

Clinical case: NAFLD



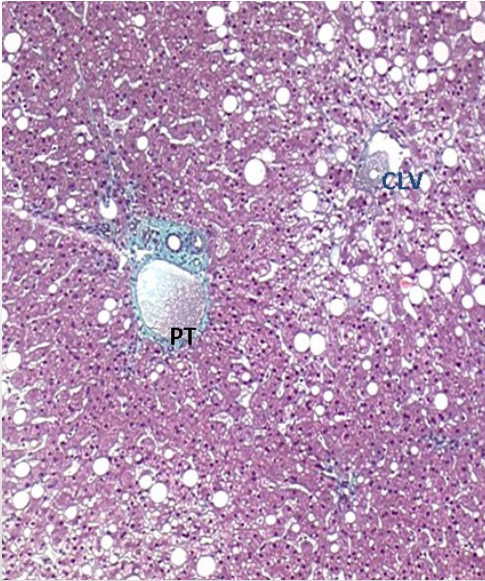
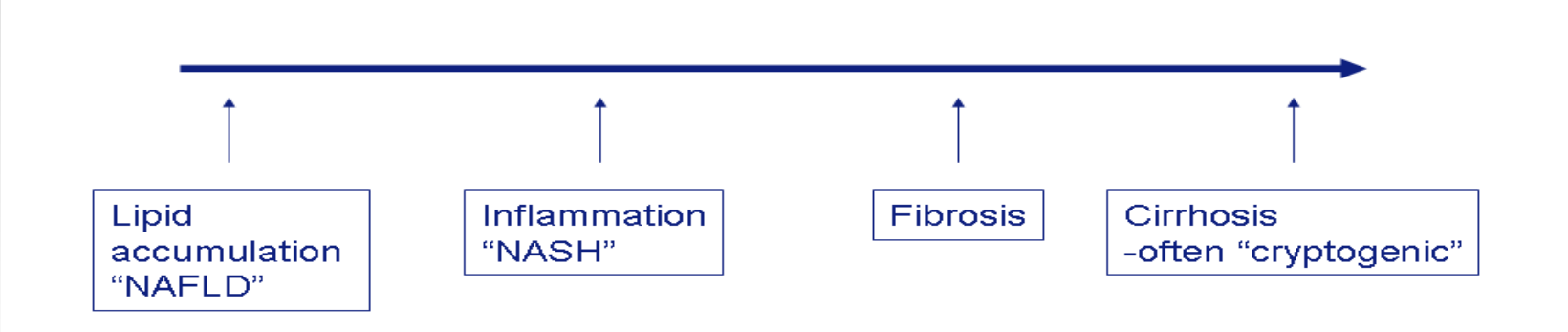
Victor de Lédighen

Centre d'Investigation de la
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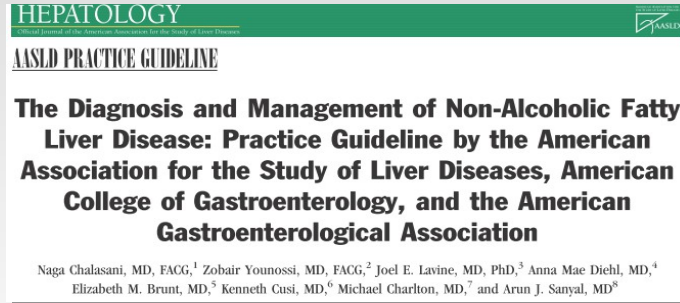
CHU Bordeaux

France

Non-alcoholic fatty liver disease (NAFLD)



Current AASLD guidelines in NAFLD (2012)



- ***“Liver biopsy should be considered in patients with NAFLD who are at increased risk to have steatohepatitis and advanced fibrosis”***
- ***“The presence of metabolic syndrome and the NAFLD Fibrosis Score may be used for identifying patients who are at risk for steatohepatitis and advanced fibrosis”***

