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Use of Fibroscan Liver Elastography in the Rapid Diagnosis and Monitoring of MASLD Treatment

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Abstract

Steatohepatitis associated with metabolic dysfunction is the most common chronic liver disease worldwide, usually detected incidentally and affecting nearly 30% of the adult population and nearly 10% of the child population. It is one of the leading causes of hepatocellular carcinoma, cirrhosis and liver transplantation in developed countries. It is also a significant factor in the development of cardiovascular disease, which is the leading cause of death in this group of patients. It is estimated that the number of patients with MASLD could double by 2030. Its long-standing asymptomatic nature means that at the time of diagnosis it is usually an advanced disease, with advanced liver fibrosis, and it is not uncommon for the diagnosis to be made at the stage of cirrhosis or liver cancer or extrahepatic complications. Hence, non-invasive diagnostic methods are still being sought that will detect minimal steatosis of the hepatocytes, still in the subclinical phase in patients at risk - obesity, pre-diabetes or type 2 diabetes, lipid disorders or hypertension - faster than classic ultrasound. Such tools include FibroScan® liver elastography, which enables the detection of hepatic steatosis at its early stage and the assessment of liver fibrosis. It is also used to monitor treatment and estimate possible complications. It can also be used in the paediatric population. This paper discusses the feasibility of Fibro Scan as a diagnostic and treatment monitoring tool for MASLD, its advantages, potential disadvantages, how the test can be performed and interpreted, and the use of specialised scales based on the FibroScan® test and selected laboratory parameters to assess the development of liver complications, as well as its place in current guidelines of scientific societies.

Keywords: MASLD; Steatosis; Fibroscan; Liver Elastography; Cirrhosis.

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease worldwide, detected most often incidentally and affecting nearly 30% of the adult population and nearly 10% of the child population. It is one of the leading causes of hepatocellular carcinoma, cirrhosis and liver transplantation in the developed world - the first cause of cirrhosis and liver transplantation in women in the USA and the second in men. Also, in Europe, there is a noticeable increase in end-stage cirrhosis of MASLD aetiology and liver transplantation due to this cause. It is also an important factor in the development of cardiovascular disease. On the one hand, it is the most common liver disease in the world, with a year-on-year increase in prevalence in both adults and the paediatric population, which is very worrying, as it is estimated that the number of patients with MASLD could double by 2030.On the other hand, epidemiological data are still underestimated due to the low awareness of patients as well as physicians regarding early detection of the disease and the lack of basic screening. The long-term asymptomatic course means that it is not uncommon for MASLD to be diagnosed at the stage of advanced liver fibrosis or cirrhosis or only after a cardiovascular incident, which is the most common cause of death in this group of patients.

Hence, it seems necessary to pay attention to patients at risk of developing MASLD, i.e. those with excessive body weight - overweight, abdominal obesity or obesity, type 2 diabetes in or pre-diabetes, hypertension or lipid disorders, and in these patients screening for hepatic steatosis should be performed periodically. MASLD can occur in about 50% of dyslipidaemic patients, in 70% of those with type 2 diabetes, but up to 90% in patients with giant obesity. Some of these individuals, especially patients with type 2 diabetes, may have advanced liver fibrosis, while some will develop cirrhosis. Some patients will develop primary hepatocellular carcinoma (HCC), the incidence of which is independent of the progression of liver fibrosis to cirrhosis, as MASLD risk factors such as type 2 diabetes and obesity are independent risk factors for also developing HCC. Hence, the incidence of HCC in patients with MASLD is higher and unfortunately still increasing [1-11].

It is also a growing problem in the paediatric population and affects children of all ages. It is particularly associated with the growing epidemic of obesity in children and the associated diseases dependent on excessive body weight - type 2 diabetes, hyperlipidaemia or hypertension and even metabolic syndrome in children over 10 years of age according to IDF criteria. In addition, the lack of regular physical activity exacerbates this phenomenon [12-14].

