

Non invasive tests for NASH

Are we there yet?

P Mathurin

Hôpital Claude Huriez

Lille

Medical History

2018

- Female 45 years old, caucasian
- Referred by the bariatric Surgeon for screening of NASH

Past history: Type 2 diabetes, hypertension, sleep apnea syndrome, severe obesity (BMI 48)

No over comorbidities

No active or past alcohol consumption.

Physical examination

- Weight: 128; Height: 1.61 m, **BMI: 49.4 kg/m²**
- **Abdominal circumference: 104 cm**
- No signe of chronic liver disease or excessive alcohol consumption
- No hepatomegaly or splenomegaly

Abdominal ultrasound

- Grade 2, liver steatosis
- Normal pancreas & biliary tree
- No ascites

- Gastrointestinal endoscopy : no oesophageal varices, no portal hypertension

Laboratory data

Haemoglobin	14,7	g/dL
Platelets	140 000	cel/L
AST	150	U/L
ALT	179	U/L
Total bilirubin	0.7	mg/dL
Alkaline phosphatase	48	U/L
gGT	280	U/L
Total cholesterol	228	mg/dL
Triglyceride	403	mg/dL

Glucose	180	mg/dL
Hb A1C	9.2%	
INR	1.1	

Question #1

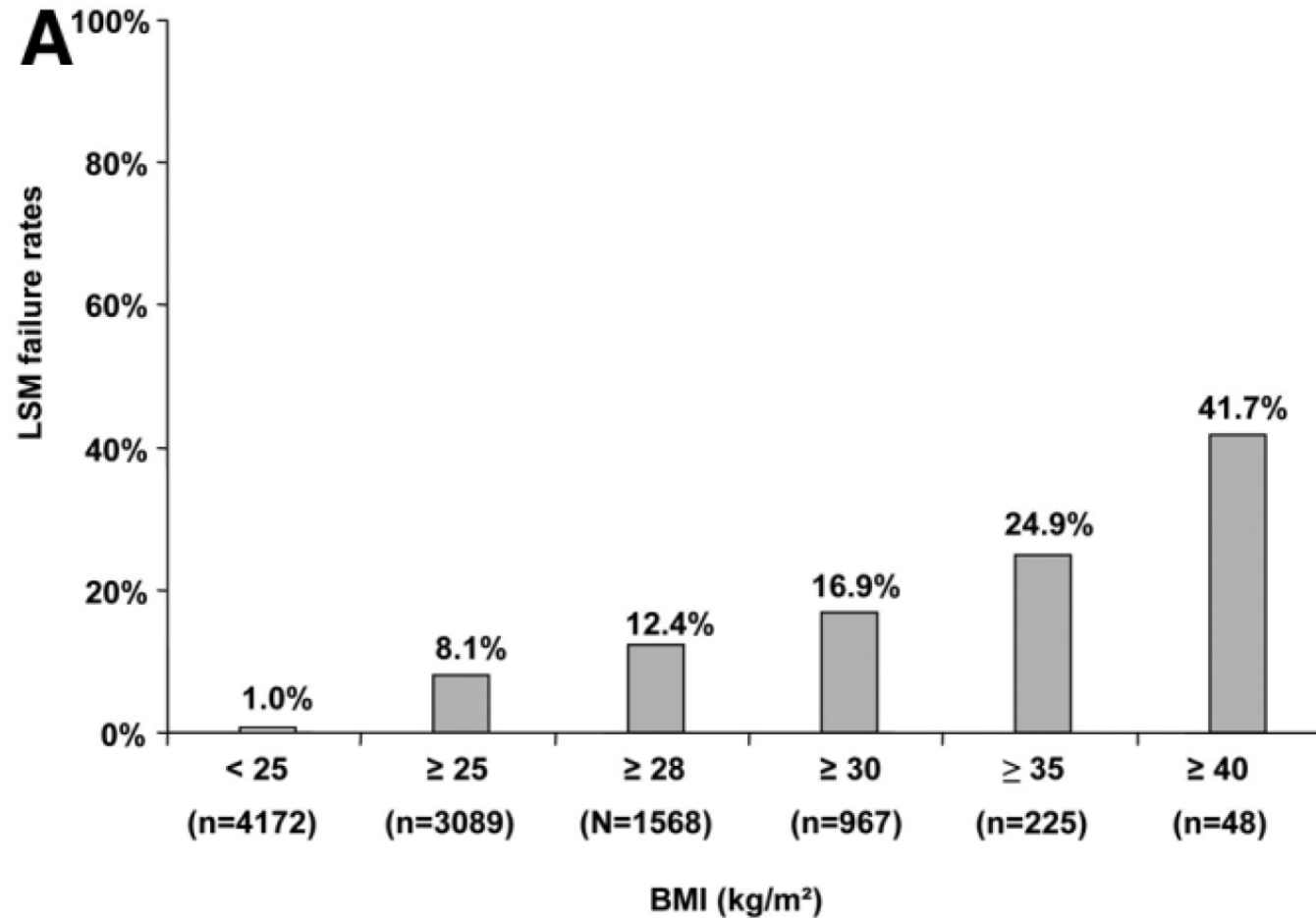
Which method would you use in your daily clinical practice to evaluate liver fibrosis in this patient ?

1. FIB4
2. Fibrotest / FibroMeter / ELF
3. Fibroscan
4. ARFI
5. MRE
6. Liver biopsy

Non Invasive screening of Fibrosis

FIB-4	3.9
Fibrotest	0.6
Fibroscan XL Probe	Failure to measure

Fibroscan in severely obese patients



WITTGENSTEIN - PICASSO

Théodore

Né le 01.02.03

Code : 012547696366

Examen FibroScan M

05.01.10

Courbe de flexion

08 : 12

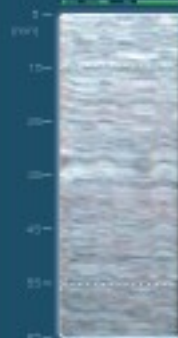
Taux de réussite

100 %

Mesures valides

2

Mesures Valides **15**



CAP (dB/m)

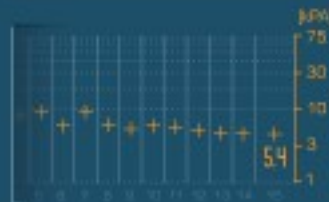
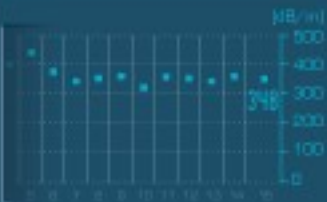
IGR
330
IGR/méd.
10 %

MÉDIANE
350

E (kPa)

MÉDIANE
5.6

IGR
3.9
IGR/méd.
18 %



- 19.4 kPa
- 19.4 kPa
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- 5.4 kPa

