa)
- Significant correlation with fibrosis and histological stage
  Corpechot, Hepatology 2006

- N= 55 pt with TE and LB
- Statistically significant correlation of fibrosis stage and LSM
- AUROC 0.89  F>2, 0.96  F=4

Gomez -Dominguez, APT 2008
Noninvasive evaluation of liver fibrosis stage and disease progression in PBC with TE

- Diagnostic cohort, n=103 pt
- Monitoring cohort, n=150 pt
- Follow up for up to 5 y
- Rx UDCA

Corpechot C, Hepatology 2012
Table 2. Performance Profile of TE in Differentiating Liver Fibrosis Stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>No.</th>
<th>Cutoff</th>
<th>Se</th>
<th>Sp</th>
<th>PPV</th>
<th>NPV</th>
<th>PLR</th>
<th>NLR</th>
<th>ACC</th>
<th>AuROC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>7.1 ± 0.3</td>
<td>0.64 ± 0.07</td>
<td>1.00 ± 0.00</td>
<td>0.25 ± 0.00</td>
<td>+∞</td>
<td>0.36 ± 0.00</td>
<td>0.68 ± 0.00</td>
<td>0.80 ± 0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8.8 ± 0.9</td>
<td>0.67 ± 0.08</td>
<td>1.00 ± 0.00</td>
<td>0.75 ± 0.00</td>
<td>4.41</td>
<td>0.17 ± 0.00</td>
<td>0.84 ± 0.00</td>
<td>0.91 ± 0.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10.7</td>
<td>0.90 ± 0.08</td>
<td>0.84 ± 0.00</td>
<td>0.96 ± 0.00</td>
<td>13.14</td>
<td>0.11 ± 0.00</td>
<td>0.92 ± 0.00</td>
<td>0.95 ± 0.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>16.9</td>
<td>0.93 ± 0.00</td>
<td>0.93 ± 0.00</td>
<td>0.99 ± 0.00</td>
<td>82.13</td>
<td>0.07 ± 0.00</td>
<td>0.98 ± 0.00</td>
<td>0.99 ± 0.00</td>
</tr>
</tbody>
</table>

Bootstrap statistic

<table>
<thead>
<tr>
<th>Stage</th>
<th>No.</th>
<th>Cutoff</th>
<th>Se</th>
<th>Sp</th>
<th>PPV</th>
<th>NPV</th>
<th>PLR</th>
<th>NLR</th>
<th>ACC</th>
<th>AuROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥F1</td>
<td>9,219</td>
<td>7.1 ± 0.3</td>
<td>0.67 ± 0.04</td>
<td>0.99 ± 0.03</td>
<td>1.00 ± 0.00</td>
<td>0.26 ± 0.00</td>
<td>+∞</td>
<td>0.34 ± 0.03</td>
<td>0.70 ± 0.06</td>
<td>0.80 ± 0.05</td>
</tr>
<tr>
<td></td>
<td>(5.9-7.5)</td>
<td>(0.54-0.84)</td>
<td>(0.88-1.00)</td>
<td>(0.99-1.00)</td>
<td>(0.15-0.39)</td>
<td>(0.18-0.46)</td>
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<td>≥F2</td>
<td>5,225</td>
<td>8.7 ± 0.9</td>
<td>0.78 ± 0.08</td>
<td>0.93 ± 0.07</td>
<td>0.93 ± 0.07</td>
<td>0.81 ± 0.07</td>
<td>12.1 ± 10.4</td>
<td>0.23 ± 0.03</td>
<td>0.86 ± 0.04</td>
<td>0.91 ± 0.03</td>
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<td>(7.9-9.8)</td>
<td>(0.61-0.94)</td>
<td>(0.77-1.00)</td>
<td>(0.78-1.00)</td>
<td>(0.67-0.93)</td>
<td>(3.7-13.3)</td>
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<td>≥F3</td>
<td>3,002</td>
<td>10.9 ± 0.8</td>
<td>0.90 ± 0.06</td>
<td>0.93 ± 0.04</td>
<td>0.85 ± 0.07</td>
<td>0.96 ± 0.02</td>
<td>16.5 ± 9.1</td>
<td>0.10 ± 0.03</td>
<td>0.92 ± 0.03</td>
<td>0.95 ± 0.02</td>
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<td>(10.7-11.5)</td>
<td>(0.79-1.00)</td>
<td>(0.86-0.98)</td>
<td>(0.71-0.94)</td>
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<td>(6.0-34.5)</td>
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<td>≥F4</td>
<td>1,492</td>
<td>16.1 ± 1.8</td>
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<td>0.96 ± 0.04</td>
<td>0.82 ± 0.16</td>
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<td>(0.00-0.07)</td>
<td>(0.90-1.00)</td>
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Cutoffs are expressed in kPa and bootstrap estimates as mean ± SD (95% CI).