According to US guidelines, early detection of MASLD is fundamental. Hence, it is best to perform liver elastography by Fibro Scan in patients with risk factors for MASLD as a screening test to detect minimal, subclinical hepatic steatosis and, if this is not possible, to at least perform liver ultrasound. On the other hand, in any patient with liver steatosis detected by imaging studies, a differential diagnosis of hepatic steatosis should be made, based on history, physical examination and laboratory tests, including cardiometabolic tests. Patients diagnosed with MASLD should be periodically monitored for liver fibrosis using the FIB-4 calculator and, if warranted, Fibro Scan liver elastography, and should be screened for hepatocellular carcinoma, as well as systematically monitored for cardiovascular risk. Early detection of MASLD aims to bring the patient under interdisciplinary care as soon as possible and to include appropriate treatment aimed at reducing disease progression, both in terms of hepatic complications - progression of steatosis, development of inflammation, or progression of fibrosis and development of cirrhosis and hepatocellular carcinoma - and extrahepatic, aimed at correcting cardio diabetic factors (Table 1) [5,6,15,16].

MASLD risk factors

- Genetic factors - PNPLA3, TM6SF2, E167K, MBOAT7, GCKR, HSD17B13 gene variants,
- Environmental factors - high calorie diet, excessive intake of sugars and saturated fatty acids,
- Low physical activity,
- Overweight, obesity/abdominal obesity,
- Pre-diabetes/type 2 diabetes,
- Dyslipidaemia,
- Hypertension.

Clinical manifestations of MASLD

The symptoms of the disease are uncharacteristic:

- can usually be asymptomatic,
- a feeling of chronic fatigue,
- a feeling of discomfort in the right lower abdomen,
- symptoms of cirrhosis.

Complications of MASLD

Complications of MASLD can be divided into two groups:

1. liver complications
2. extrahepatic complications

liver	extrahepatic
- steatohepatitis -MASH	- vascular atherosclerosis
- progression of fibrosis - from F0 to F4 (cirrhosis)	- cardiovascular diseases
- primary liver cancer (HCC)	- myocardial infarction
- liver transplantation	- stroke

Table 1: Complications of MASLD.

Management guidelines for MASLD

Due to the long-term asymptomatic course of MASLD, patients should be actively sought out, especially those burdened by cardiometabolic factors*.

The main objective is the early diagnosis of hepatic steatosis in a patient with risk factors for the development of MASLD and the assessment of disease progression, i.e. the determination of both the degree of hepatic steatosis (S0 to S3) and the degree of hepatic fibrosis (F0 to F4) and the implementation of appropriate comprehensive multidisciplinary treatment.

If advanced liver fibrosis at the F3-F4 level is found, the patient should be under the care of a specialist hepatologist or gastroenterologist. Any patient with cirrhosis should also be screened for HCC [1,5,16].

*Cardiometabolic factors considered in patients with suspected MASLD.

- BMI ≥25 kg/m2 or waist circumference ≥94 cm in men and ≥80 cm in women (or above normal depending on ethnicity),
- blood pressure ≥130/85 mm Hg or treatment of hypertension,
- Serum triglyceride concentration ≥1.7 mmol/l (150 mg/dl) or treatment of hypertriglyceridaemia,
- serum HDL cholesterol concentration ≤1.0 mmol/l (<40 mg/dl) in men and ≤1.3 mmol/l (<50 mg/dl) in women or treatment of hypercholesterolaemia,
- fasting glucose ≥5.6 mmol/l (100 mg/l) or 2 h after a glucose load ≥7.8 mmol/l (140 mg/dl) or HbA1c ≥5.7% (39 mmol/mol) or type 2 diabetes or treatment of type 2 diabetes.

The place of classical liver biopsy in the diagnosis of MASLD

For many years, virtually the only method of assessing the progression of liver fibrosis was histopathological examination of material taken during classical liver biopsy, less frequently during surgery.

Of course, it is still the case that the classic coarse-needle biopsy of the liver is the gold standard for hepatological diagnosis in many disease entities or is used in the differential diagnosis of abnormal liver parameters, abnormal radiological images or the diagnosis of focal liver lesions (Table 2).

Liver biopsy in MASLD is mainly used to diagnose the disease in clinically doubtful cases, when overlap syndromes are suspected or to differentiate the progression of steatosis to steatohepatitis-MASH or cirrhosis. However, in most cases of suspected MASLD, it is not necessary to perform, and the limitation of availability to perform it may delay diagnosis and early treatment [17-21].

