Non-invasive liver fibrosis assessment: Opportunities for enhanced liver disease assessment and treatment in the drug and alcohol setting

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Available non-invasive methods
2 different but complementary approaches

« Biological » approach
Serum Biomarkers

« Physical » approach
Liver stiffness

Castera & Pinzani. Lancet 2010; 375: 419-20
Serum Fibrosis Biomarkers

« Direct » markers

- Hyaluronate
- PIIINP
- Laminin
- Type IV Collagen
- MMP
- TIMP-1
- TGF-beta
- YKL-40

« Indirect » markers

- Prothrombine time
- Platelet count
- AST/ALT Ratio
# Serum Fibrosis Biomarkers: Scores

<table>
<thead>
<tr>
<th>HCV</th>
<th>HBV</th>
<th>HIV-HCV</th>
<th>NAFLD</th>
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<td>Fibrotest</td>
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<td>Virahep-C model</td>
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</table>
Measuring Liver Stiffness

TE (FibroScan)  pSWE/ARFI  2D-SWE
FibroScan: a Non Invasive Tool to Assess Liver Fibrosis

Serum Biomarkers: Pitfalls

Risk factors for biomarkers
- hemolysis (Fibrotest)
- Gilbert (Fibrotest)
- systemic inflammation (Fibrotest)
- extra-hepatic cholestasis (Fibrotest)
- thrombocytopenia not liver-related (APRI)
Applicability Of Transient Elastography

Failure 3.1%  Unreliable 15.8%

FibroScan not applicable in 20% of cases

Valid shot =

IQR/LSM > 30%

9.2%

N=13669 examinations

Features Influencing Liver Stiffness Measurements

**LIVER CONGESTION**
- Millonig et al. Hepatology 2010
- Colli et al. Radiology 2010

**INFLAMMATION**
- Coco et al. J Viral Hepat 2007
- Arena et al. Hepatology 2008
- Sagir et al. Hepatology 2008
- Rigamonti et al. Gut 2008
- Arena et al. Gut 2008
- Fraquelli et al. J Hepatol 2011

**EXTRA-HEPATIC CHOLESTASIS**

**STEATOSIS**
- Fraquelli et al. J Hepatol 2011
Comparative Performance: Viral Hepatitis

N= 1307 patients; F2: 57%; F4: 14%

Degos et al. J Hepatol 2010; 53: 1013-21
# Fibroscan: Meta-analyses

<table>
<thead>
<tr>
<th></th>
<th>Number of included studies</th>
<th>Number of included subjects for analysis</th>
<th>AUROC</th>
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<td>Talwalkar\textsuperscript{15}</td>
<td>9</td>
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<td>Tsochatzis et al\textsuperscript{18}</td>
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<td>Chon et al</td>
<td>18</td>
<td>2,772</td>
<td>0.859</td>
</tr>
</tbody>
</table>

\textsuperscript{15} Talwalkar et al. CGH 2007
\textsuperscript{16} Stebbing et al. APT 2010
\textsuperscript{17} Friedrich-Rust et al. Gastroenterology 2008
\textsuperscript{18} Tsochatzis et al. J Hepatol 2011
\textsuperscript{18} Chon et al. PLoS ONE 2012
Transient Elastography For Cirrhosis (N=1007 Patients With Various CLD, 165 With Cirrhosis)

- Correctly classified 92%

- F < 4
  - 96% misclassified
  - 3.5% classified

- F = 4
  - 74% misclassified
  - 4.5% classified

Ganne-Carrié et al. Hepatology 2006; 44: 1511-7
The EASL/ALEH Guidelines On Non Invasive Methods

- TE and serum biomarkers have equivalent performance for detecting significant fibrosis in patients with viral hepatitis (A1)

- TE is the most accurate non-invasive method for detecting cirrhosis in patients with viral hepatitis (A1)

- For the diagnosis of significant fibrosis a combination of tests with concordance may provide the highest diagnostic accuracy (A2)
What do HCV Guidelines Recommend?

Considerable evidence suggest that non-invasive methods can now be used instead of liver biopsy to assess liver disease severity. Liver stiffness measurement can be used to assess liver fibrosis in patients with chronic hepatitis C. Well-established panels of biomarkers of fibrosis can also be applied.


(1) Non-invasive assessments have a reduced risk and greater acceptance than liver biopsy, may enhance HCV screening and disease assessment among PWID, and should be offered, if available (Class I, Level B).

(2) Combining multiple non-invasive assessments is recommended, when possible (Class I, Level B).

298 PWID offered Transient elastography:
- 100% acceptance rate
- 9% new HCV cases detected

221 (76.2%) agreed to a blood sample
Transient Elastography is the Preferred Method To Assess Disease Staging: The LiveRLife Study

Noninvasive Tests for Fibrosis and Liver Stiffness Predict 5-year Outcomes of Patients with Chronic Hepatitis C

Transient Elasticography Evolution Predicts Survival in HCV

Transient Elastography Evolution Predicts Survival in HCV

Ultrasound Elastography for Fibrosis Surveillance Is Cost Effective in Patients with Chronic Hepatitis C Virus in the UK

C. Canavan · J. Eisenburg · L. Meng · K. Corey · C. Hur
IDENTIFICATION OF PATIENTS WHO CAN SAFELY AVOID SCREENING ENDOSCOPY

Patients with a **liver stiffness < 20 kPa** and with a **platelet count > 150,000** have a very low risk of having varices requiring treatment, and can avoid screening endoscopy (1b,A).

These patients can be followed up by yearly repetition of TE and platelet count (5,D).

If liver stiffness increases or platelet count declines, these patients should undergo screening esophagogastroduodenoscopy (5,D).
Liver Steatosis: A Confounder For Transient Elastography Results

Non-invasive assessment of liver fibrosis in chronic hepatitis C patients

Diagnostic LSM with US steatosis
High risk of false positive results

Diagnostic LSM without US steatosis
Low risk of false positive results

Is There A Need For Inflammation Based Cut-offs In Patients With HCV & ALD?

Mueller S et al, Liver International in press
Fibroscan Diagnosis of Residual Cirrhosis in Patients with a Five-year SVR to Peg/RBV

Diagnosis of Residual Cirrhosis by Fibroscan Is Biased By Liver Morphometry

TE vs Liver biopsy

| TE > 12Kpa | 8/9 F4 by LB |
| TE < 12Kpa | 5/24 F4 by LB |

Cut off of 12 Kpa for F4

Specificity = 95% (85-100%)
Sensitivity = 61% (35-87%)

D’Ambrosio et al, J Hepatol 2013;59:251–256
ELF Test for Diagnosis of Residual Cirrhosis in Patients with a Five-year SVR to Peg/RBV

D'Ambrosio et al, submitted
Conclusions

- Non Invasive methods to stage HCV are
  - The SOC for pre-treatment assessment
  - Accurate in ruling out cirrhosis
  - Well accepted by patients
  - A tool to increase screening and access to care in PWID

- Non invasive methods still require expert interpretation due to confounders that are common in PWID or alcohol abusers