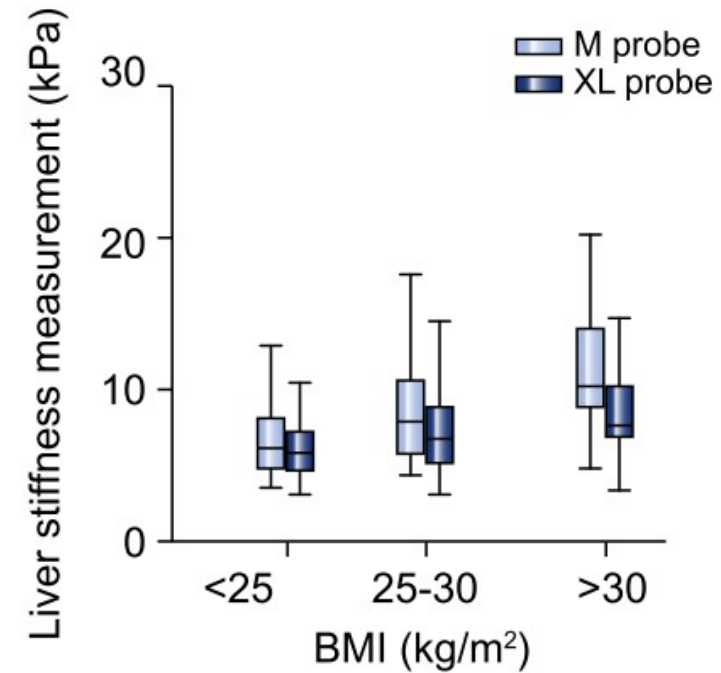
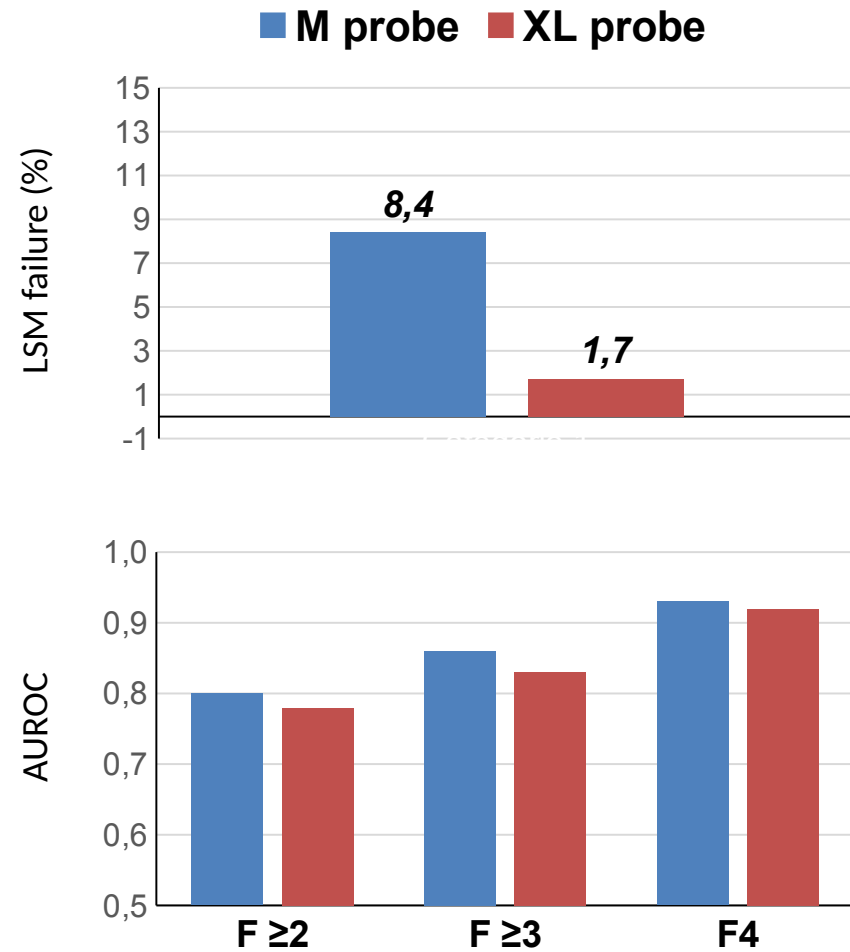
Note