Liver stiffness measurement



FibroScan – ARFI - SSI

Fasting at least 2 hours

FibroScan



FibroScan examination: screen

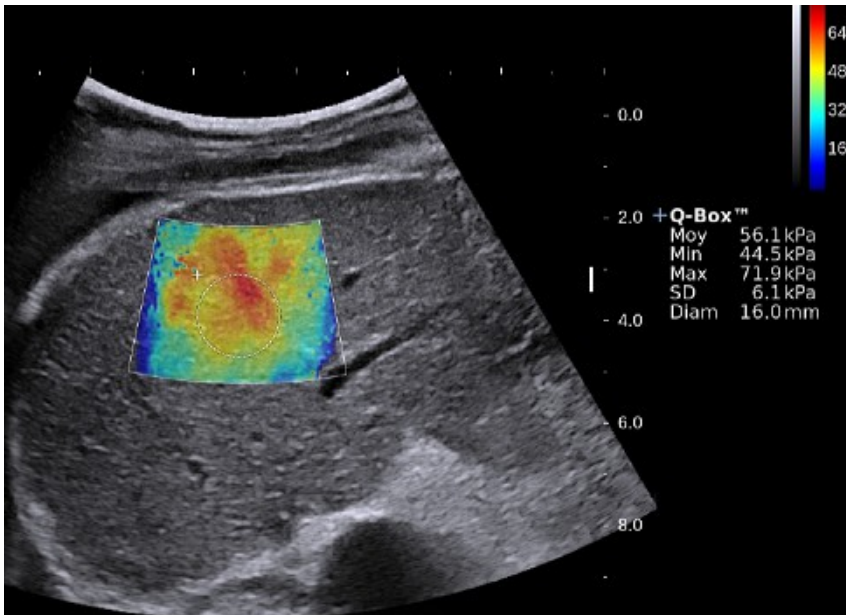


CAP : 100 to 400 dB/m

E : 2 to 75 kPa

Shear wave elastography

SSI is integrated into a conventional ultrasound device (Aixplorer™, Supersonic Imagine, Aix-en-Provence, France).



Shear Wave elastography is based on the measurement of the velocity of a focal shear wave through soft tissue. Elasticity is displayed using a color mapping of the elasticity encoded pixel by pixel in an image superimposed on the standard mode.

Mr C. works in a « château »

- Male (birthdate 1970)
- No alcohol
- Statin

In 2004:

- BMI 27 kg/m², elevated waist circumference
- ALT 64 IU/L GGT 66 IU/L
- FibroMeter 0.02
- Fibrotest 0.19
- Fibroscan 5.8 kPa

Would you perform a liver biopsy?

Clinical case

- ❑ A liver biopsy is performed
- ❑ F1
- ❑ Steatosis 15%
- ❑ No NASH (NAS < 5)

Clinical case

| | FibroMeter | Fibrotest | FibroScan | CAP | F | S (%) |
|------|------------|-----------|-----------|-----|----------|-----------|
| 2004 | 0,2 | 0.19 | 5.8 | | 1 | 15 |
| 2005 | | 0.21 | 5.3 | | | |
| 2006 | | 0.35 | 5.6 | | | |
| 2007 | | 0.67 | 5.1 | | | |
| 2008 | | 0.32 | 6.6 | | | |

BMI from 27 to 32 kg/m²

NAFLD fibrosis score

NAFLD fibrosis score Online calculator

Angulo P, Hui JM, Marchesini G et al. The NAFLD fibrosis score
A noninvasive system that identifies liver fibrosis in patients with NAFLD
Hepatology 2007; 45 (4): 846-854 [doi:10.1002/hep.21496](https://doi.org/10.1002/hep.21496)

Age (years)

BMI (kg/m²)

IGF/diabetes

AST

ALT

Platelets (x10⁹/l)

Albumin (g/l)

Score

< -1.455: predictor of **absence** of significant fibrosis (F0-F2 fibrosis)