	MASLD	MASH	Cirrhosis
Steatosis of the liver	>5%	>5%	+/-
Lobular and portal inflammation	+/-	Yes	Yes
Ballooning degeneration	Not	Yes	Yes
Liver fibrosis	Not	F0-F3*	F4*
*Fibrosis severity scale according to Metavir - F0 - no fibrosis, F1 - mild fibrosis (periventricular), F2 - moderate fibrosis, F3 - advanced fibrosis (bridging fibrosis), F4 - cirrhosis.			

Table 2: Histopathological evaluation of liver biopsy in patients with MASLD.

Histopathological scales used in the assessment of hepatic steatosis:

NAS (NAFLD Activity Score), reflects disease activity: unweighted composite of

- Steatosis (0 to 3)
- Lobular inflammation (0 to 3)
- Ballooning (0 to 2)

SAF Score: semi-quantitative score of

- Steatosis (0 to 3)
- Activity (lobular inflammation + ballooning) = NAS (0 to 8)
- Fibrosis (0 to 4)

Non-invasive methods in the diagnosis of MASLD

Radiological methods for the assessment of hepatic steatosis play a key role in the diagnosis and monitoring of disease progression. Most commonly, non-invasive imaging modalities such as ultrasonography or liver elastography are used in outpatient diagnosis. Computed tomography or magnetic resonance imaging are used less frequently due to availability and cost.

Ultrasonography (USG)

Liver ultrasound (USG) is currently the primary screening tool for liver steatosis in most countries due to its availability and low cost. It has a high diagnostic accuracy: sensitivity 88% and specificity 91%.

Unfortunately, usg detects steatosis if a minimum of 20-30% of the hepatocytes are affected, so this is already advanced steatosis.

Characteristic features on ultrasound:

- Increased echogenicity (hyperechogenicity) of the liver parenchyma (so-called "bright liver")
- Blurring of liver vessels and diaphragm border (less visible vessels),
- Focal hyposteatosis.

Computed Tomography (CT)

It uses differences in tissue density, measured in Hounsfield units (HU).

Characteristics in CT: Reduced liver density compared to spleen density (difference ≥10 HU suggests steatosis). becomes more hypodense in relation to other tissues.

Pros: Ability to quantify steatosis.

Limitations: Exposure to ionising radiation. sensitivity at low stealth levels.

Magnetic Resonance Imaging (MRI)

Considered the gold standard in the assessment of hepatic steatosis.

Techniques used in MRI:

-Dixon (in-phase and out-of-phase imaging): allows differentiation of tissues based on fat content.

-Proton Density Fat Fraction (PDFF): quantitative measurement of liver fat content, highly accurate and reproducible.

Pros: High sensitivity and specificity. Possibility of quantitative fat analysis.

Limitations: High costs of the study. accessible compared to ultrasound.

Magnetic Resonance Spectroscopy (MRS)

An advanced MRI technique that allows accurate analysis of tissue chemistry.

Application: Quantitative measurement of fat in liver parenchyma. as a reference method in scientific research.

Limitations: High cost and limited availability in routine diagnostics.

hybrid techniques

Modern techniques, such as PET/MRI or PET/CT, can provide additional metabolic information. However, they are rarely used in the assessment of steatosis itself.

liver elastography

Technical advances in medicine, particularly in ultrasound techniques, have meant that it is now possible to assess the extent of liver damage non-invasively using elastographic techniques. These techniques are used worldwide and their availability is also increasing [22-30].

Types of liver elastography:

Shear Wave Elastography (SWE), allowing quantitative non-invasive assessment of the extent of liver damage/fibrosis:

A. One-dimensional dynamic impulse elastography (Transient Elastography- TE);

B. Point wave elastography (Point SWE): - Acoustic Radiation Force Impulse Elastography (ARFI), elastography using the ElastPQ technique;

C. Real Time Shear Wave Elastography.

Quasi-static real-time elastography (Strain Elastography - SE). This method only allows a qualitative, non-invasive, subjective assessment of fibrosis progression.

Elastographic methods can be used depending on the type of elastography to assess the degree of liver fibrosis, as well as to assess hepatic steatosis, which can be used for the early diagnosis of MASLD [22].

