

# Combination of blood test and elastometry improves the diagnosis of liver fibrosis or cirrhosis and markedly reduces the biopsy requirement in algorithms

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## Introduction

- Blood tests, liver stiffness evaluation (LSE) by ultrasonographic elastometry, and Doppler-ultrasonography (US) are accurate tools to diagnose liver fibrosis.
- Our aim was to evaluate whether their synchronous combination could improve the diagnostic accuracy and reduce biopsy requirement in algorithm.

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## Material and Methods

- 540 patients with chronic liver disease were included into 3 groups according to fibrosis tests availability:
  - #1 (n=150): blood tests + Doppler US
  - #2 (n=194): blood tests + Doppler-US + LSE
  - #3 (n=196): blood tests + LSE
- Exclusion criteria: ascites, variceal bleeding, hepatocellular carcinoma, infection
- Liver fibrosis reference: Metavir F score
- Non invasive liver fibrosis tests:
  - Blood tests: FibroMeter, Fibrotest, Hepascore, APRI, Fib-4
  - Liver stiffness evaluation: Fibroscan®

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## Patients characteristics

	Group				p
	All	#1	#2	#3	
Patients (n)	540	150	194	196	-
Age (years)	51.0±13.1	47.5 ± 11.6	50.8±12.7	53.9±14.0	<10 <sup>-3</sup>
Male sex (%)	68.1	68.7	68.0	67.9	0.99
Cause (%)					<10 <sup>-3</sup>
- Virus	54.3	68.1	54.1	43.4	
- Alcohol	25.0	19.3	26.3	28.1	
- NAFLD	5.6	7.3	9.8	0.0	
- Others	15.2	4.7	9.8	28.6	
Metavir F≥2 (%)	72.4	67.3	76.3	72.4	0.18
Metavir F=4 (%)	28.7	22.7	22.7	39.3	<10 <sup>-3</sup>
Reliable biopsy <sup>a</sup> (%)	87.4	82.4	95.3	82.6	<10 <sup>-3</sup>
IQR / median <sup>b</sup> <0.21 (%)	59.4	-	58.5	60.3	0.73

<sup>a</sup> length ≥15 mm and/or portal tract number ≥8 ; <sup>b</sup> LSE : ratio IQR (kPa) / median (kPa)

## Fibrosis tests: AUROC<sup>a</sup> according to diagnostic target

	Metavir F≥2	Metavir F=4
FibroMeter	0.836	0.834
Fibrotest	0.826	0.813
Hepascore	0.799	0.806
Fib-4	0.787	0.793
APRI	0.762	0.691
LSE	0.858	0.915

<sup>a</sup> In the 332 patients having all blood tests and LSE available

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## Diagnosis by combined fibrosis tests

Diagnostic target	Group	Independent variables <sup>a</sup>	p	Score <sup>b</sup>
Metavir F≥2	#2 <sup>c</sup>	1. FibroMeter	<10 <sup>-3</sup>	FS-index
		2. LSE	<10 <sup>-3</sup>	
	#3	1. FibroMeter	<10 <sup>-3</sup>	
		2. LSE	0.012	
Metavir F=4	#2 <sup>c</sup>	1. LSE	<10 <sup>-3</sup>	C-index
		2. FibroMeter	0.031	
	#3	1. LSE	<10 <sup>-3</sup>	
		2. FibroMeter	0.017	

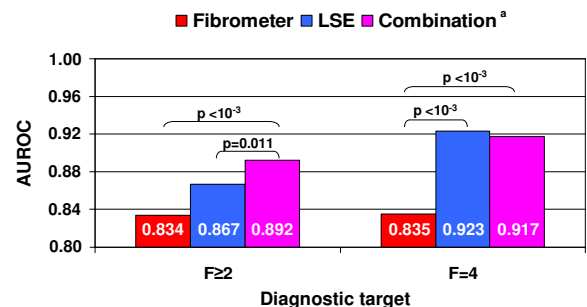
<sup>a</sup> By stepwise binary logistic regression

<sup>b</sup> Constructed with the regression score of the multivariate analysis

<sup>c</sup> No Doppler-US variable was independently associated with the diagnostic target

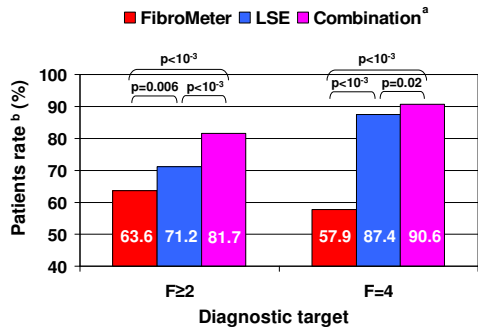
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## Accuracy of fibrosis tests and their combination according to diagnostic target