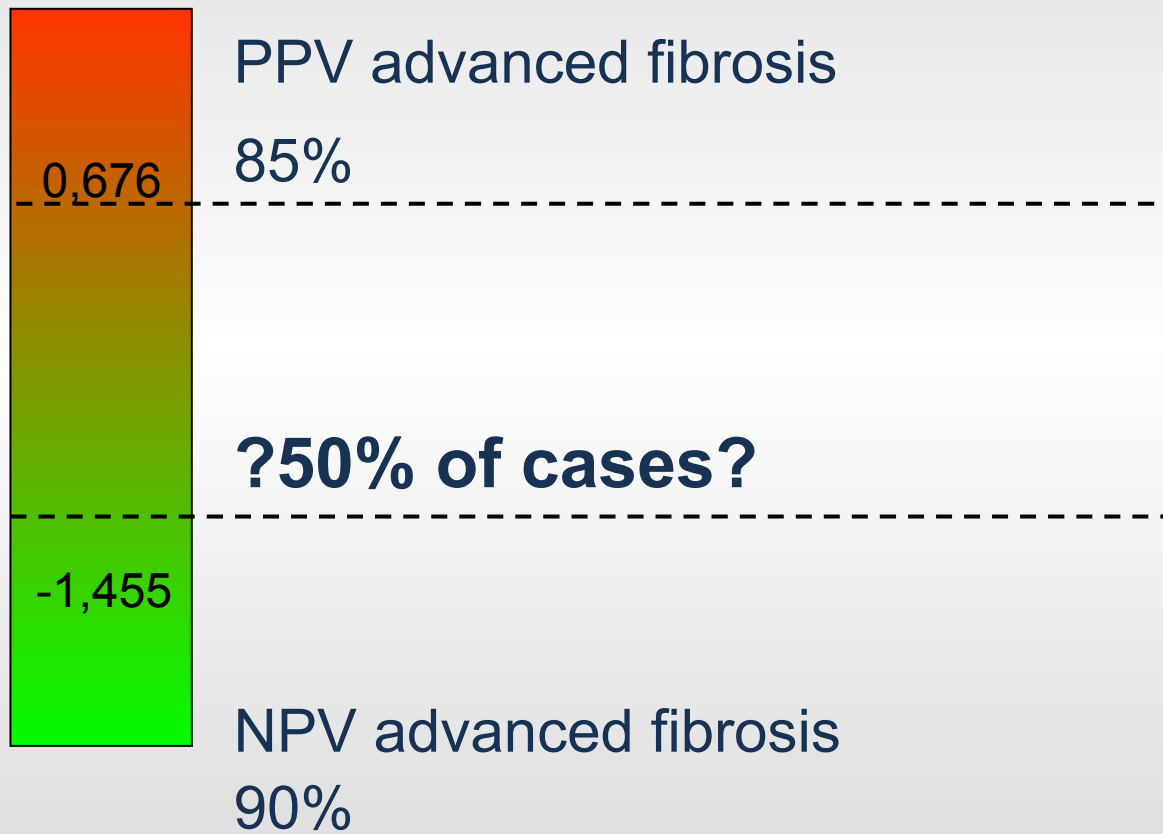
≤ -1.455 to ≤ 0.675: indeterminate score

> 0.675: predictor of **presence** of significant fibrosis (F3-F4 fibrosis)