Modern medicine offers several advanced elastographic technologies for the assessment of hepatic steatosis, the most important of which are Controlled Attenuation Parameter (CAP™) and Attenuation Imaging (ATI) [31-33].

Technical bases for the measurement of steatosis

The basis of techniques such as CAP™ and ATI is the analysis of the attenuation of the ultrasound wave in liver tissue. This attenuation occurs as a result of:

- Scattering: Ultrasound waves scatter at the boundaries between structures with different acoustic impedances, such as fat cells and hepatocytes.
- Absorption: The energy of the ultrasound wave is absorbed and converted into heat, which is intensified in the presence of fat.

The intensity of attenuation is expressed in units of decibels per centimetre per megahertz (dB/cm/MHz) and correlates with the degree of stealth.

Controlled Attenuation Parameter (CAP™)

CAP™ is a patented technique developed by Echosens and integrated into the FibroScan® device. It uses 3.5 MHz ultrasound waves that pass through the liver parenchyma. The system measures the attenuation of these waves, which is proportional to the fat content of the hepatocytes [33-35].

CAP™ test procedure:

- Patient preparation: The patient should be fasted for at least 3-6 hours to eliminate the influence of gastrointestinal contents.
- Patient positioning: The patient lies in a supine position with the right arm raised above the head (positioning as for classical liver biopsy),
- Measurement: The probe of the FibroScan® device emits an ultrasound wave that penetrates the liver parenchyma. The system analyses the attenuation of the ultrasound signals at a depth of 25 to 65 mm. The result is presented in dB/m and calculated from the averaged measurements.

Interpretation of CAP™ results:

- S0 (no stealth): CAP™ < 238 dB/m
- S1 (mild steatosis): 238-260 dB/m
- S2 (moderate steatosis): 260-290 dB/m
- S3 (significant steatosis): > 290 dB/m

CAP™ is particularly useful for screening for early-onset steatosis and for monitoring disease progression.

Attenuation Imaging (ATI)

ATI is a modern ultrasound technique available on advanced ultrasound systems. Like CAP™, it is based on the analysis of ultrasound attenuation in the liver, but differs in the way it is measured and interpreted [27-29,32].

ATI test procedure:

- Equipment and settings: A standard convex probe with a frequency of 2-5 MHz is used.
- The region of measurement (Region of Interest, ROI) is selected in the homogeneous liver parenchyma, away from the vessels and internal structures.
- Performance of the examination: Ultrasound passes through the liver parenchyma and the system analyses the changes in amplitude of the reflected signals as a function of depth. Measurement depth 20-60 mm.
- The results are automatically converted into an attenuation coefficient value (ATI Score).
- Repeatability of measurements: It is recommended to take at least 3-5 measurements at different liver sites to obtain reliable results.

Interpretation of ATI results:

- Healthy liver: ATI < 0.55 dB/cm/MHz.
- Mild steatosis: 0.55-0.65 dB/cm/MHz.
- Moderate steatosis: 0.65-0.75 dB/cm/MHz.
- Significant steatosis: > 0.75 dB/cm/MHz.

Potential use of FibroScan liver elastography in MASLD

The most widely used in hepatology practice is the dynamic pulse elastography (TE (vibration-controlled elastography -VCTE,) available on the FibroScan, which has been in use since 2003. This method involves measuring the speed of propagation of a mechanical pulse (elastic wave) using ultrasound. A special transducer applied to the skin of the subject (right side) generates a mechanical impulse that penetrates the skin towards the liver. At the same time, the ultrasound transducer takes a series of measurements of the propagation of the mechanical pulse.

The velocity of wave propagation is greater the greater the fibrosis in the liver. The test result, expressed quantitatively in kPa, is converted into degrees of fibrosis from F0 to F4 according to Metavir:

- F0 - no fibrosis,
- F1 - light fibrosis (circular),
- F2 - moderate fibrosis,
- F3 - advanced fibrosis (bridging fibrosis),
- F4- cirrhosis

(Validation of liver fibrosis depends on the aetiology, which is why the potential diagnosis/cause, suspected liver disease, is so important.