Abbreviations: Se, sensitivity; Sp, specificity.
Noninvasive Elastography-Based Assessment of Liver Fibrosis Progression and Prognosis in Primary Biliary Cirrhosis

Fig. 3. Time course of LSM as observed from the whole individual data (A) or estimated by the four-stage model as a function of baseline fibrosis stage (B). In (B), trends in liver stiffness progression are shown as linear regression straight lines (black lines) with 95% CIs (gray areas).
PORTAL HYPERTENSION

TE in predicting clinically significant portal hypertension

- N=61, CHC, METAVIR F3-F4
- Strong correlation of TE and HVPG, $r = 0.81$, $p < 0.0003$
  - **BUT**
    - HVPG < 10 mmHg, $r = 0.81$
    - HVPG $\geq 10$ mmHg, $r = 0.35$
    - HVPG $\geq 12$ mmHg, $r = 0.17$
- Not good for prognosis and classification of oesophageal varices
- Pathophysiology of portal hypertension involves not only fibrosis but also other complicated hemodynamic mechanisms

Vizzutti, Hepatology 2007
PORTAL HYPERTENSION

Garcia-Samaniego and Forns, Hepatology 2007

Vizzutti F et al, Hepatology 2007
“Non invasive evaluation of portal hypertension using transient elastography”

- HVPG and upper GI endoscopy are considered the gold standards for portal hypertension assessment in patients with cirrhosis.
- Need for non invasive methods able to predict:
  - portal hypertension clinically significant, i.e. HVPG P10 mmHg
  - portal hypertension clinically severe, HVPG P12 mmHg
  - presence and size of oesophageal varices
- TE has a good correlation with liver stiffness and HVPG as well as the presence of oesophageal varices,
- Diagnostic performance of TE is acceptable in prediction of clinically significant portal hypertension.
- Not satisfactory to predict the presence of OV and screen cirrhotic without endoscopy.

Castera L et al. J Hepatol 2012
“Non invasive evaluation of portal hypertension using transient elastography”

<table>
<thead>
<tr>
<th>Authors, [Ref.]</th>
<th>Patients (n)</th>
<th>Etiologies</th>
<th>Study design</th>
<th>Prevalence of clinically significant portal hypertension (%)</th>
<th>Cut-offs HVPG ≥10 mmHg (kPa)</th>
<th>AUC</th>
<th>Se (%)</th>
<th>Sp (%)</th>
<th>PPV (%)</th>
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*Hepatic venous pressure gradient (HVPG) ≥6 mm Hg; **severe portal hypertension HVPG ≥12 mm Hg.

AUC, area under ROC curve; Se, sensitivity; Sp, specificity; +LR, positive likelihood ratio; –LR, negative likelihood ratio; HCV, chronic hepatitis C; HCV-LT, liver transplant for hepatitis C; CLD, chronic liver diseases; Pro. mono., prospective monocentric; Retro. mono., retrospective monocentric.

Castera L et al. J Hepatol 2012
“Non invasive evaluation of portal hypertension using transient elastography”

<table>
<thead>
<tr>
<th>Authors, [Ref.]</th>
<th>Patients (n)</th>
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<th>Child-Pugh A (%)</th>
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<th>Saved endoscopy (%)</th>
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*CROV: clinically relevant OV requiring primary prophylaxis of bleeding, i.e. patients carrying LOV or OV with red signs or Child-Pugh class C.

CLD, chronic liver diseases; HCV, chronic hepatitis C; HIV-HCV, co-infection with human deficiency virus and hepatitis C virus; HBV, hepatitis B virus; AUC, area under ROC curve; Se, sensitivity; Sp, specificity; PPV & NPV, positive and negative predictive values; +LR & -LR, positive and negative likelihood ratios; Pro. mono., prospective monocentric; Pro. multi., prospective multicentric; Retro. mono., retrospective monocentric.

The percentage of saved endoscopy was calculated as the percentage of correctly classified patients by pooling true negative and true positive.

Castera L et al. J Hepatol 2012
CONCLUSIONS

- Painless, safe, rapid and practical method
- Reliable and accurate in assessment of liver fibrosis in various liver diseases
- High reproducibility and accuracy
- High diagnostic accuracy in detecting cirrhosis
- Useful in assessing portal hypertension and cirrhosis complications
- Reduction of biopsies
CONCLUSIONS

- TE is the only established imaging modality for non-invasive diagnosis of liver fibrosis at the present time

- Interpretation of results should always be done by expert clinicians according to clinical context
THANK YOU!