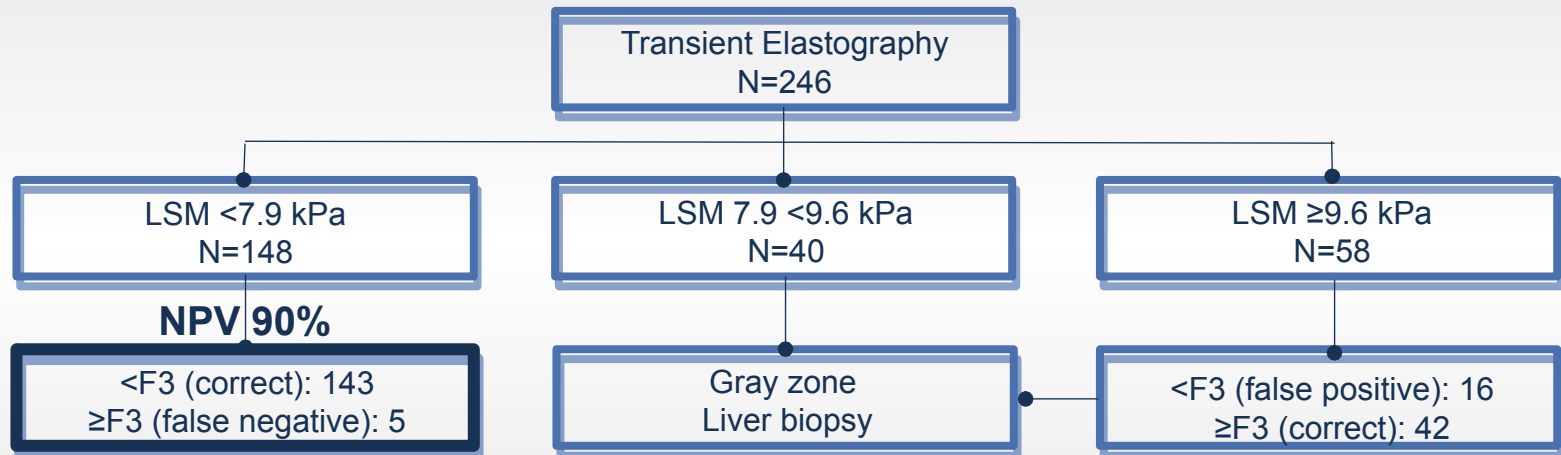
BMI: body mass index

IGF: impaired fasting glucose

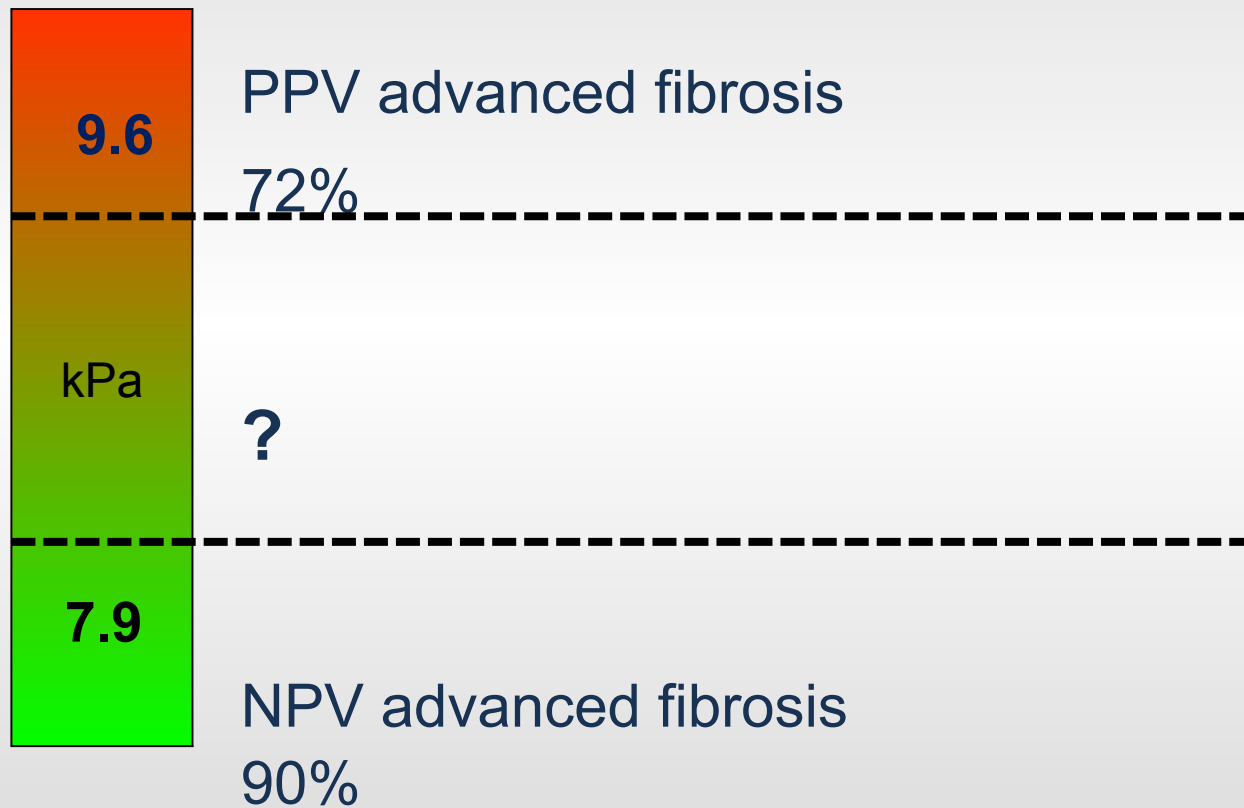
NAFLD fibrosis score



FibroScan (M probe) is useful in NAFLD patients



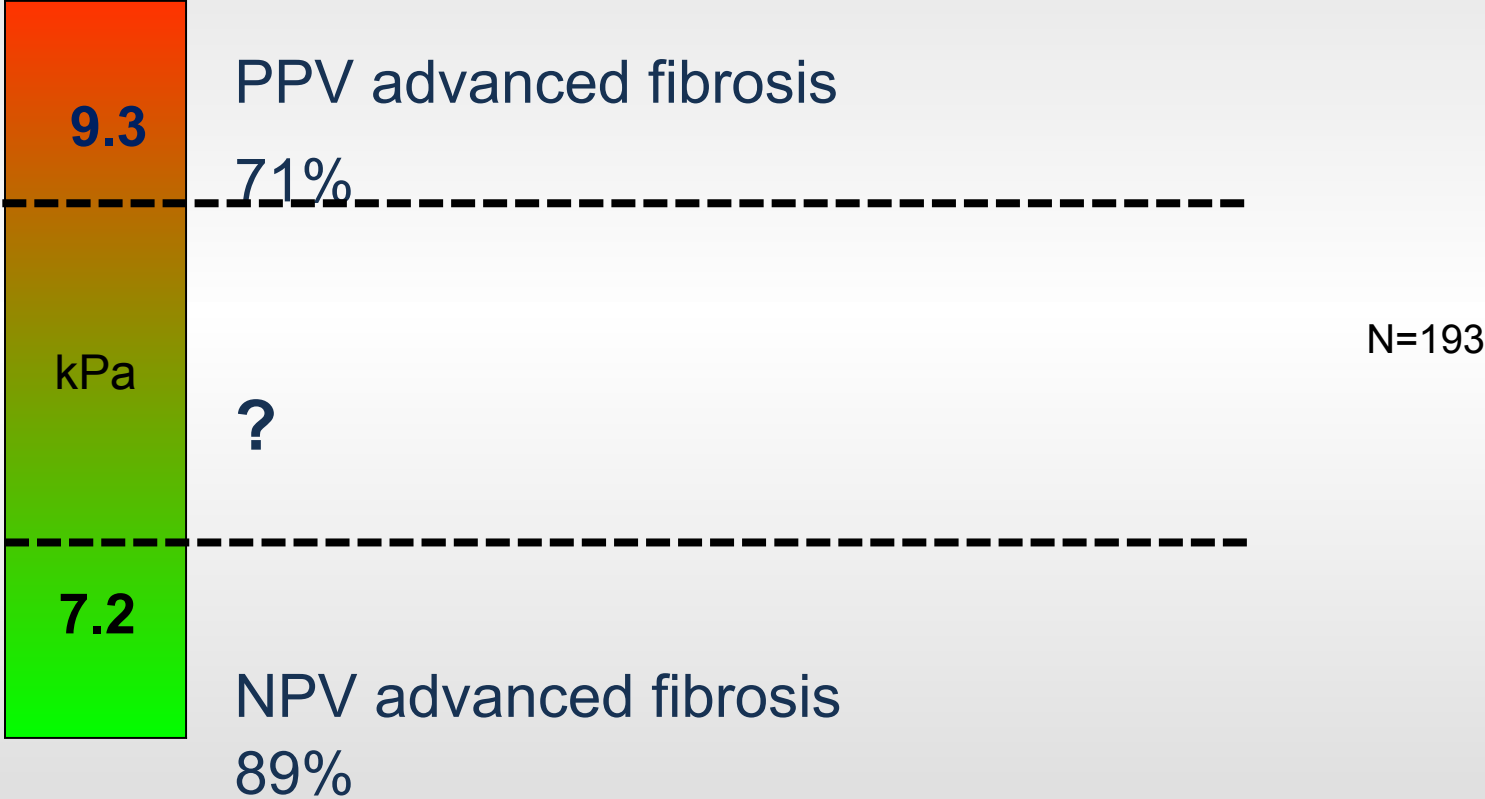
FibroScan M probe



FibroScan M versus XL probes in NAFLD

| | M | XL |
|--------|----------|-----------|
| F2F3F4 | 0.83 | 0.80 |
| F3F4 | 0.87 | 0.85 |
| F4 | 0.89 | 0.91 |

FibroScan XL probe



Liver stiffness is better than biomarker for the diagnosis of fibrosis or cirrhosis

| N=349 | F2F3F4 | F3F4 | F4 |
|-----------|-------------|-------------|-------------|
| SSI | 0.89 | 0.92 | 0.92 |
