Liver Biopsy versus Noninvasive Methods – Fibroscan and Fibrotest in the Diagnosis of Non-alcoholic Fatty Liver Disease: A Review of the Literature

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The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing in general population so it is impossible to perform liver biopsy in such a large number of patients to identify those with advanced fibrosis or non-alcoholic steatohepatitis. Liver biopsy has a potential sampling error, it is invasive and prone to complications, so it is no longer considered as mandatory as first line screening tools for chronic liver disease.

The development of non-invasive biomarkers, FibroTest-ActiTest in 2001 and more recently FibroMax, as well as transient elastography (TE) has changed the management of chronic liver disease.

The aim of this review is to summarize the advantages and limits of the available non-invasive biomarkers of liver fibrosis, in comparison with liver biopsy in NAFLD patients.

**Key words:** fatty liver, steato-hepatitis, non-alcoholic, liver fibrosis, liver biopsy, FibroTest, FibroScan.

Nonalcoholic fatty liver (NAFLD) disease represents a spectrum of conditions characterized by micro vesicular hepatic steatosis in the absence of alcohol consumption [1]. There are two main histological patterns of NAFLD: simple steatosis and steatohepatitis (steatosis, inflammation and fibrosis).

Obesity, hyperglycemia, type 2 diabetes mellitus and hypertriglyceridemia are the best known risk factors for NAFLD. The increasing incidence of obesity, currently calculated to approach 40% of the U.S. population by the year 2025, and the attendant rise in insulin resistance and diabetes in up to 10% of obese subjects raise serious concerns for occurrence and progression of liver disease due to NAFLD and NASH [2].

NAFLD is an increasingly recognized cause of liver-related morbidity and mortality.

It is estimated that 20% to 30% of adults in the United States and Western Europe have NAFLD and up to 10% of these people, which means about 2% to 3% of adult population, may meet the diagnosis criteria for progressive lesion of nonalcoholic steatohepatitis (NASH) [3].

The presence of severe fibrosis, the most worrisome feature in liver biopsies in patients with NASH, has been noted in 15%–50% of patients, and cirrhosis has been documented in 7%–26% of patients at the time of diagnosis. [4] Age, activity of steatohepatitis, and established fibrosis predispose to cirrhosis, which has a 7- to 10-year liver-related mortality of 12% to 25%. Many cases of cryptogenic cirrhosis are likely end stage NASH which currently accounts for 4% to 10% of liver transplants [5].

Differentiation between NAFLD and NASH requires histopathologic evaluation. A composite index for distinguishing steatosis from NASH was calculated by summing the risk factors of age > 50 years, female gender, AST > 45 IU/l, BMI > 30 kg/m2, AST/ALT ratio > 0.80, Hyaluronic acid > 55 mcg/l. The presence of three or more risk factors had a sensitivity, specificity, positive and negative predictive value of 73.7%, 65.7%, 68.2% and 71.4% respectively [6].

Powell et al. [7] originally proposed 3 criteria for the diagnosis of NASH: (1) a histological picture of steatohepatitis, (2) convincing evidence of minimal or no alcohol consumption (< 40 g/wk), and (3) absence of serologic evidence of viral hepatitis. Although these criteria are used widely in clinical practice, each criterion has specific limitations that bear discussion.

Two recent studies derived scores from clinical and laboratory values to predict fibrosis, [8] the BAAT (BMI, ALT, Age, Triglycerides) score or the
presence of NASH [9] and the HAIR (Hypertension, ALT, Insulin Resistance) score in obese subjects. These scoring systems are subjects of biases and controversies, so until recently, liver biopsy remained the most reliable method to assess the severity and progression of fibrosis in NAFLD patients.

In this paper we will review the accuracy and the place of liver biopsy versus non-invasive methods for the diagnosis and staging of NAFLD and NASH.

**LIVER BIOPSY**

Until recently, the consensus in many conference statements recommended and considered liver biopsy the “gold standard” in the management of almost all patients with chronic liver disease related to hepatitis B, C, alcoholic and non-alcoholic fatty liver disease.

