

# **INHSU 2015**



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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



# « Physical » approach



#### **Liver stiffness**

#### Serum Biomarkers

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**

## HCV

Fibrotest
Forns Index
APRI
FibroSpect
MP3
ELF score
FPI
Hepascore
FibroMeters
Fibroindex

Virahep-C model



# HBV



# HIV-HCV

# NAFLD

NFS

# **Measuring Liver Stiffness**



# FibroScan: a Non Invasive Tool to Assess Liver Fibrosis







Ziol M, Hepatology 2005;41:48-54; Castéra L, Gastroenterology 2005;128:343-50; Fraquelli M, Gut 2007;56:968-973

## **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** 



Castéra et al. Hepatology 2010;51:828-35.

## **Features Influencing Liver Stiffness Measurements**

#### LIVER CONGESTION

Millonig et al. Hepatology 2010 Colli et al. Radiology 2010

#### STEATOSIS

Lupsor et al. J Gastrointestin Liver Dis 2008 Fraquelli et al. J Hepatol 2011

#### 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

Millonig et al. Hepatology 2008

## **Comparative Performance: Viral Hepatitis**

Significant fibrosis

Cirrhosis

Biomarkers <sup>†‡</sup>		AUC			AUC		
Fibrotest®	1197	0.48	0.78 (0.75-0.81)		0.74	0.82 (0.79-0.85) <sup>†</sup>	
Fibrometre®	1204	P-	NC)		P-	N <b>S</b> 9) (	
APRI	1272		(0.69-0.75)		2.0	(0.73-0.81)†	
Hepascore	1238	0.5	0.78 (0.75-0.80)		0.84	0.86 (0.83-0.88) <sup>‡</sup>	

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

Degos et al. J Hepatol 2010; 53: 1013-21

## **Fibroscan: Meta-analyses**

	Number of included studies	Number of included subjects for analysis	AUROC			
			≥ F2		F4	
Talwalkar <sup>15</sup>	<u>9</u>	2,083	0.870		0.957	
Stebbing <sup>16</sup>	22	4,760	0.84		0.94	
Fredrich-rust et al <sup>17</sup>	50	8,206	0.84		0.94	
Tsochatzis et al <sup>18</sup>	<u>40</u>	7,723	N/A		N/A	
Chon et al	<u>18</u>	2,772	0.859		0.929	

Talwalkar et al. CGH 2007 Stebbing et al. APT 2010 Friedrich-Rust et al. Gastroenterology 2008 Tsochatzis et al. J Hepatol 2011

Chon et al. PLoS ONE 2012

# Transient Elastography For Cirrhosis (N=1007 Patients With Various CLD, 165 With Cirrhosis)



83%		17%	
3	14.6		75
F < 4 96%	F = 4 74%		
3.5 % misclassified		4.5% misclassified	

Ganne-Carrié et al. Hepatology 2006; 44: 1511-7

- 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)

EASL-ALEH Clinical practice Guidelines. J Hepatol 2015; 63: 237-64.

## 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.

EASL HCV Treatment Recommendations. J Hepatol 2015;63:199–236.

(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).

Grebely J et al. International Journal of Drug Policy 2015;26:1028–1038.

#### Transient Elastography as a Tool to Increase Screening and Access to Therapy

Journal of Viral Hepatitis, 2009, 16, 121-131

doi:10.1111/j.1365-2893.2008.01050.x

FibroScan used in street-based outreach for drug users is useful for hepatitis C virus screening and management: a prospective study

J. Foucher,<sup>1</sup> B. Reiller,<sup>2</sup> V. Jullien,<sup>2</sup> F. Léal,<sup>3</sup> E. S. di Cesare,<sup>2</sup> W. Merrouche,<sup>1</sup> J.-M. Delile<sup>2</sup> and V. de Lédinghen<sup>1,4</sup> <sup>1</sup>Centre d'Investigation de la Fibrose hépatique, Hôpital Haut-Lévêque, CHU Bordeaux, Pessac, France; <sup>2</sup>CEID, Centre Planterose, Bordeaux, France; <sup>3</sup>Médecins du monde, La Case, Bordeaux, France; <sup>4</sup>INSERM U889, Université Victor Segalen Bordeaux 2, Bordeaux, France

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



Marshall AD, et al. International Journal of Drug Policy 2015;26:984-991

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



FIBROSCAN

FIBROTEST

Vergniol J. et al, Gastroenterology 2011;140:1970-1979

#### **Transient Elastography Evolution Predicts Survival in HCV**



Vergniol J. et al, Hepatology. 2014;60(1):65-76

#### **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

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PROGNOSIS	Good	Intern	nediate	Bad

**Position Paper** 



#### Expanding consensus in portal hypertension Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension

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#### 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



Macaluso et al, Journal of Hepatology. 2014;

# 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 _ specificity _ sensitivity	a for F4 = 95% (85-100%) = 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