| Fibroscan | 0.83 | 0.86 | 0.90 |
| ARFI | 0.81 | 0.85 | 0.84 |
| Fibrotest | 0.74 | 0.78 | 0.81 |
| FIB-4 | 0.75 | 0.77 | 0.82 |
| APRI | 0.71 | 0.72 | 0.74 |

Clinical case

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Do you think we need a follow-up?

If yes, every year?

Do we need to perform a new liver biopsy?

Clinical case

| | FibroMeter | Fibrotest | FibroScan | CAP | F | S(%) |
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| 2007 | 0,11 | 0.67 | 5.1 | | | |
| 2008 | 0,1 | 0.32 | 6.6 | | | |
| 2009 | 0,05 | 0.47 | 5.9 | | | |

Liver biopsy : F1

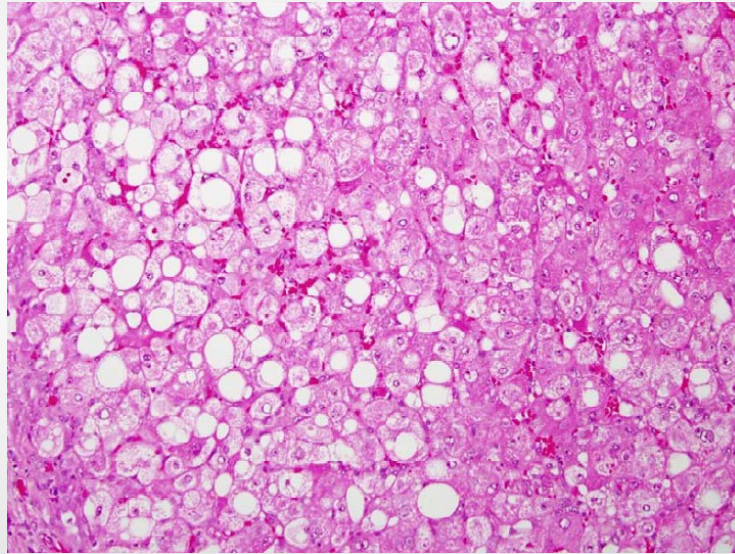
Steatosis : 70%

No NASH

How can we diagnose steatosis?