Liver biopsy allows the diagnosis of the type of NAFLD (simple steatosis or steatohepatitis), and provides information on the severity of the disease (necroinflammatory activity and fibrosis stages).

A scoring system for grading and staging the histological lesions in NAFLD was proposed by Brunt et al. (Table I) [10].

Equally important, liver biopsy is the gold standard for measuring changes in disease severity in single or groups of patients, whether induced by treatment, diet or lifestyle modifications or occurring spontaneously throughout the natural course of the disease. Therefore, the information provided by liver biopsy is important and often determinant in the management of patients with NAFLD [11].

### Table 1
Grading and staging of NAFLD

<table>
<thead>
<tr>
<th>Grading NAFLD</th>
<th>Staging NAFLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macro vesicular steatosis</td>
<td>1. Stage 1</td>
</tr>
<tr>
<td>Grade 0</td>
<td>Zone III perisinoidal/pericellular fibrosis; focally or extensively present</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Zone III perisinoidal/pericellular fibrosis with focal or extensive periportal fibrosis</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Zone III perisinoidal/pericellular fibrosis and portal fibrosis with focal or extensive bridging fibrosis</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Necroinflammatory activity</td>
<td>2. Stage 2</td>
</tr>
<tr>
<td>Grade 0 (mild)</td>
<td>Steatosis up to 60%, occasional ballooned hepatocyte (mainly zone 3), scattered intra-acinar neutrophils (PMN) +/– lymphocytes, no or mild portal inflammation</td>
</tr>
<tr>
<td>Grade 2 (moderate)</td>
<td>Steatosis of any degree, obvious zone III ballooning degeneration, intra-acinar PMNs, zone III perisinoidal fibrosis may be present, mild to moderate, portal and intra-acinar inflammation</td>
</tr>
<tr>
<td>Grade 3 (severe)</td>
<td>Panacinar steatosis, widespread ballooning, intra-acinar inflammation, PMNs associated with ballooned hepatocytes, mild to moderate portal inflammation</td>
</tr>
</tbody>
</table>

The place of liver biopsy in the management of NAFLD patients is summarized by the following proposed algorithm (Fig. 1) [12].

An important limitation of liver biopsy is sampling variability. The size of the biopsy specimen, which varies between 1 and 3 cm in length and between 1.2 and 2 mm in diameter, represents 1/50,000 of the total mass of the liver. Usually, for evaluation of diffuse liver disease, a specimen of 1.5 cm in length is adequate for a diagnosis to be made [13].

Recently, there are several studies demonstrating that sampling variability of liver biopsy has the potential to alter significantly the diagnosis and staging of NAFLD.

Ratziu et al. [14] demonstrated that hepatocyte ballooning, which is essential to the diagnosis of NASH, can be absent on one sample and present on the other in 18% of patients, in a study of 51 patients (2 liver biopsy samples collected, samples size > 15 mm length). Comparing the results of one sample
Liver biopsy vs. noninvasive methods

Fig. 1. – Management algorithm for NAFLD.

with the other, the negative predictive value for hepatocyte ballooning was only 0.78, meaning that the probability of finding ballooning on an additional biopsy is as high as 22%. In the same study, 22% of patients had perisinusoidal fibrosis on one sample but not on the other. The negative predictive value of perisinusoidal fibrosis was 60%, meaning that there is a 40% chance of detecting perisinusoidal fibrosis if an additional biopsy is collected.

Another study of 50 patients, [15], demonstrated that steatosis, lobular inflammation and fibrosis scores were significantly higher when 3 samples of liver biopsy were analyzed, compared with 2 samples. In the same study, the length of the biopsy sample correlated with the percentage of patients found to have definite NASH (29%, 46%, 56% and 65% in biopsies measuring < 10mm, 10–14 mm, 15–24 mm, and ≥ 25 mm; P<0.001).