Note sur un détail éventuel intéressant à garder en mémoire

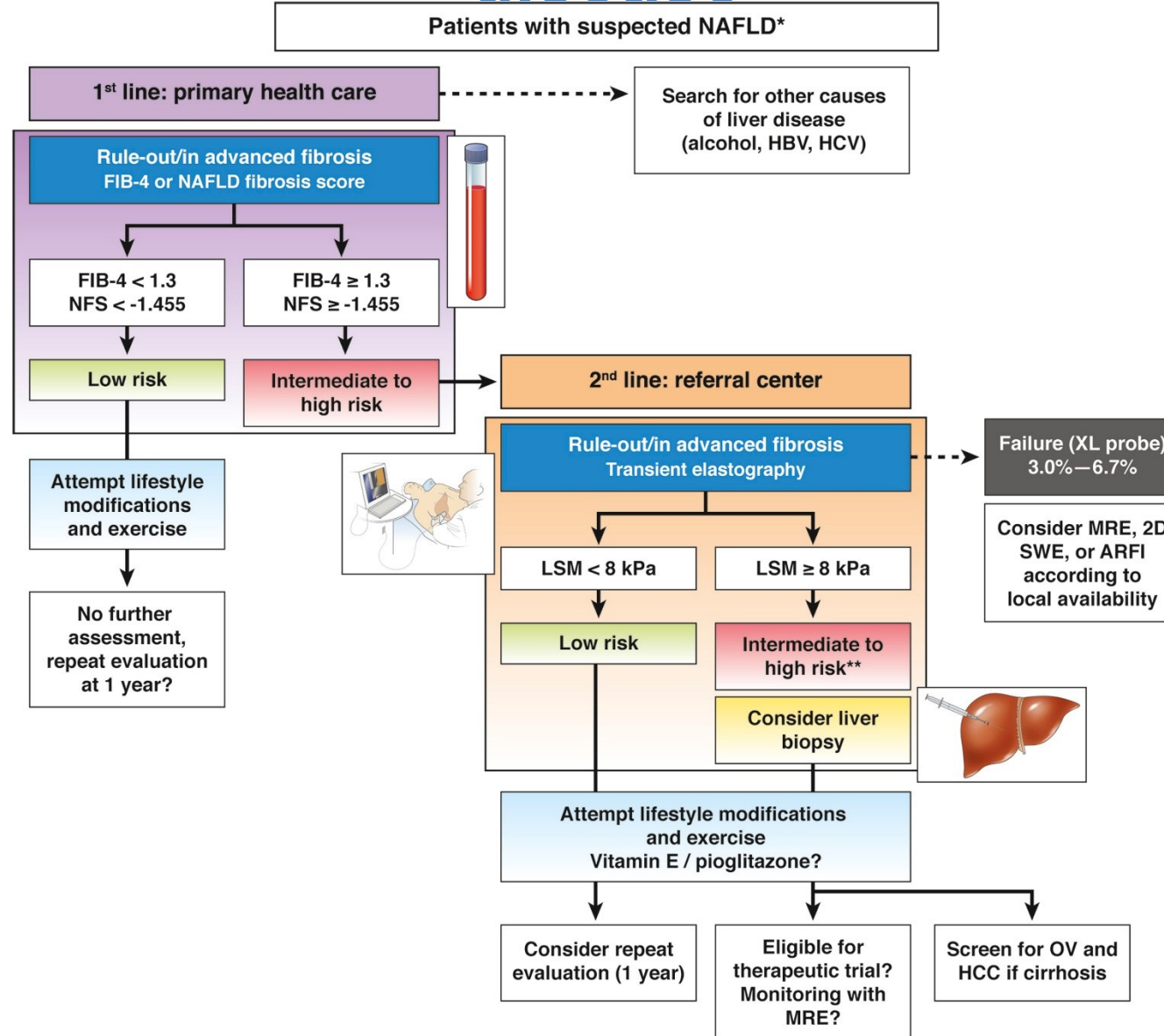
S₁ S₂ m XL

Type d'examen

Fibroscan XL probe

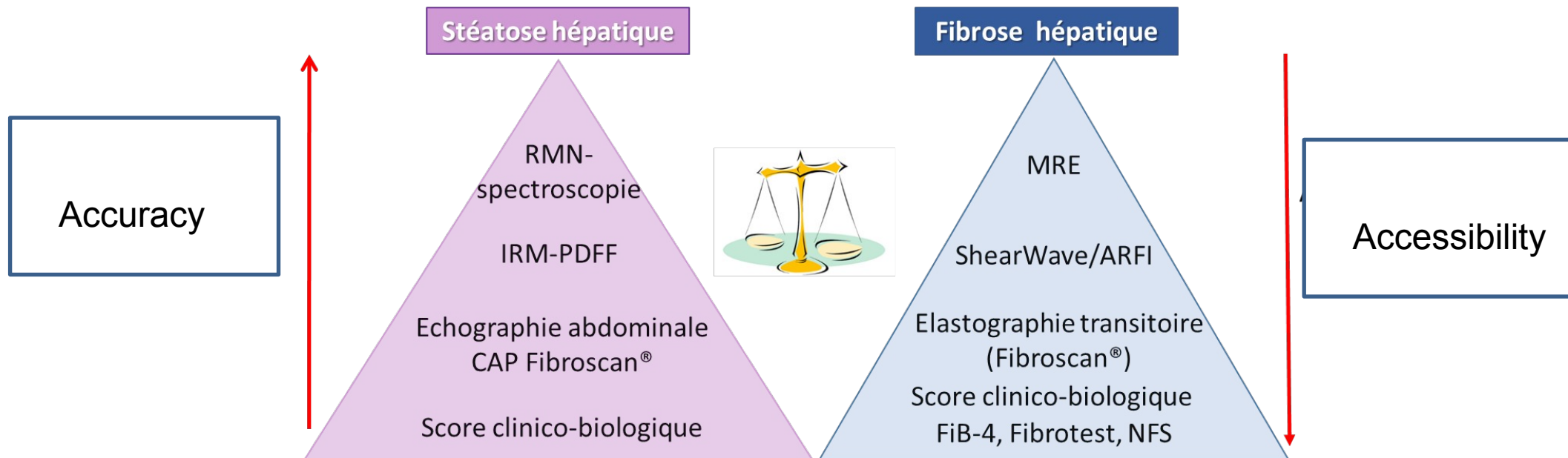


Fibrosis screening in patients with Liver disease



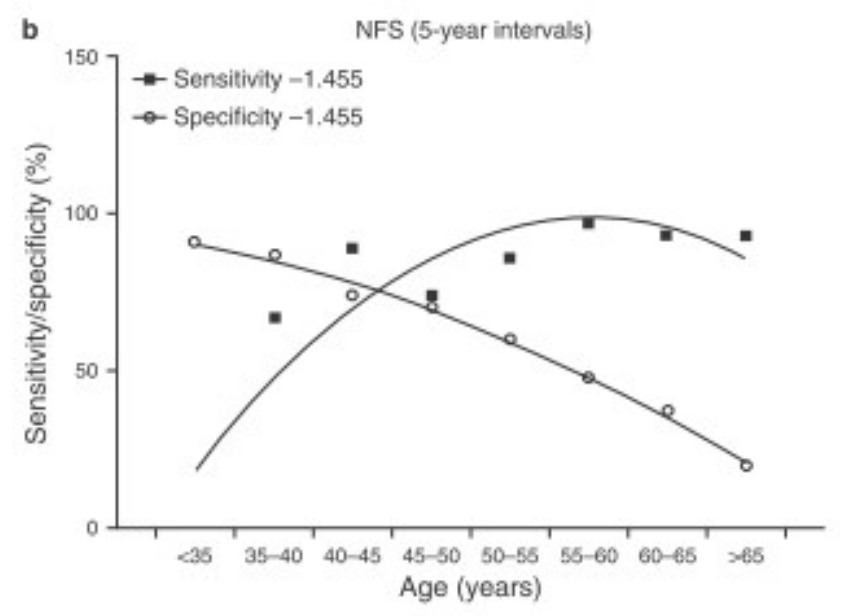
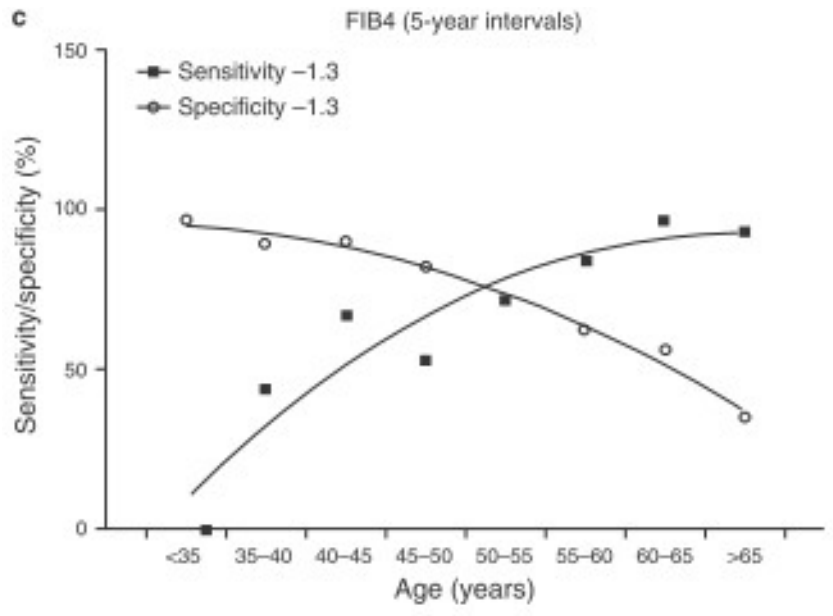
Non invasive tests for NAFLD