Liver
biopsy

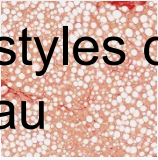


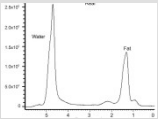
US
CT
MRI



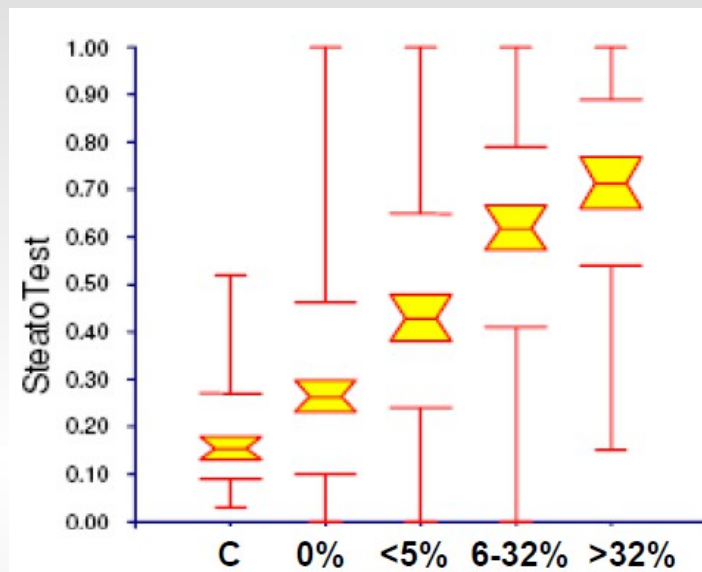
Biomarkers

CAP

Methods for liver steatosis evaluation

| Methods | Advantages | Drawbacks |
|---|---|---|
| Liver biopsy  | Reference Steatosis quantification | Invasive Sample bias Moderate inter-observer reproducibility Cost |
| Ultrasound • Cinquième niveau  | Non-invasive Widely available | Poor sensitivity if steatosis <30% Moderate inter-observer reproducibility |
| MRI • Cinquième niveau  | Non-invasive Steatosis quantification | Poorly available Cost |
| MRS  | Non-invasive Steatosis quantification « Reference » | Poorly available Cost |

Steatotest



NPV 93%

Steatosis >5%

PPV 63%

CAP™ examination on FibroScan®

- CAP: Controlled Attenuation Parameter
- CAP has been devised to target liver steatosis specifically
- CAP quantifies ultrasonic attenuation in the liver, directly related to steatosis amount.
- Stiffness and CAP measurements are performed simultaneously on a 3cm³ volume of liver tissue
- CAP is expressed in dB/m (range from 100 to 400 dB/m)

The more steatosis, the higher CAP will be

Clinical case

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| 2009 | 0,05 | 0.47 | 5.9 | | 1 | 70 |
| 2010 | | 0.4 | 6.3 | | | |
| 2011 | | 0.35 | 5.9 | 347 | | |
| 2012 | | | 6.3 | 246 | | |

Factors associated with CAP

| Multivariate analysis | CAP =]250-300] dB/m | | | CAP > 300 dB/m | | |
|--|----------------------|-----------|--------|----------------|-------------|--------|
| | OR | 95% CI | P | OR | 95% CI | P |
| Male gender | 1.38 | 1.18-1.62 | <0.001 | 1.37 | 1.14-1.64 | 0.001 |
| Age > 55 years | 1.46 | 1.25-1.71 | <0.001 | 1.32 | 1.10-1.59 | 0.003 |
| BMI]25–30] versus ≤ 25 kg/m ² | 3.21 | 2.70-3.81 | <0.001 | 5.86 | 4.64-7.39 | <0.001 |
| > 30 versus]25–30] kg/m ² | 1.71 | 1.34-2.17 | <0.001 | 3.69 | 2.93-4.65 | <0.001 |
| > 30 versus ≤ 25 kg/m ² | 5.47 | 4.28-7.00 | <0.001 | 21.61 | 16.47-28.36 | <0.001 |
| Metabolic syndrome | 1.46 | 1.20-1.78 | <0.001 | 2.73 | 2.23-3.34 | <0.001 |
| Alcohol abuse | 1.72 | 1.37-2.16 | <0.001 | 2.22 | 1.72-2.88 | <0.001 |
| Liver stiffness > 6 kPa | 1.32 | 1.12-1.54 | 0.001 | 2.00 | 1.67-2.41 | <0.001 |