It has also been shown that NASH biopsy specimen longer than 1.6 cm had a significantly lower heterogeneity of fibrosis than biopsy specimens 1.6 cm or shorter [16]. The same study demonstrated that fibrosis heterogeneity is significantly greater in NASH than in HCV patients.

Sampling error should not be regarded as an artifact of liver biopsy, but rather as the reflection of the heterogeneity of the distribution of pathologic lesions throughout the liver parenchyma. The mechanism responsible for fibrosis heterogeneity in NASH is not completely elucidated. The potential regional factors operating at the regional, lobular (acinar) levels responsible for this heterogeneity might be the intrahepatic free fatty acid levels, the oxygen saturation of sinusoidal blood and the sinusoidal blood levels of antioxidants received from the gut [17][18].

Sampling variability is an important factor to be considered in the assessment of histological progression of nonalcoholic fatty liver disease. A critical analysis of natural history studies, [11], showed an improvement of steatosis (47% vs. 8%), significantly higher than expected from sample variability but no change in activity grade or ballooning. There was only a marginal effect on fibrosis with no convincing demonstration of worsening of fibrosis, a conclusion contrary to what individual studies have claimed.

Moreover, liver biopsy is an invasive procedure, prone to the complications. Up to 30% of patients experience pain after the procedure, severe complications occur in 0.3% of patients, and death in 0.01% [19][20].

Due to the high prevalence of NAFLD in general population, [3] the limitations of biopsy [17–20], and the developing of reliable non-invasive tests, liver biopsy is no longer considered as mandatory as first line screening tools for chronic liver disease.

NONINVASIVE BIOMARKERS FOR SCREENING FOR FIBROSIS – FIBROTEST, FIBROMAX EXPERIENCE

The development of FibroTest (FT) – ActiTest (AT) (BioPredictive, Paris, France) in 2001 and its widespread use in clinical practice has changed the management with chronic liver disease [21].

A nationwide survey conducted recently in France revealed that among 546 hepatologists, 81% used noninvasive biomarker FibroTest – ActiTest and 32% used elastography (Fibroscan), with a decrease
in the use of liver biopsy for more than 50% of the patients with chronic hepatitis C, with a subsequent increase in the number of patients treated [22].

In order to improve this diagnostic tool, three new simple tests were developed to provide an estimate of associated or worsening factors of fibrosis: liver steatosis (SteatoTest), nonalcoholic steatohepatitis (NashTest) and alcoholic steatohepatitis (AshTest). More recently developed FibroMax, is a method of concomitant calculation of all these fibrosis-related tests in a single procedure [23].

FibroTest (FT), the fibrosis index, includes alpha 2 macroglobulin, apolipoprotein A1, haptoglobin, total bilirubin and GGT adjusted for age and gender. FT score ranges from 0 to 1. SteatoTest (ST) combines the FT-AT components plus BMI, glucose, triglycerides and cholesterol adjusted for age and gender. ST score ranges from 0 to 1. NashTest (NT) combines FT-AT components plus height, weight, AST, glucose, triglycerides, cholesterol and ST adjusted for age and gender. The five indices are summarized in Table II.

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>FibroTest</th>
<th>ActiTest</th>
<th>SteatoTest</th>
<th>NashTest</th>
<th>FibroMax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Gender</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Alpha 2 macroglobulin, g/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Haptoglobin, g/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Apolipoprotein A1, g/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Total bilirubin, µmol/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>GGT, IU/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>ALT, IU/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>AST, IU/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Height, m</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

The conversion between FibroTest score and fibrosis stages, SteatoTest Score and steatosis grade, and between NashTest score and nonalcoholic steatohepatitis categories in patient with NAFLD are summarized in Table III and Fig. 2 [24].