In addition, instruments with the option to assess the controlled attenuation parameter (controlled attenuation parameter-CAP) provide a quantitative assessment of steatosis expressed in dB/m, which is converted into steatosis grades S0 to S3 relating to the Brunt scale:

- S0 - no steatosis,
- S1 - steatosis < 33%,
- S2 - steatosis 34-66%,
- S3 - steatosis > 66% of hepatocytes

(Validation of the degree of hepatic steatosis also depends on its aetiology, hence, as in the determination of liver fibrosis, a suspicion or diagnosis of liver disease is indicated.

FibroScan® liver elastography is recommended in the recommendations *of the European Association for the Study of the Liver*- EASL, *American Association for the Study of Liver Diseases*-AASLD, *Asian-Pacific Association for the Study of the Liver* APASL, as a method to assess the degree of fibrosis - liver damage.

This technique is used both for screening diagnosis and for the evaluation of diagnosed liver diseases. In addition, the method can be used to monitor liver fibrosis during and after treatment.

As a highly reproducible method, FibroScan® is used in the majority of ongoing clinical trials. Numerous scientific studies, involving several thousand patients, have shown high concordance in determining the extent of fibrosis between the elastographic method and histopathological examination of the liver biopsy [22,30,32, 36-40].

The FibroScan® liver elastography test allows the detection of minimal hepatic steatosis - detection of less than 5%. It is also characterised by a high correlation of the CAP parameter with the determination of hepatic steatosis by proton MRI spectostropy -1-H-MRS (Table 3) [41].

Steatosis	AUC	CAP	1-H-MRS
>5%		0,93	0,87
>34%		0,94	0,88
>67%		0,82	0,85

Table 3: Correlation of CAP* with liver steatosis determination by proton spectostropy MRI (1-H-MRS).

Interpretation of the results obtained, expressed in kPa and dB/m, can be checked using the freely available MyFibroScan app, where by substituting the obtained parameters and selecting the suspected disease aetiology, the degree of liver fibrosis and steatosis can be quickly obtained.

The AASLD recommends the use of FibroScan® liver elastography as a screening test for liver steatosis in all patients with MASLD risk factors: overweight and obesity, elevated serum lipids, type 2 diabetes, hypertension.

Assessment of liver fibrosis in patients with MASLD

In line with AASLD recommendations, every patient diagnosed with MASLD should be assessed for risk or progression of liver fibrosis.

According to recommendations in primary care, we should assess approximate liver fibrosis using the FIB 4 scale (free FIB-4 app or at www.fib4.pl) based on simple biochemical parameters - ALT, AST, platelets - and the patient's age. If the centre has a device using elastography technology, fibrosis can be assessed using liver elastography instead of the FIB-4 calculator (Table 4) [4,5,8,16].

Risk of fibrosis	<1,45 Low	1,45-2,67 Unspecified/indirect	>2,67 High
Degree of fibrosis	F0	F1 - F2	F3-F4
Recommended treatment:	Control as before in GP. Repeat the study after 1-2 years.	Indicated more accurate assessment of liver fibrosis by liver elastography e.g. FibroScan method Referral to a specialist gastroenterologist/hepatologist.	Specialist care indicated: Referral to a specialist gastroenterologist/hepatologist.

Table 4: Algorithm for the management of patients with MASLD after assessment of fibrosis based on the FIB-4 calculator.

On the other hand, if, after reading the fibrosis severity in the FIB-4 application, the result indicates intermediate (indeterminate) fibrosis (FIB-4 1.45- 2.67), such a patient should have fibrosis assessed by liver elastography, e.g. by FibroScan®.

In hepatology practice in patients with MASLD, liver elastography by FibroScan® is also used to assess the risk of developing steatohepatitis - MASH (using the FAST scale in the MyFibroScan app - need to determine the degree of liver fibrosis and steatosis and AST for assessment). It can also be used to assess patients with advanced liver fibrosis at the F3 level according to Metavir to assess the prediction of the risk of complications - Agile 3+ scale and to assess the risk of developing and the need for screening for HCC in patients with F4 fibrosis according to Metavir - Agille 4 scale (these scales use assessment of liver fibrosis, age, sex, presence of diabetes, AT, AST, PLT) [42-48].