CAP for the diagnosis of steatosis

| | S 1 | S 2 | S=3 |
|------------|------|------|------|
| SteatoTest | 0.70 | 0.73 | 0.75 |
| FLI | 0.72 | 0.71 | 0.75 |
| CAP | 0.83 | 0.86 | 0.91 |

P<0.05

CAP in chronic liver diseases

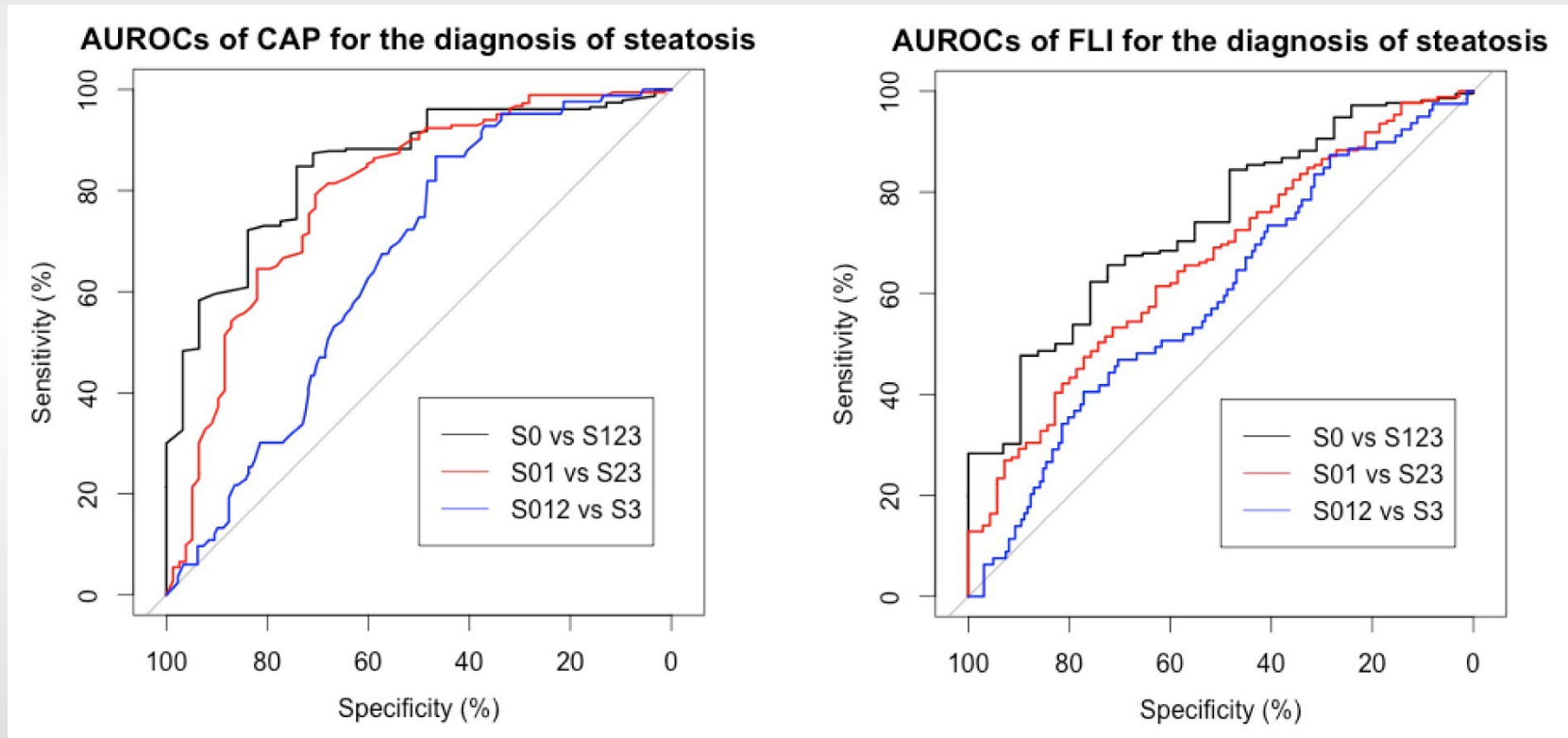
- CAP correlated with steatosis ($r=0,456$, $p<0.0001$) but slightly with fibrosis ($r=0,095$, $p=0,01$).

| | CAP | | FLI | |
|------|------|-----------|------|-----------|
| S123 | 0.79 | 0.75-0.84 | 0.74 | 0.69-0.79 |
| S23 | 0.84 | 0.80-0.88 | 0.79 | 0.75-0.84 |
| S3 | 0.84 | 0.80-0.88 | 0.76 | 0.70-0.84 |