Available options in routine practice

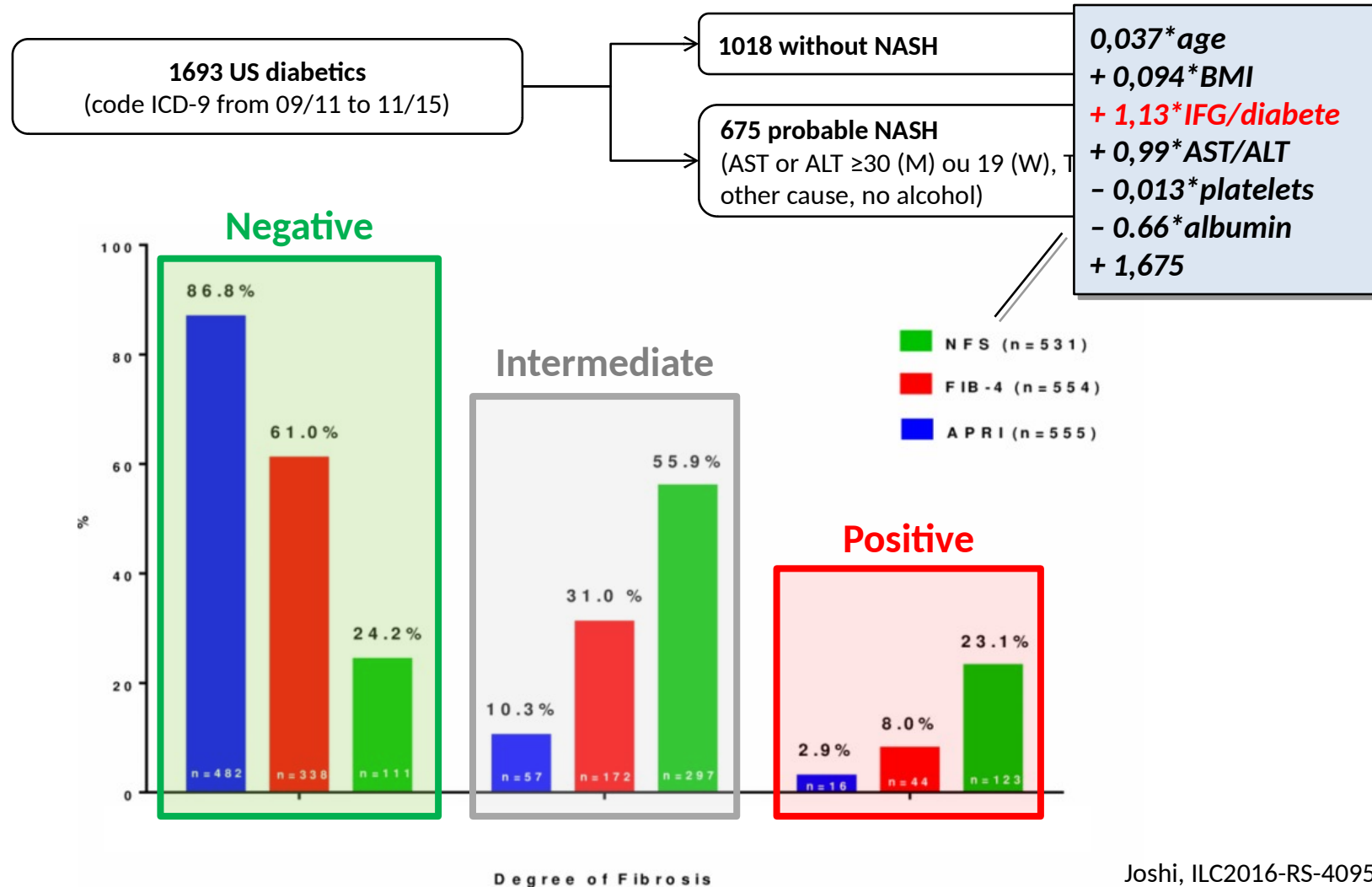


Blood fibrosis tests in NAFLD: age is an issue to consider!

634 patients with biopsy-proven NAFLD



NFS: a good fibrosis test in diabetics?



Comparison of Laboratory Tests, Ultrasound, or Magnetic Resonance Elastography to Detect Fibrosis in Patients With Nonalcoholic Fatty Liver Disease: A Meta-Analysis

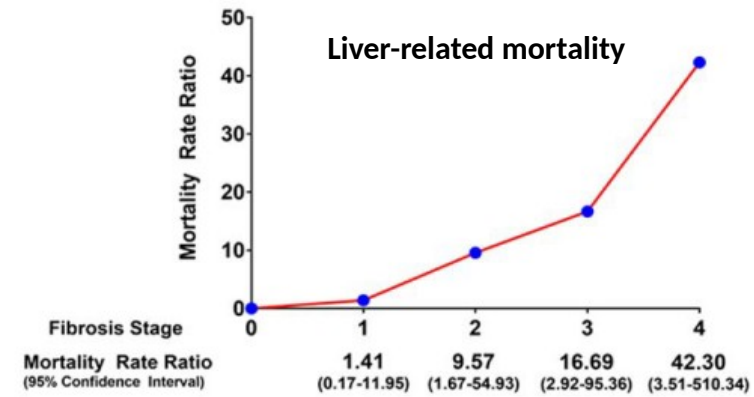
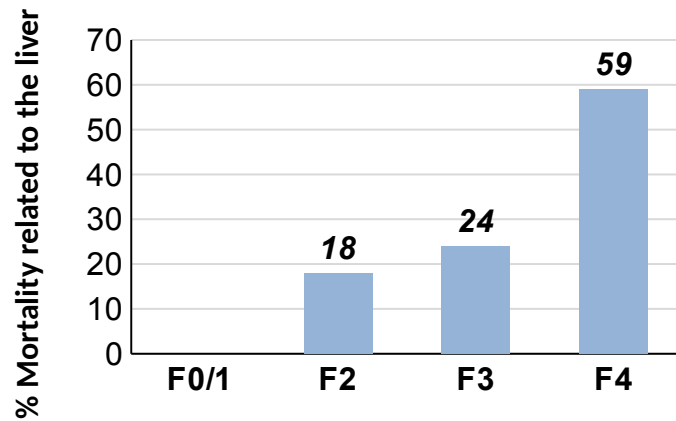
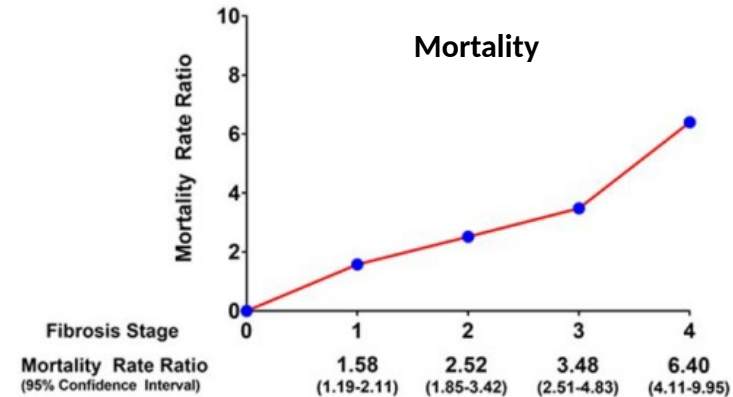
Guangqin Xiao,¹ Sixian Zhu,² Xiao Xiao,³ Lunan Yan,⁴ Jiayin Yang,⁴ and Gang Wu¹

TABLE 2. Summary Sensitivities, Specificities, PPV, and NPV of APRI, FIB-4, BARD Score, NAFLD Score, FibroScan, SWE, and MRE at Various Diagnostic Thresholds for Prediction of SF, AF, and Cirrhosis

	Cutoff Values	No. of Studies (No. of Patients)	Summary Sensitivity, %, Mean (Range)	Summary Specificity, %, Mean (Range)	Summary PPV, %, Mean (Range)	Summary NPV, %, Mean (Range)
FibroScan XL probe						
SF	4.8-8.2	4 (654)	75.8 (57.0-92.0)	64.8 (37.0-90.0)	65.5 (54.0-83.0)	78.8 (72.0-84.0)
AF	5.7-9.3	3 (579)	75.3 (57.0-91.0)	74.0 (54.0-90.0)	58.7 (45.0-71.0)	88.7 (84.0-93.0)
Cirrhosis	7.2-16	4 (654)	87.8 (71.0-100)	82.0 (70.0-91.0)	39.8 (31.0-53.0)	97.8 (95.0-100)
SWE						
SF	2.67-9.4	2 (233)	85.0 (84.0-86.0)	94.4 (88.9-100)	93.9 (87.8-100)	84.8 (82.5-87.0)
AF	3.02-10.6	3 (429)	89.9 (88.2-91.5)	91.8 (90.0-94.0)	88.2 (83.3-93.1)	93.4 (92.6-94.2)
Cirrhosis	3.36	1 (181)	100	85.6	55.2	100
MRE						
SF	3.4-3.62	3 (384)	73.2 (65.7-87.3)	90.7 (85.0-95.7)	83.2 (76.7-88.4)	86.2 (83.6-88.9)
AF	3.62-4.8	5 (628)	85.7 (74.5-92.2)	90.8 (86.9-93.3)	71.0 (67.9-74.5)	93.4 (81.0-98.1)
Cirrhosis	4.15-6.7	3 (384)	86.6 (80.0-90.9)	93.4 (91.4-94.5)	53.4 (44.4-58.8)	98.8 (98.1-99.2)

Liver fibrosis and prognosis in NAFLD

- Meta-analysis, 5 studies
- 1 495 patients
- 17 452 person-years



Question #1

In selection of candidates for bariatric surgery, are you performing in screening of fibrosis ?