In patients with MASLD and cirrhosis, splenic stiffness can also be examined using FibroScan® to screen for portal hypertension and the need for subsequent gastroscopy to assess for possible oesophageal varices. According to the Baveno VII guidelines, the cut-off points for splenic stiffness considered as a predictive value for the development of portal hypertension is a result > 40-45 kPa [49].

Liver elastography performed with the FibroScan® device is completely non-invasive, painless, safe, characterised by the absence of absolute contraindications and fast performance - the average execution time is about 5 minutes, with the result available immediately after the test.

How to perform a FibroScan® test

- The patient should report for the examination on an empty stomach - a minimum of 3 hours,
- He should rest in a supine position on the bed before the examination,
- The patient should lie on the bed as for a classic liver biopsy - supine, with the right hand behind the head, the right lower limb assumed - crossed over the left and slightly arched,
- The examination should be performed by a certified person trained by the manufacturer of the device - this does not have to be a doctor, unlike other elastography techniques based on conventional ultrasound equipment,
- The appropriate choice of transducer (M, XL or S) is important, depending on the patient's anatomical conditions - adult/thin/obese/child. Most current devices have a built-in electronic system to support the operator's decision on the type of transducer.
- The transducer should be placed between the ribs at the height where the liver parenchyma layer is thickest - usually the right intercostal region in the mid axillary line. This can be done by typically palpating the patient as for a classic liver biopsy or by conventional ultrasound [40,50].

What can interfere with the reliability of FibroScan® testing

In order for the FibroScan liver elastography result to be reliable, the patient should be advised to fast for a minimum of three hours prior to the scheduled test, as a meal may temporarily increase liver stiffness. In addition, liver diseases with high aminotransferase activity (e.g. acute viral hepatitis, exacerbation of autoimmune hepatitis), ascites or exacerbation of congestive heart failure may temporarily increase liver stiffness and the test should be repeated once the above-mentioned factors have subsided [40,51].

The FibroScan-AST (FAST) scale is a diagnostic tool developed by Echosens for the assessment of *advanced liver fibrosis* (ALF) in patients with non-alcoholic fatty liver disease (NAFLD). The FAST scale uses non-invasive methods, combining liver stiffness (LSM) measurements with the FibroScan device, *Controlled Attenuation Parameter* (CAP) and serum AST (aspartate aminotransferase) enzyme levels (table 4,5,6) [39, 42-46].

Application of the FAST scale

The FAST scale is particularly useful in patients:

- With non-alcoholic fatty liver disease (NAFLD).

- With metabolic syndrome, obesity or type 2 diabetes.
- To select patients who may require more intensive hepatological care.

How is the FAST score calculated?

- The FAST score is based on an algorithm that combines:
- **LSM (Liver Stiffness Measurement):** Obtained with FibroScan (assessment of liver stiffness, measured in kPa).
- **CAP (Controlled Attenuation Parameter):** Assessment of the degree of hepatic steatosis (measured in dB/m).
- **AST (aspartate aminotransferase):** Laboratory result (U/l).

The algorithm requires advanced software integrated into the FibroScan device.

Elements of the FAST Scale	Description	Scope/Values
LSM (Liver Stiffness Measurement)	Measurement of liver stiffness using the FibroScan device, expressed in kPa.	2.5-75 kPa (higher values = higher risk)
CAP (Controlled Attenuation Parameter)	Measurement of hepatic steatosis, expressed in dB/m.	100-400 dB/m (higher values = more steatosis)
AST (aspartate aminotransferase)	Biochemical marker assessing potential liver damage, expressed in U/l.	Normal < 40 U/l; higher values indicate liver damage

Table 4: Detailed FAST Scale (FibroScan-AST).

Scale objective:

- Assesses the likelihood of advanced fibrosis (F≥3) in patients with NAFLD.
- It helps avoid invasive liver biopsies, which are costly and have a risk of complications.

FAST range	Risk of advanced fibrosis (F≥3)	Clinical recommendations
FAST ≤ 0.35	Low	Regular monitoring, modification of risk factors (obesity, diabetes).
FAST ≥ 0.67	High	Urgent specialist diagnosis (e.g. liver biopsy, further imaging studies).
FAST 0.35-0.67	Indirect	Further diagnostic tests (e.g. elastography, detailed biochemical markers).