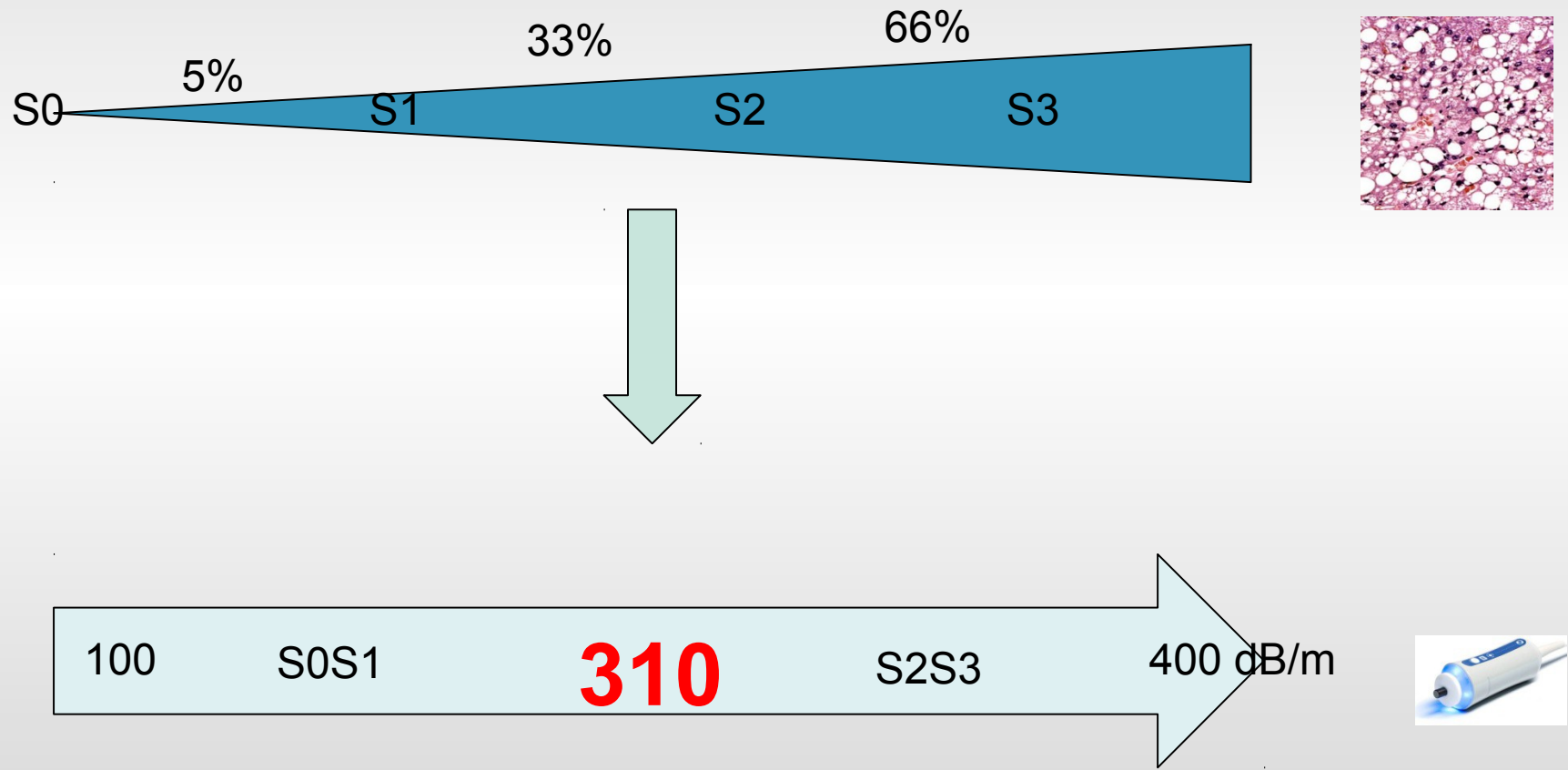
P<0.01

CAP in NAFLD patients

N=261 NAFLD patients with Fibroscan + liver biopsy



CAP in NAFLD patients



Clinical case

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What do you think?
Do we perform a new liver biopsy?

Clinical case

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| 2010 | | 0.4 | 6.3 | | | |
| 2011 | | 0.35 | 5.9 | 347 | | |
| 2012 | | | 6.3 | 246 | | |
| 2013 | | 0.18 | 6.7 | 355 | 1 | 40 |
| 2014 | | | 6.5 | 336 | | |

Take home messages

- Liver stiffness measurement by FibroScan® is an accurate methods to rule out or rule in advanced fibrosis in NAFLD.
- Steatosis can easily be diagnosed using ultrasonography for S>30%.
- Steatosis could be quantified and followed using CAP™ measured by FibroScan®.



ASSOCIATION FRANÇAISE POUR L'ÉTUDE DU FOIE



www.afef.asso.fr