In a series of 267 patients [26] with suspected NAFLD, a FT cutoff value of 0.30 had 77% sensitivity and 90% negative predictive value for advanced fibrosis. An FT score of 0.70 had 98% specificity and 76% positive predictive value. FT was highly sensitive for the detection of bridging fibrosis or cirrhosis (F3F4): an FT equal to or higher than 0.30, had 92% sensitivity and 98% negative predictive value for F3F4. In this study, an increased level of alpha 2 macroglobulin was correlated with advanced fibrosis and insulin resistance and a decreased level of apolipoprotein A1 was correlated with necrosis, polymorphonuclear infiltrate and Mallory bodies. The same study population was used for the validation of NashTest for nonalcoholic steatohepatitis. The NashTest Sp for Nash was 94% (PPV = 66%) and Se was 33% (NPV = 81%); for borderline Nash or Nash, Sp was 50% (PPV = 74%) and Se was 88% (NPV = 72%) [27].

SteatoTest (ST) was separately analyzed in a study of 884 subjects divided into four groups – hepatitis C, former hepatitis C, alcoholic liver disease and control [28]. A cut-off value of ST of 0.30 had 90% sensibility and a cut-off of 0.72 had 90% specificity permitting to achieve a useful predictive value, 93% NPV and 63% PPV for a steatosis prevalence of 30%.

The usefulness of non-invasive biomarkers in screening for liver fibroses was also demonstrated in patients with hyperlipidaemia and diabetes, both components of metabolic syndrome. Advanced fibrosis was identified by FT in 53 of 1909 (2.8%) hyperlipidaemic patients, advanced steatosis in 569 of 1893 (30.1%), and NASH in 132 of 1893 (7%) hyperlipidaemic patients. The authors found a
A meta-analysis of 30 studies, which pooled 6378 subjects with both FT and biopsy (3501 HCV, 1457 HBV, 267 NAFLD, 429 ALD, and 724 mixed), demonstrated that FT is an effective alternative for liver biopsy and its value is

significant association between the number of metabolic syndrome components and liver disease prevalence, the highest for type 2 diabetes: 66% advanced steatosis, 24% NASH and 6% advanced fibrosis [29, 30].
similar for the diagnosis of intermediate and extreme fibrosis stages [31].

Table III
Conversion between FibroTest score and fibrosis stages (Panel A), SteatoTest score and steatosis grades (Panel B) and between NashTest score and nonalcoholic steatohepatitis categories (Panel C) in patients with non-alcoholic liver disease

<table>
<thead>
<tr>
<th>Panel A</th>
<th>FibroTest Fibrosis stage (METAVIR scoring system)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.75–1.00</td>
<td>F4</td>
</tr>
<tr>
<td>0.73–0.74</td>
<td>F3–F4</td>
</tr>
<tr>
<td>0.59–0.72</td>
<td>F3</td>
</tr>
<tr>
<td>0.49–0.58</td>
<td>F2</td>
</tr>
<tr>
<td>0.32–0.48</td>
<td>F1–F2</td>
</tr>
<tr>
<td>0.28–0.38</td>
<td>F1</td>
</tr>
<tr>
<td>0.22–0.27</td>
<td>F0–F1</td>
</tr>
<tr>
<td>0.00–0.21</td>
<td>F0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Panel B</th>
<th>SteatoTest Steatosis percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.69–1.00</td>
<td>S2S3 &gt;32%</td>
</tr>
<tr>
<td>0.57–0.68</td>
<td>S2 6–32%</td>
</tr>
<tr>
<td>0.38–0.56</td>
<td>S1 1–5%</td>
</tr>
<tr>
<td>0.00–0.37</td>
<td>S0 0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Panel C</th>
<th>NashTest Nonalcoholic steatohepatitis class</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.75</td>
<td>Nonalcoholic steatohepatitis (NASH)</td>
</tr>
<tr>
<td>0.50</td>
<td>Borderline NASH</td>
</tr>
<tr>
<td>0.25</td>
<td>No NASH</td>
</tr>
</tbody>
</table>

Munteanu et al., [24]

There are several limitations of Fibromax biomarkers, with the non-interpretability of results in about 5% of cases [32]. The most frequent cause leading to false negative result was high haptoglobin in acute inflammation or sepsis. The most frequent cause of false positive results was extremely low haptoglobin associated with intravascular hemolysis and high bilirubin in hemolysis and Gilbert disease [24][32].