Table 5: Detailed Inxterpretationx of FAST Results.

Aspect	Description
Non-invasiveness	Eliminates the need for a liver biopsy, reducing the risk of complications.
Speed	Results available immediately after FibroScan and blood analysis.
Savings	Reduces diagnostic costs associated with invasive tests.
Application	Useful for patients with NAFLD and risk factors, e.g. type 2 diabetes, obesity.

Table 6: Benefits and Application of the FAST Scale.

The Agile scale is a diagnostic tool developed by **Echosens** to assess the degree of liver fibrosis and identify patients at risk of advanced fibrosis (F≥2), advanced fibrosis (F≥3), and cirrhosis (F=4). It is particularly useful in the assessment of various chronic liver diseases such as:

- Non-alcoholic fatty liver disease (NAFLD),
- Chronic viral hepatitis (HBV, HCV),

- Other chronic liver diseases [47,48].

Elements of the Agile scale

The Agile scale uses three main parameters:

1. **LSM (Liver Stiffness Measurement):**

- Measurement of liver stiffness using the FibroScan device, expressed in kPa.
- Higher values indicate a higher risk of fibrosis and advanced liver disease.

2. **ALT (alaninotransferase):**

- Liver enzyme used to assess inflammatory activity in the liver.
- Increased ALT values may indicate the presence of hepatocyte damage.

3. **AST (aspartate aminotransferase):**

- Another liver enzyme that provides information on inflammatory activity and potential liver fibrosis.
- When combined with LSM, it helps to increase diagnostic accuracy.

Operating principle

The Agile scale combines measurements of liver stiffness (LSM) with biochemical results (ALT, AST) using a developed algorithm. This makes it possible to:

- Recognition of early stages of fibrosis (F≥2),
- Identification of advanced fibrosis (F≥3),
- Cirrhosis risk assessment (F=4).

Interpretation of Agile Scale Results

Scope of Agile	Clinical relevance	Recommendations
Agile ≤ Threshold 1	Low risk of advanced fibrosis.	Monitoring and prevention, without the need for further invasive investigations.
Threshold 1 < Agile < Threshold 2	Intermediate risk of fibrosis.	Requires further diagnostic testing, such as elastography or more sophisticated tests.
Agile ≥ Threshold 2	High risk of advanced fibrosis or cirrhosis.	Urgent specialist diagnosis, consideration of liver biopsy or intensive treatment.

Agile benefits of scale

1. **Non-invasive:** Allows assessment of fibrosis without the need for liver biopsy.
2. **Speed and convenience:** result available immediately after FibroScan and blood analysis.
3. **Accuracy:** Highly effective in differentiating between different stages of fibrosis.
4. **Versatility:** It can be used in a variety of chronic liver diseases, not just NAFLD.
5. **Cost-effectiveness:** Reduces diagnostic costs, reducing the need for invasive and costly methods.

Clinical use

The Agile scale is mainly used in:

- Assessment of patients with chronic liver disease (NAFLD, HBV, HCV),
- Screening in risk groups (obesity, type 2 diabetes, metabolic syndrome),
- Monitoring liver disease progression.

Agile Scale - Elements and Interpretation of Results

Element	Description	Scope
LSM (Liver Stiffness Measurement)	Measurement of liver stiffness, expressed in kPa. Helps determine the degree of fibrosis (F≥2, F≥3, F=4).	2.5-75 kPa
ALT (alaninotransferase)	Biochemical marker indicating hepatic inflammatory activity, expressed in U/l.	Normal < 40 U/l
AST (aspartate aminotransferase)	Biochemical marker to assess liver damage and fibrosis, expressed in U/l.	Normal < 40 U/l