1. NASH is a contraindicated for bariatric surgery
2. Cirrhosis is contraindicated for bariatric surgery
3. Fibrosis regression occurs after bariatric surgery
4. Fibrosis is stable after bariatric surgery in 80% of cases after bariatric surgery
5. Bariatric surgery may be proposed in highly selected patient with cirrhosis

Cirrhosis and Bariatric surgery: without selection there is an increased risk

NIS Register (National Inpatients Sample): 1998-2007

- Mortality in patients with compensated cirrhosis (N=3888):
 - 0,9% vs 0,3%
 - Increased risk of mortality x 2-3
- Mortality in patients with de compensated cirrhosis(N=62):
 - 16,3% vs 0,3%
 - Increased risk of mortality x 21

Cirrhosis and Bariatric surgery highly selected

3) Morbidity: Early post-operative complications (<30 days)

Characteristics of the procedure and outcome	Cirrhosis N = 28	No Cirrhosis N = 1996	p
Duration of the surgical procedure	202 min	161 min	0.03
Complication rate	25%	11.4%	0.04
Hemorrhage	3.6%	1.2%	0.2
Infection	14.3%	2.3%	<0.001
Thrombotic event	0	0.65	1
Rhabdomyolysis	7.1%	1.1%	0.04

Patients with cirrhosis	Before surgery	1 year after surgery	p
IMC (kg/m ²)*	49 (45-55)	39 (35-45)	< 0.001 [§]
Bilirubin (mg/L)*	6 (4-8)	5 (4-8.8)	0.09 [§]
PT (%) *	91 (85-98)	88 (81-97)	0.7 [§]
ALT (IU/L) *	39 (33-60)	24 (16.8-39)	<0.001 [§]
AST (IU/L) *	47.5 (32-70)	26 (22-37.5)	0.003 [§]
GGT (IU/L) *	98 (58-160)	54 (28-77)	0.02 [§]
Platelets (G/mm ³) *	173 (111-218)	193 (150-250)	0.2 [§]
HbA1c (%) *	8 (5.6-9)	5.6 (5.4-6.3)	<0.001 [§]
Fasting glucose (mmol/L) *	8.4 (6.8-11.4)	4.8 (4.5-6.4)	<0.001 [§]

Cirrhosis and Bariatric surgery

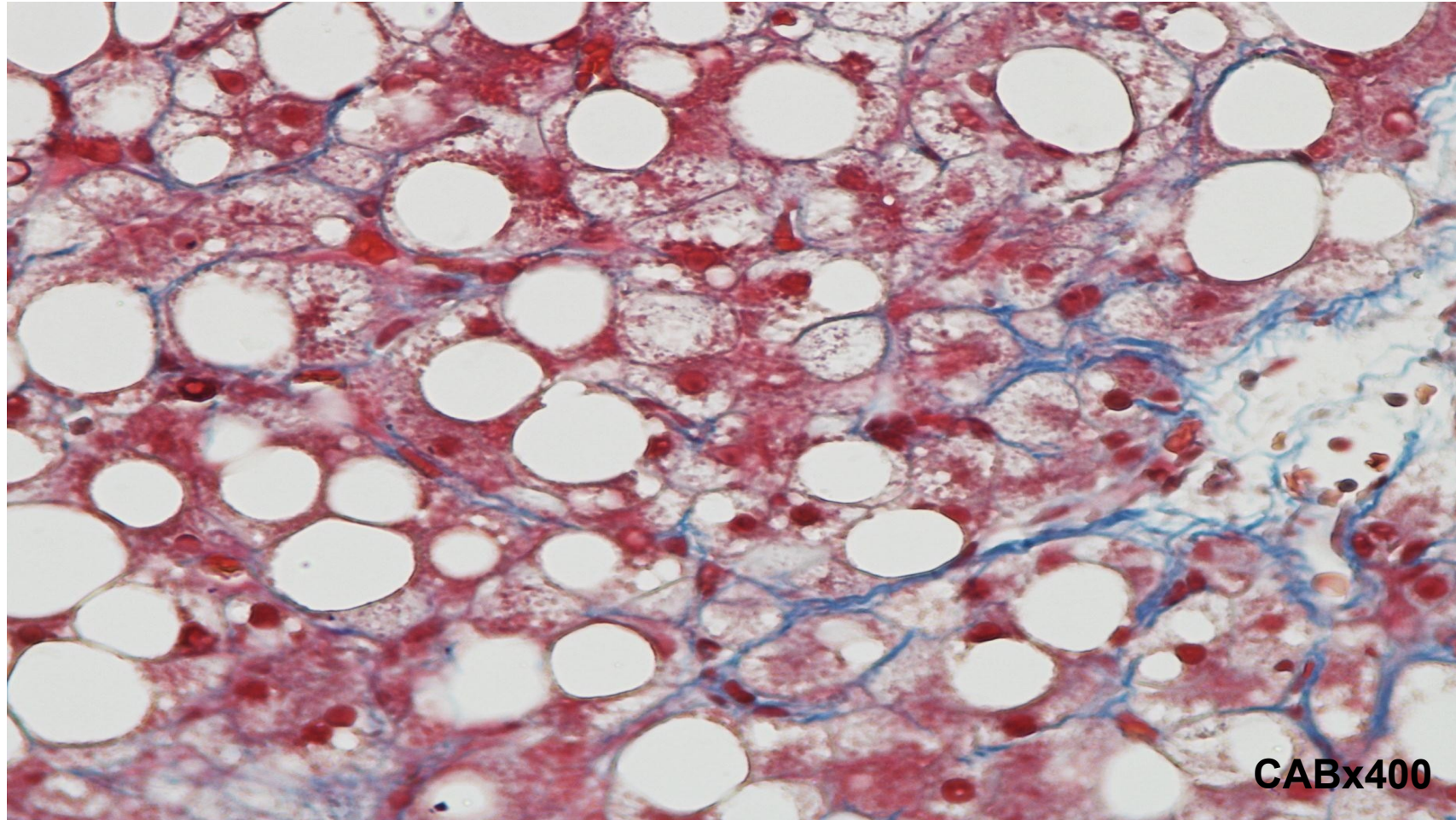
	Cirrhosis	No Cirrhosis	p
Survival (median follow-up 5 y)*	95.5 ± 0.04 %	98.9 ± 0.01%	0.32