**TRANSIENT ELASTOGRAPHY**

Transient elastography (FibroScan, EchoSens, Paris) is a recently developed technique for the detection of fibrosis by measuring liver stiffness in patients with chronic liver disease.

Briefly, an ultrasound transducer probe is mounted on the axis of a vibrator. The principle is one in which a painless, mechanical impulse is delivered to the skin above the liver, using a low-frequency elastic wave at 50 MHz. This produces a wave of mechanical deformation that propagates toward the liver. Pulse-echo ultrasound acquisition is used to follow the propagation of the shear wave and to measure its velocity, which is directly related to tissue stiffness: the stiffer the tissue, the faster the shear wave propagates [33–35].

The results are expressed in kilopascals and vary from 2.5 to 75 KPa, corresponding to the median value of 10 successful acquisitions in the same patients. TE measures liver stiffness in a volume that approximates a cylinder 1 cm wide and 4 cm long, between 25 mm and 65 mm below the skin surface. Finally, hepatic elastography reports on around 1/500th of the liver’s total mass, versus around 1/50 000th for a liver biopsy [36][37].

The main advantages [38][39] of transient elastography compared with other methods used in the assessment of liver fibrosis are:
- it is a non-invasive, painless method, easy to perform at the bedside or in outpatients clinic
- short time of examination
- the results are not modified with cardiac or respiratory movement
- the results are not influenced by associated co-morbidities
- no inter-observer variability
- the fibrosis is estimated in a liver volume that exceeds 150–400 times those obtained by liver biopsy

The method has been validated in several chronic liver diseases: viral hepatitis C [40–43], viral hepatitis B [44][45], HCV-HIV co-infection [46][47], liver transplant [48–51], cholestatic liver disease [52], hemochromatosis [53].

In a systematic review of 50 studies, Friedrich-Rust et al. reported summary AUROCs (95% CI) for the diagnosis of septal fibrosis (≥ F2), bridging fibrosis (≥ F3) and cirrhosis (F4) of 0.84 (0.82–0.86), 0.89 (0.88–0.91), and 0.94 (0.93–0.95), respectively [54].

Until now there are just a few studies published in the literature to investigate the role of transient elastography in the assessment of fibrosis stages in NAFLD patients [55–57]. AUROC values were 0.93–0.97 (fibrosis ≥ F1), 0.86–0.99 (fibrosis ≥ F2), 0.90–1 (fibrosis ≥ F3) and 0.99 (cirrhosis). (Table IV).

The efficacy and cutoff values of liver stiffness measurement for the detection of fibrosis stages should be reevaluated in NAFLD patients. Further cohort studies are needed in NAFLD patients to establish if liver stiffness is correlated only with fibrosis stages or there is also a correlation with steatosis or necroinflammatory activity.
Liver biopsy vs. noninvasive methods

Table IV

<table>
<thead>
<tr>
<th>Fibrosis Stages (Brunt)</th>
<th>Author</th>
<th>Cutoff (kPa)</th>
<th>Sn(%)</th>
<th>Sp(%)</th>
<th>PPV(%)</th>
<th>NPV(%)</th>
<th>AUROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>F≥1</td>
<td>Yoneda [56]</td>
<td>5.9</td>
<td>86</td>
<td>89</td>
<td>97</td>
<td>59</td>
<td>0.93</td>
</tr>
<tr>
<td></td>
<td>Nobili [57]</td>
<td>5.1</td>
<td>97</td>
<td>91</td>
<td>97</td>
<td>91</td>
<td>0.97</td>
</tr>
<tr>
<td>F≥2</td>
<td>Yoneda [56]</td>
<td>6.6</td>
<td>88</td>
<td>74</td>
<td>79</td>
<td>85</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>Nobili [57]</td>
<td>7.4</td>
<td>100</td>
<td>92</td>
<td>80</td>
<td>100</td>
<td>0.99</td>
</tr>
<tr>
<td>F≥3</td>
<td>Yoneda [56]</td>
<td>9.8</td>
<td>85</td>
<td>81</td>
<td>64</td>
<td>93</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>Nobili [57]</td>
<td>10.2</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>F4</td>
<td>Yoneda [56]</td>
<td>17.5</td>
<td>100</td>
<td>97</td>
<td>75</td>
<td>100</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>Nobili [57]</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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</tr>
</tbody>
</table>

The main limitation of TE in clinical practice is the impossibility of obtaining any liver stiffness measurements in around 5% of cases, mainly obese patients, which may represent a concern for its use in NAFLD patients [58].