Comparison of Agile and FAST Scales

Criterion	FAST scale (FibroScan-AST)	Agile scale
Diagnostic objective	Assessment of advanced liver fibrosis (F≥3) in patients with NAFLD.	Assessment of liver fibrosis at different stages (F≥2, F≥3, F=4).
Elements of scale	**- LSM (Liver Stiffness Measurement)**: Measurement of liver stiffness.	**- LSM (Liver Stiffness Measurement)**: Measurement of liver stiffness.
	- CAP (Controlled Attenuation Parameter): Fatigue measurement.	**- ALT (alaninotransferase)**: Marker of inflammatory activity.
	- AST (aspartate aminotransferase): Indicator of liver damage.	**- AST (aspartate aminotransferase)**: Fibrosis index.
Range of parameters	- LSM: 2.5-75 kPa	- LSM: 2.5-75 kPa
	- CAP: 100-400 dB/m	- ALT/AST: Normal < 40 U/l
Interpretation of results	- FAST ≤ 0.35: Low risk of fibrosis.	- Agile ≤ Threshold 1: Low risk of fibrosis.
	- FAST 0.35-0.67: Intermediate risk.	- Threshold 1 < Agile < Threshold 2: Intermediate risk of fibrosis.
	- FAST ≥ 0.67: High risk of fibrosis.	- Agile ≥ Threshold 2: High risk of fibrosis/marring.
Clinical purpose	- Optimising the diagnosis of advanced fibrosis in NAFLD.	- Assessment of fibrosis in a range of liver diseases, including HBV/HCV.
Main benefits	- Non-invasive, fast and accurate.	- Comprehensive assessment of fibrosis at different stages.
	- Reduction in liver biopsies.	- Useful in assessing both fibrosis and inflammatory activity.
Restrictions	- Focused on advanced fibrosis (F≥3).	- Requires detailed biochemical data (ALT/AST).

Key differences

Diagnostic scope

- The FAST scale is more specialised in identifying advanced fibrosis (F≥3) in patients with NAFLD.
- The Agile scale assesses a broader spectrum of fibrosis (F≥2, F≥3, F=4), making it more versatile in a variety of chronic liver diseases.

Elements of measurement

- FAST is based on LSM, CAP and AST.
- Agile uses LSM, ALT and AST to better assess inflammatory activity and fibrotic status.

Scope of application

- FAST is mainly aimed at patients with NAFLD.
- Agile is applicable in a broader context, including patients with HBV, HCV and other liver diseases.

Use of FibroScan in the assessment of liver damage in MASLD:

- Screening for hepatic steatosis (CAP*)in patients with MASLD risk factors and screening for steatohepatitis (MASH) in patients with MASLD (use of Fast score*),
- Screening for assessment of liver fibrosis - any patient diagnosed with MASLD and assessment of its severity in patients diagnosed with MASLD (Agile 3 and 4 score*),
- Monitoring of treatment efficacy/effects: assessment of liver fibrosis and quantitative steatosis at time intervals after treatment,
- Screening for the risk of developing portal hypertension in patients with MASLD and advanced liver fibrosis (assessment of splenic stiffness).

Steatohepatic disease associated with metabolic dysfunction is currently a challenge for modern medicine. On the one hand, it is the most common liver disease in the world, with a year-on-year increase in prevalence among both adults and the paediatric population. On the other hand, epidemiological data are still underestimated due to low awareness of patients as well as physicians regarding early detection of the disease and lack of screening. The long-term asymptomatic course means that MASLD is usually detected incidentally, often at the stage of advanced liver fibrosis or cirrhosis or only after a cardiovascular incident, which is the most common cause of death in this group of patients. Hence, MASLD is now of interest not only to hepatologists or gastroenterologists, but also to paediatricians, cardiologists, diabetologists, lipidologists or obesitologists. Education of both the public and physicians to raise awareness of early diagnosis of MASLD, prevention methods and treatment seems necessary.

It seems necessary to pay attention to patients, including children, at risk of developing MASLD, i.e. patients with obesity, type 2 diabetes mellitus or pre-diabetes, hypertension or lipid disorders, and in these patients, it is best to periodically perform liver elastography using the FibroScan method to detect minimal, subclinical degree of hepatic steatosis and, if this is not possible, to at least perform liver ultrasound. Based on the available studies and many years of clinical experience in performing liver elastography by FibroScan, this method seems to be the most suitable and optimal for preventive, screening tests for the early detection of hepatic steatosis in patients of all ages, as well as for monitoring liver fibrosis and assessing the progress of treatment. It is an easy to perform, non-invasive, painless and reproducible method recommended by all liver research societies.

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