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Liver biopsy

Steatosis grade 3

Fibrosis grade 2

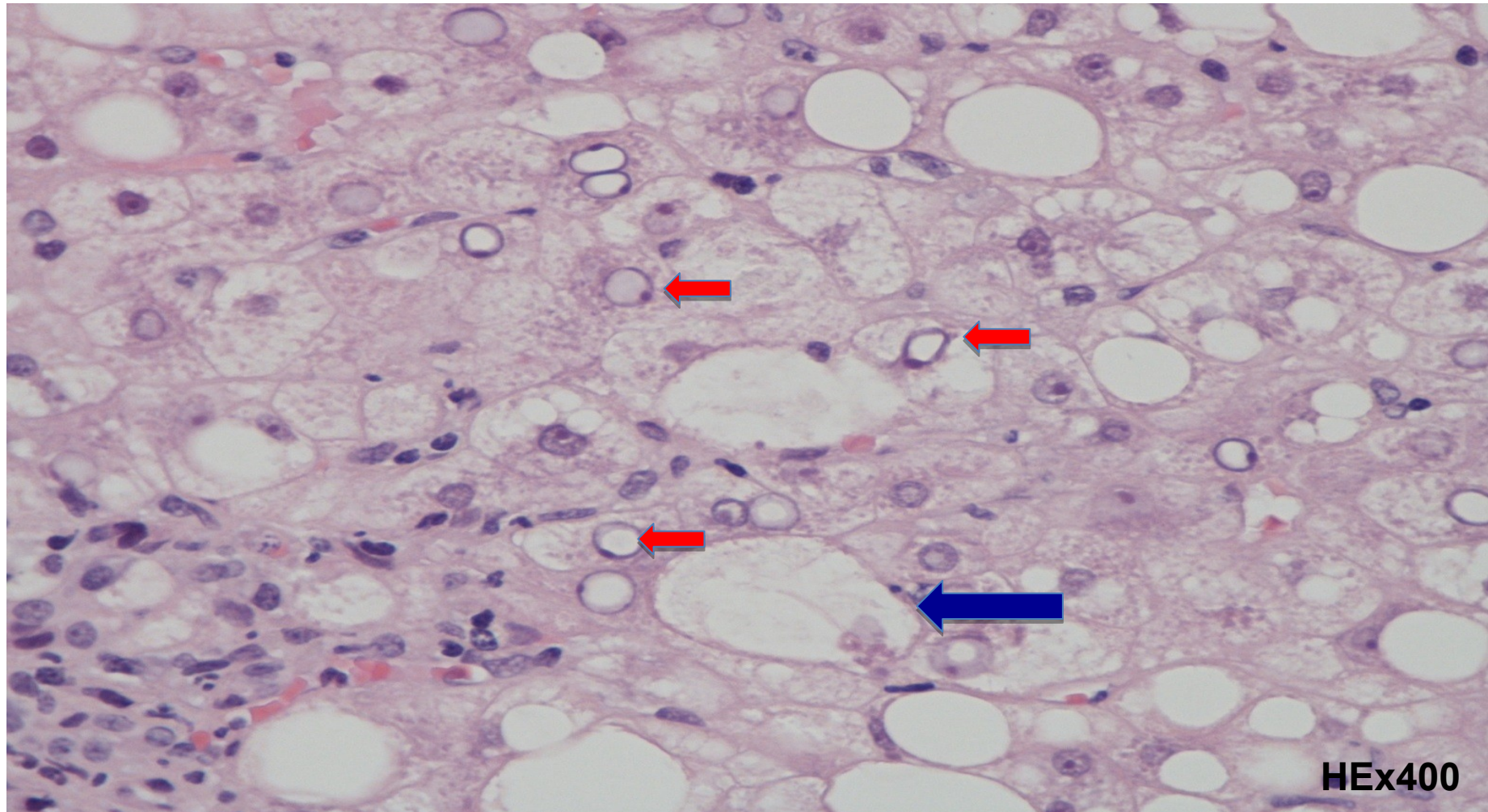


CABx400

Liver biopsy

Glycogenated nuclei

Hepatocyte ballooning grade 2



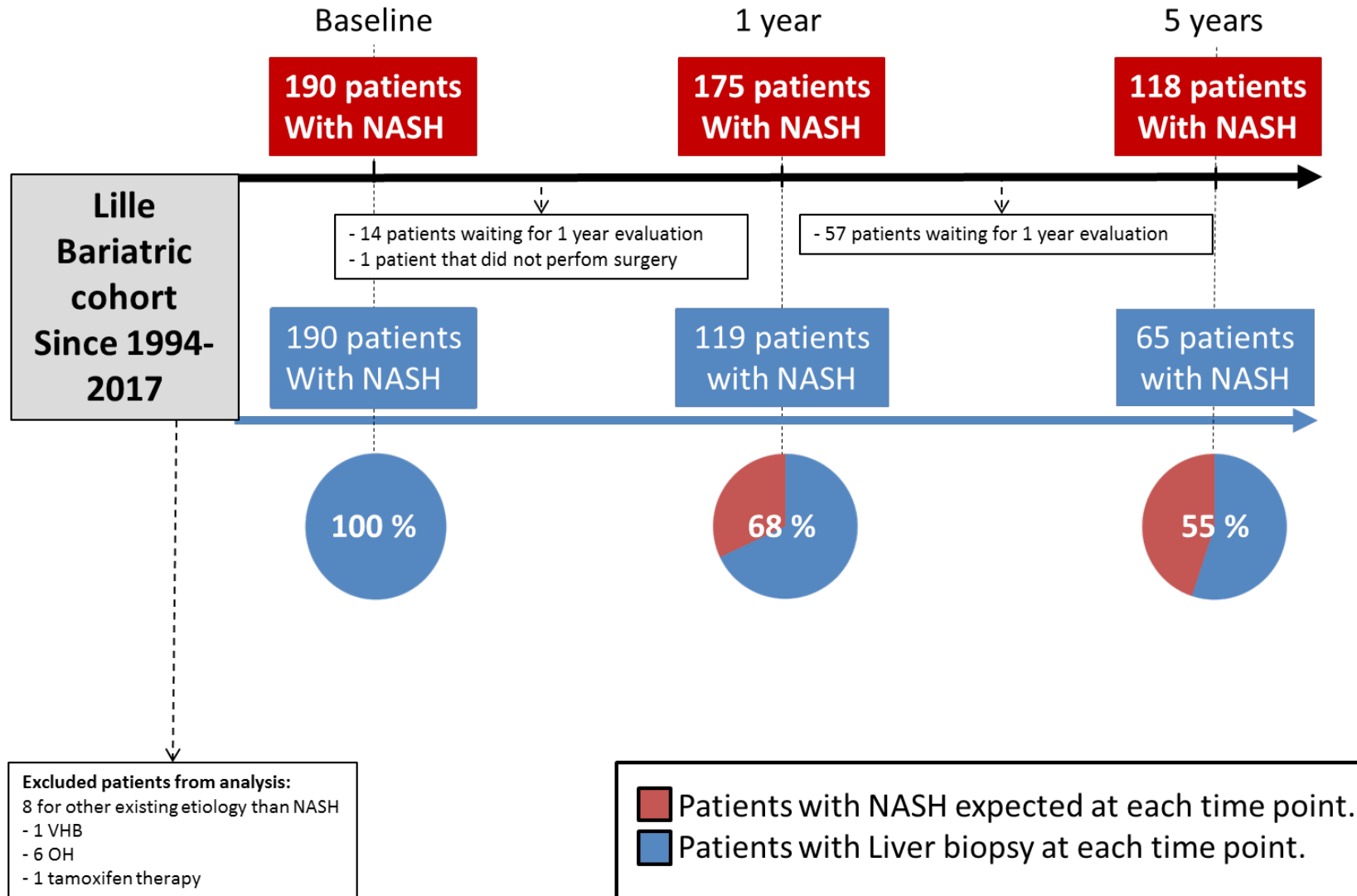
Regression of Fibrosis after Disappearance of Nash in Morbidly Obese Patients: A Prospective Bariatric Surgery Cohort with Sequential Liver Biopsies

G. Lassailly^{1,2}, **R. Caiazzo**^{3,4}, **V. Gnemmi**⁵, **L.C. Tanja Wandji**¹, **H. Verkindt**^{3,4}, **A. Louvet**^{1,2}, **E. Leteurtre**⁵, **F. Artru**^{1,2}, **M. Ningarhari**^{1,2}, **S. Dharancy**^{1,2}, **V. Canva-Delcambre**¹, **F. Pattou**^{3,4}, **P. Mathurin**^{1,2}.