Additional limitations of TE include: ascites (the vibrations are not transmitted in the liquid), the qualities of liver parenchyma and intrahepatic structures, the presence of large vascular structures in the acquisition window [34].

In a study of 2114 patients, Foucher [59] et al. demonstrated that liver stiffness could not be measured in 4.5% of cases; the only factor of error identified by multivariate analysis was the body mass index of more than 28 kg/m².

TE is difficult to perform in obese patients, because the vibrations are attenuated in the subcutaneous tissue. This is a frequent situation in NAFLD patients [1][60][61]. There is a 4–6% failure rate of TE in NAFLD patients, [56][57], but the results should be interpreted with caution due to the limited external validity of reported studies (small samples size, two studies were conducted in a Japanese and Chinese population and one in a pediatric population, with a low mean BMI).

To overcome these limitations in obese patients, a new probe for FibroScan was designed. This new probe specially designed for obese patients has a central US frequency of 2.5 MHz (as compared with 5 MHz of the usual probe) and a measurement depth of 35–75 mm (as compared with 25–65 mm). In patients with a BMI_30 kg/m², 49% of patients who cannot be measured with the usual probe can be measured with the new probe choosing the optimized measurement point with an ultrasound imaging system [62].

TE might be an alternative to liver biopsy in staging fibrosis, but it cannot establish the etiology of liver disease and cannot distinguish between steatosis and steatohepatitis [63][64].

CONCLUSION

Due to the epidemics of obesity and diabetes, the screening for liver fibrosis in NAFLD patients will be an important medical challenge in the years to come.

Liver biopsy is still useful, but not as a first line estimate of liver injury in HCV, HBV, NAFLD and ALD, the most frequent chronic liver diseases. Biopsy is still indicated when noninvasive methods like FT and Fibroscan (FS) are discordant or not applicable.

In France, non-invasive biomarkers (FT and FS) were approved by the Health Authorities and the component costs have been covered by social security since 2002, while reimbursement of the algorithms has been approved since 2006 [65].

This dramatically decreased the number of liver biopsies, from 1200 per year in 2000 to 300 per year in 2007, while the number of FibroTest and FibroScan investigations performed in 2007 was 7000 and 3000 respectively (results reported by Pitié-Salpêtrière working group) [66].

Deoarece prevalenţa steatozei hepatice non-alcoolice (SHNA) este în continuă creştere în populaţia generală, este imposibil să se efectueze biopsie hepatică la toţi aceşti pacienţi în scopul identificării celor cu stadii avansate de
fibroză. Noile ghiduri clinice nu mai recomandă biopsia hepatică de primă intenție în screening-ul afecțiunilor hepatice cronice, deoarece metoda este invizivă și susceptibilă la complicații. În plus, s-a demonstrat că există o variabilitate a rezultatelor obținute în funcție de caracteristicile fragmentului de biopsie analizat.

Dezvoltarea markerilor non invazivi – FibroTest-Actitest (2001), și mai recent FibroMax precum și posibilitatea aprecierii prin elastografie a gradului de fibroză hepatică, a determinat schimbarea algoritmului diagnostic al afecțiunilor hepatice cronice. Scopul acestei lucrări este acela de a realiza o sinteză a principalelor avantaje și dezavantaje ale metodelor neinvazive comparativ cu biopsia hepatică în aprecierea gradului de severitate a afectării hepatice la pacienții cu steatoză hepatică non-alcoolică.

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