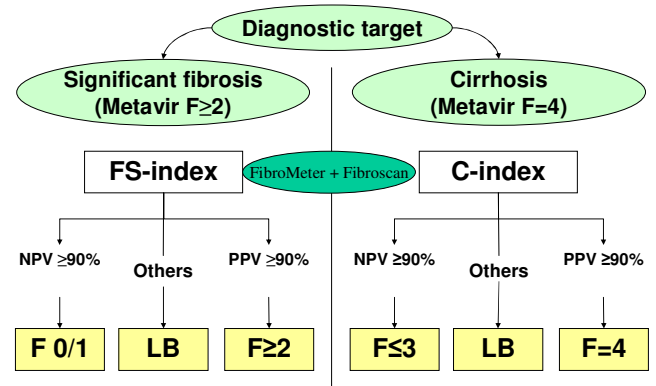
<sup>a</sup> FS-index for diagnostic target Metavir F≥2 ; C-index for diagnostic target Metavir F=4

### Reliable diagnosis of fibrosis tests and their combination according to diagnostic target

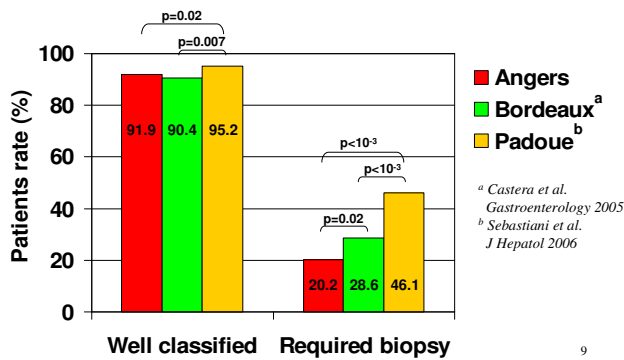


<sup>a</sup> FS-index for diagnostic target Metavir F<sub>≥2</sub>; C-index for diagnostic target Metavir F<sub>=4</sub>  
<sup>b</sup> Rate of patients with a reliable diagnosis (i.e. positive or negative predictive value ≥90%)

### Determination of new Angers diagnostic algorithms based on combined tests

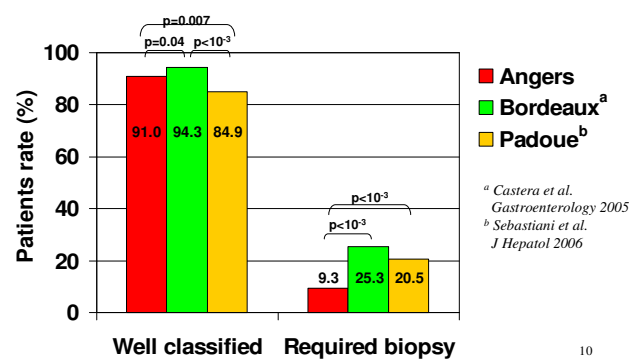


### Accuracy of diagnostic algorithms (1) for the diagnosis of significant fibrosis (Metavir F<sub>≥2</sub>)



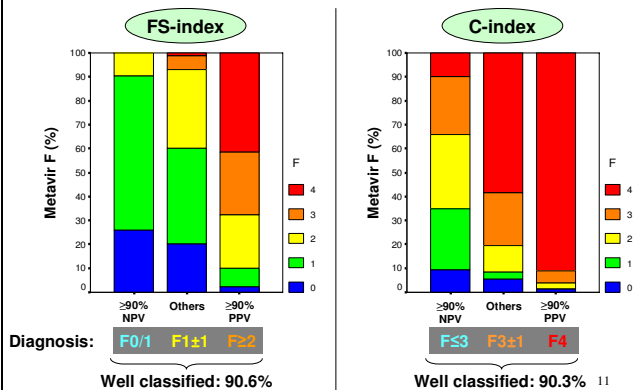
<sup>a</sup> Castera et al. Gastroenterology 2005  
<sup>b</sup> Sebastiani et al. J Hepatol 2006

### Accuracy of diagnostic algorithms (2) for the diagnosis of cirrhosis (Metavir F=4)



<sup>a</sup> Castera et al. Gastroenterology 2005  
<sup>b</sup> Sebastiani et al. J Hepatol 2006

### Reliable diagnosis with 0% liver biopsy



### Conclusions

- Compared to a single test, the synchronous combination of a blood test (FibroMeter) with LSE (Fibrosca) significantly improves:
  - the diagnostic accuracy for the diagnosis of significant fibrosis.
  - the rate of reliable individual diagnosis for significant fibrosis and cirrhosis.
- Thus, a simple sequential algorithm, based on the synchronous combination of blood test + LSE, provided a high diagnostic accuracy while lowering the requirement of liver biopsy, notably to less than 10% for cirrhosis diagnosis.