1. Service des maladies de l'appareil digestif, CHRU de Lille, Univ. Lille 2, France; 2. L.I.R.I.C., Inserm, U 995, Univ. Lille 2, France ; 3. Service de chirurgie digestive et endocrinienne, CHRU de Lille, Univ. Lille 2, France ; 4. Inserm, U 1011, Univ. Lille 2, France ; 5. Service d'anatomopathologie, CHRU de Lille, Univ. Lille 2, France

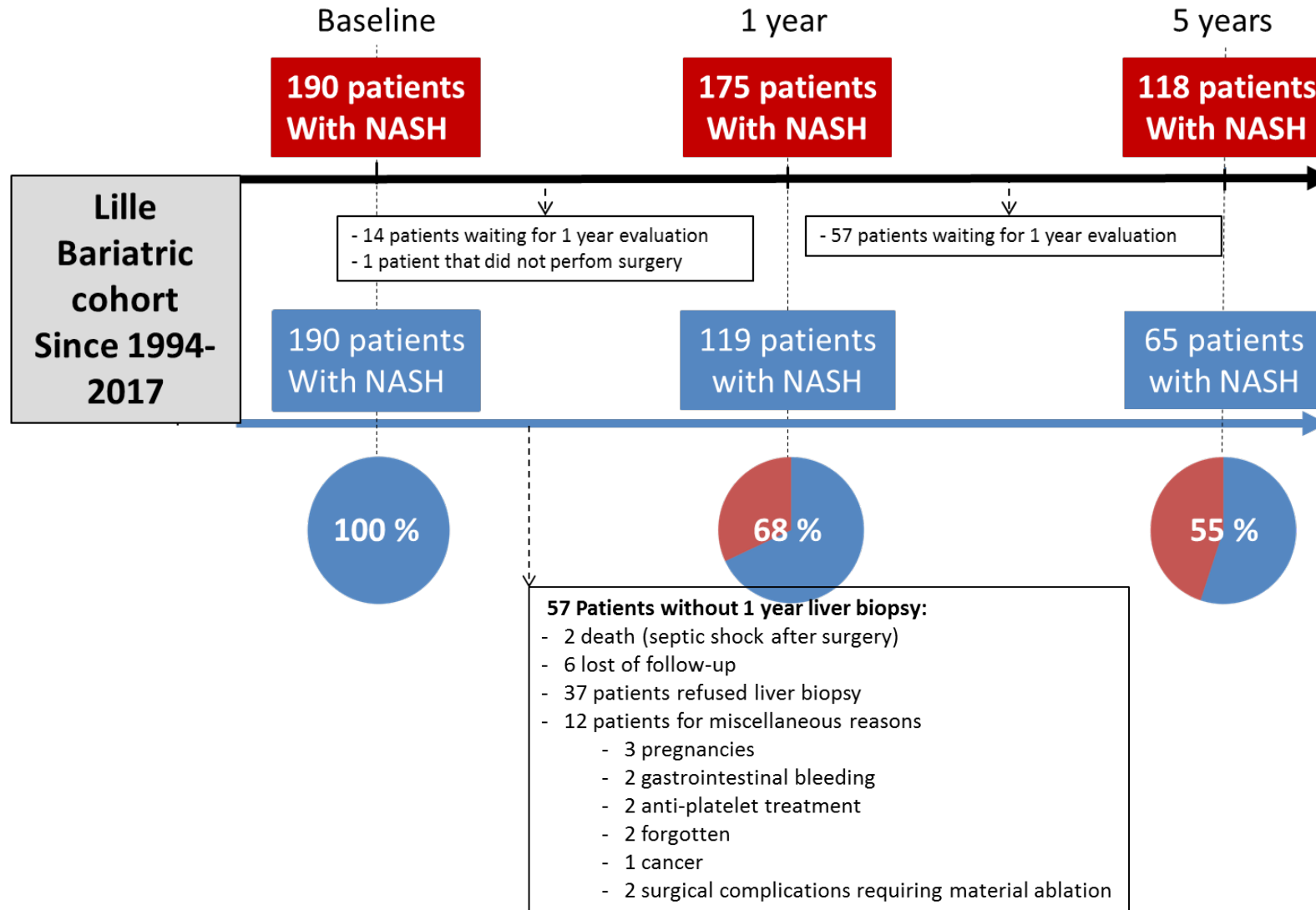
Patients & Methods

Flow Chart



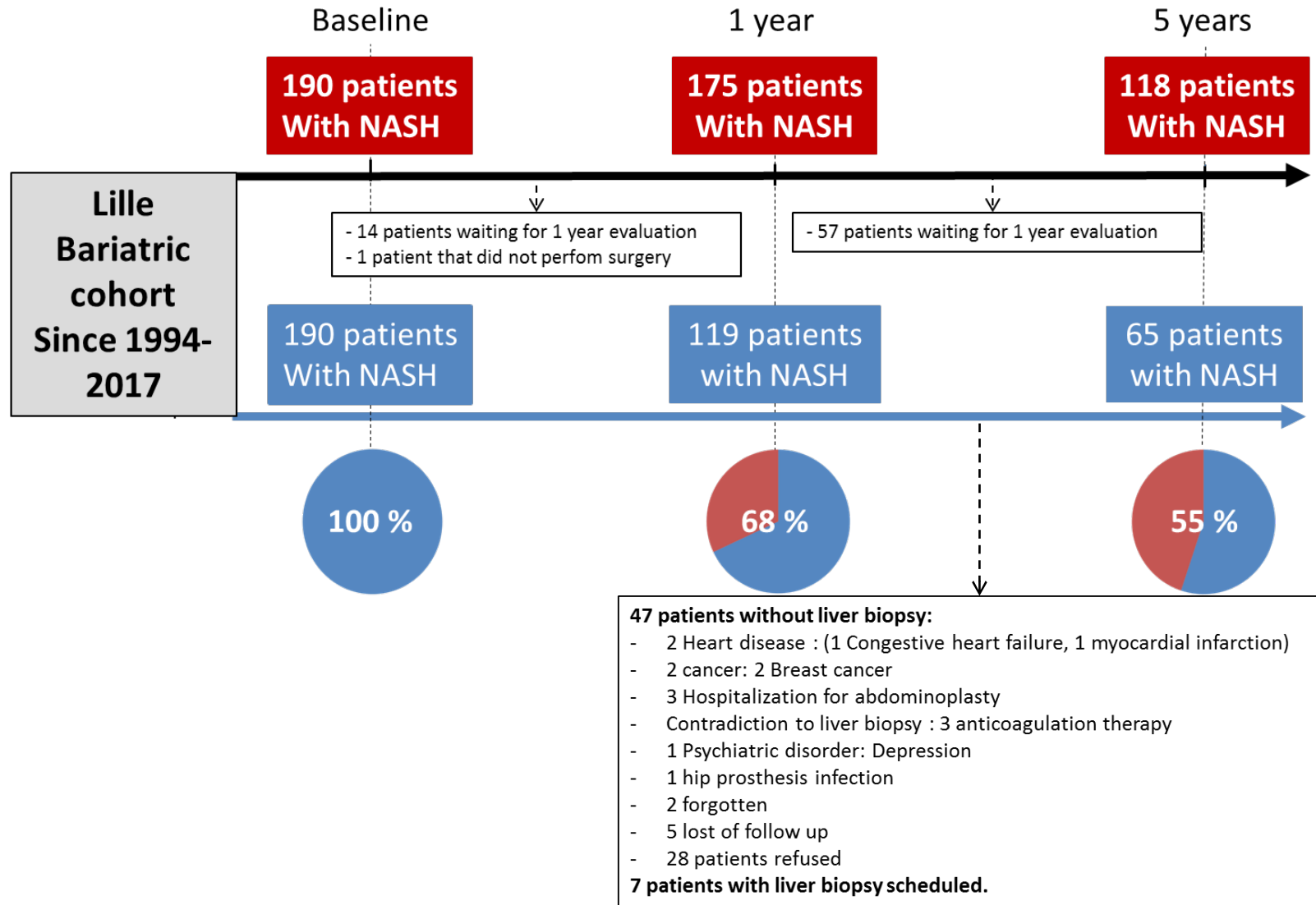
Patients & Methods

Flow Chart



Patients & Methods

Flow Chart

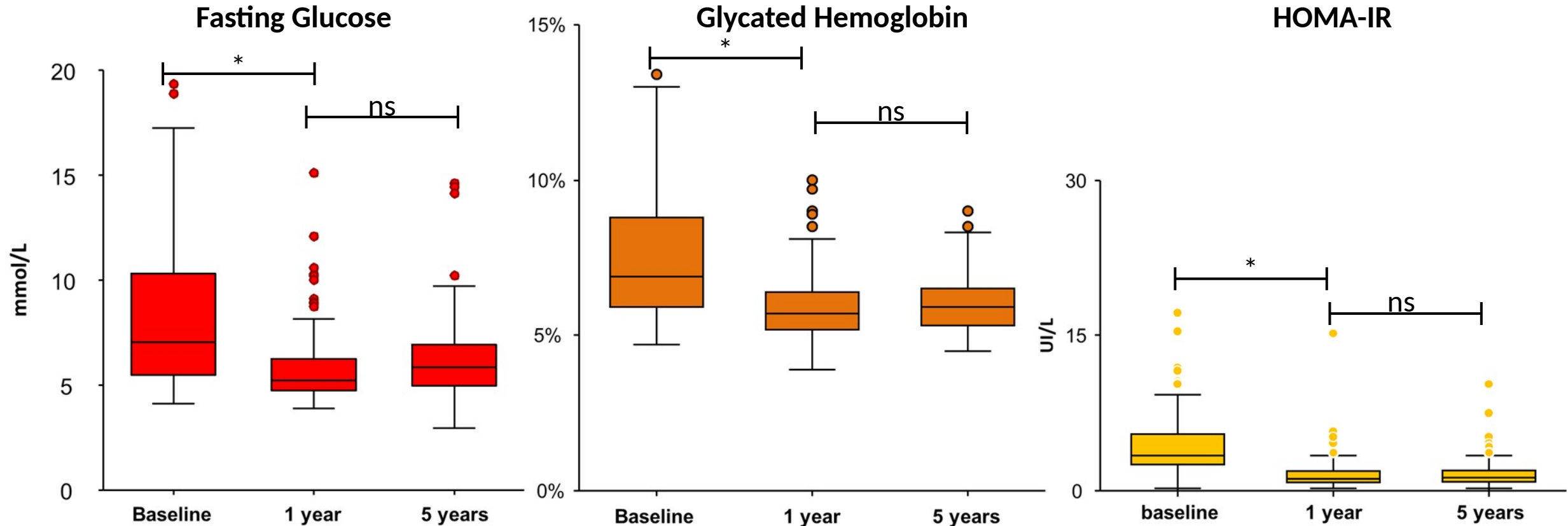


Results

Evolution of glucose metabolism parameters after surgery

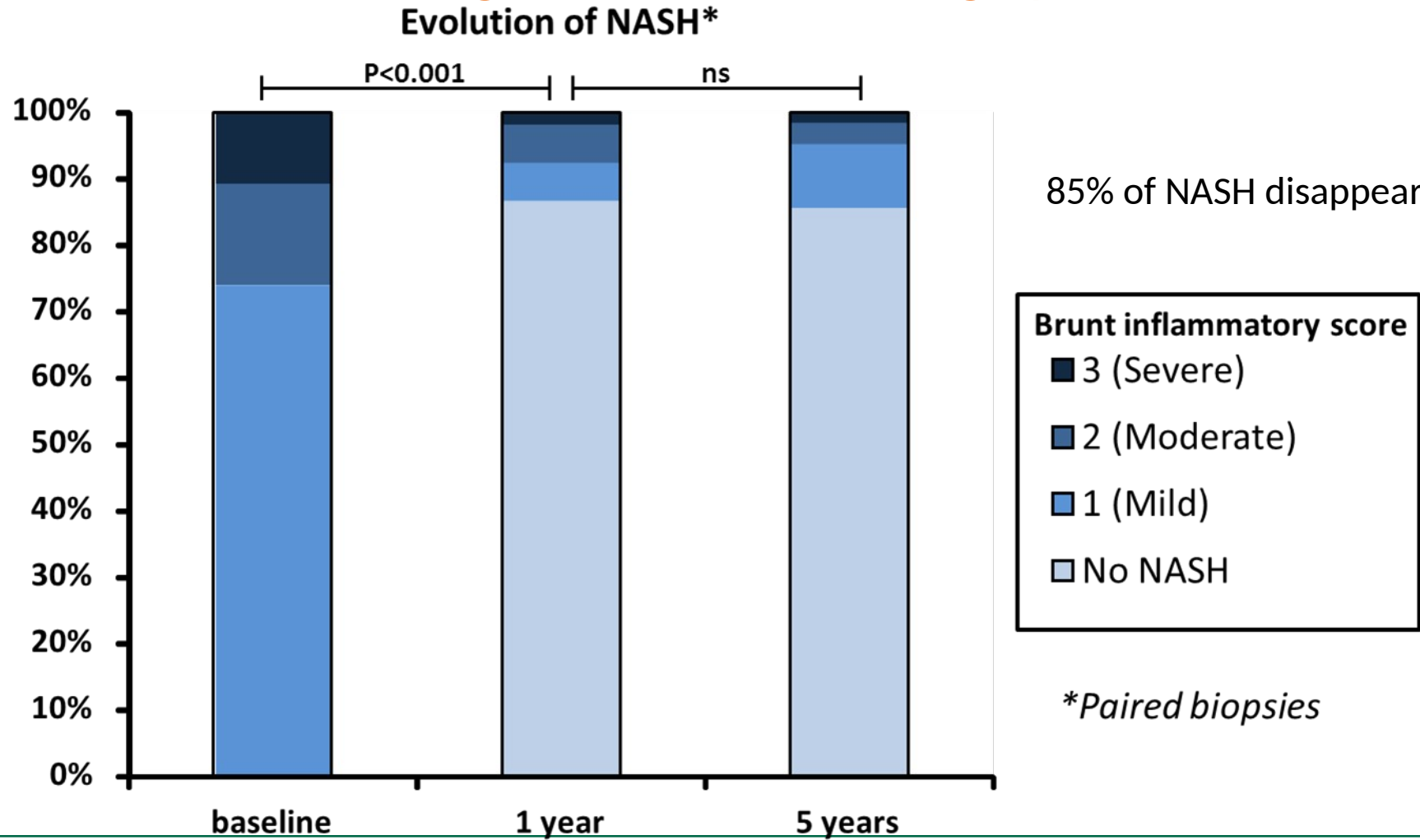
* = $p \leq .05$
ns = $p > .05$

Paired-t test.



Results

Evolution of liver histological features after surgery: NASH and Fibrosis



Results

Evolution after surgery: Histology, NASH and Fibrosis

Fibrosis	baseline	1 year	p	1 year	5 years	p
Fibrosis Brunt score	2 [1-3]	1 [0-2.5]	0.005	1 [0-2.5]	0 [0-1]	0.002

