Fibroscan®: Indications and Results inambulatory patients

ABSTRACT:
Fibroscan®, or impulsion elastometry, has become essential in the management of chronic liver diseases. It is primarily used to diagnose and monitor liver fibrosis, as well as hepatic steatosis through CAP. The aim of this study is to examine the indications and clinical applications of Fibroscan® and compare the results with current clinical practices.
Methods: This is a cross-sectional, retrospective study conducted from May 2019 to December 2023, which included all patients referred for evaluation of fibrosis and/or steatosis using FibroScan®.
Results:A total of 750 patients were included: 440 women (58.6%) and 310 men (41.4%). The mean age was 50.2 years. Clinically, 8.2% had signs of chronic liver disease and 4% had signs of portal hypertension. Abdominal ultrasound showed abnormalities in 44.5% of the patients.
The indications for Fibroscan® were distributed as follows: 34% referred for HBV, 21% for HCV, 15.7% for MASLD, 5.1% for MASH, 1.2% for AIH, 7.1% for cholestatic diseases, 2.1% for drug-induced chronic hepatitis, 0.9% for alcoholic liver disease, 1.2% for chronic liver disease of undetermined etiology, and 10.1% for portal hypertension.
The average liver elasticity value was 8.7 kPa. It was classified as F0-F1 in 70.1% of cases and F4 in 16.1%. The average values were 12.9 kPa for HCV, 7.18 kPa for HBV, 5.2 kPa for MASLD, and 13.5 kPa for MASH. The average CAP value was 231.5 dB/m. 56.1% of cases showed no steatosis, and 20.5% had steatosis classified as S3. The average CAP values were 208.7 dB/m for HCV, 227.7 dB/m for HBV, 286.3 dB/m for MASLD, and 274.6 dB/m for MASH.
In conclusion, Fibroscan® is a valuable and accessible tool that is effectively used to assess the severity of liver fibrosis and/or steatosis across a wide range of populations with commendable sensitivity and specificity.

Keywords: Fibroscan®, impulsion elastometry, fibrosis, CAP, chronic liver disease

Introduction:

Since its development in the 2000s, Fibroscan®, or transient elastography, has established itself as a tool of choice in the management of chronic liver diseases. Fundamentally non-invasive, quick, and reliable, it offers a valuable alternative to liver biopsies, thereby reducing patient risk and providing better monitoring of the progression of liver diseases.

One of the most relevant aspects of Fibroscan® is its use in the diagnosis and follow-up of hepatic fibrosis. Over the years, several studies have established elasticity thresholds corresponding to different degrees of fibrosis (Metavir) with more than satisfactory diagnostic accuracy.

Besides this role, Fibroscan® also finds applications in the diagnosis and monitoring of metabolic liver diseases by providing an estimate of liver fat content. This is the controlled attenuation parameter (CAP). The device's dual function thus allows for the estimation of both fibrosis and hepatic steatosis, and the evaluation of a patient's severity during the first visit. The scope of Fibroscan® also extends to assessing disease severity and predicting complications of portal hypertension in cirrhotic patients.

The aim of this work is to provide a comprehensive overview of the indications of Fibroscan®, exploring its current and emerging clinical applications, and closely examining the results obtained through various studies, comparing them to current clinical practices.

Methods:

This is a cross-sectional, monocentric, and retrospective study conducted from May 2019 to December 2023, which collected data on a large number of patients referred to our department for chronic liver disease follow-up, with an evaluation of fibrosis and/or steatosis using FibroScan®.
Their clinical, biological, morphological, elastometric parameters, as well as the CAP value, were recorded.
The measurement of liver elasticity and CAP was performed using a Fibroscan 530 compact. The interpretation of the Fibroscan result takes into account:

- A minimum of 10 validmeasurements
- An IQR/Median ratio < 30%

Results:

750 patients were included in our study: 440 women (58.6%), and 310 men (41.4%). The male/female sex ratio was 0.7. The average age of our patients was 50.2 years (24-90 years).

Personal medical history was foundwith varying frequencies: hypertension in 20% of cases, type 2 diabetes in 18% of cases, extra-hepatic neoplasia in 9.6% of cases, hypercholesterolemia in 8% of cases, heart disease in 3.7% of cases, and chronic kidney failure in 2.6% of cases.

On general examination, the average BMI (Body Mass Index) of the patients was 26.1 kg/m² (16.5-42.6 kg/m²). 28% (n=210) were overweight (BMI >25 kg/m²) and 25.5% (n=192) were obese (BMI >30 kg/m²). On abdominal examination, the majority of patients, 89.3% (n=670), had a normal clinical examination. 8.2% (n=62) had clinical signs of chronic liver disease, and 4% (n=30) had signs of portal hypertension, mainly abdominal collateral venous circulation.

44.5% of patients (n=334) had an abnormal abdominal ultrasound coupled with Doppler: 18% had signs of chronic liver disease, 13% had ultrasound signs of portal hypertension, and 26.5% had steatosis. 55.5% had a normal liver morphology.

The indications for Fibroscan were distributed as follows: 34% of patients (n=255) were referred for HBV, of which 70.6% (n=180) were chronic HBeAg-negative infections. 20.6% (n=53) of the patients were on Tenofovir treatment.21% of patients (n=158) were referred for HCV. Among them, 79% were referred for fibrosis assessment at diagnosis, and 21% of the patients were on direct-acting antiviral C treatment.15.7% of patients (n=118) were referred for MASLD, of which 63.6% were referred following the discovery of steatosis on ultrasound. 5.1% of patients (n=39) were referred for MASH.1.2% (n=9) were referred for AIH, and 0.3% of cases were referred for Overlap syndrome (all three patients were already on treatment).5.6% (n=42), were referred for PBC, of which 78.5% (n=33) were on ursodeoxycholic acid (UDCA).1.5% (n=11) were referred for PSC. All patients were already on UDCA treatment at the time of examination.0.3% were referred for hemochromatosis. 2.1% (n=16) were referred for drug-induced chronic hepatitis, proven by liver biopsy, of which 55% were related to Methotrexate. 0.9% (n=7) were referred for alcoholic liver disease.1.2% (n=9) were referred for fibrosis assessment related to chronic liver disease of yet undetermined etiology.10.1% (n=76), were referred for liver elasticity assessment in the face of morphological signs of portal hypertension. This was secondary to portal cavernoma in 1.8% of cases, Budd-Chiari syndrome in 0.9%, and cirrhosis in 70% of cases. Using the M probe allowed reliable results in 76.8% of cases (n=576). The use of the XL probe was necessary in 23.2% of patients (n=174).

The average liver elasticity value among all patients was 8.7 kPa, with extremes ranging from 1.9-74.5 kPa. 70.1% of patients (n=526) had mild fibrosis classified as F0-F1, 7.1% of cases (n=53) had moderate fibrosis classified as F2, 6.7% of cases (n=50) had advanced fibrosis classified as F3, and 16.1% (n=121) had severe fibrosis classified as F4.

The average liver elasticity value according to the different etiologies of chronic liver diseases was as follows: 12.9 kPa in HCV, 7.18 kPa in HBV, 5.2 kPa in MASLD, 13.5 kPa in MASH, 12.3 kPa in AIH, 11.4 kPa in PSC, and 8.2 kPa in PBC.

	HBV	HCV	MASLD	MASH
Elasticity (kPa)	7,18	12,9	5,2	13,5
F0-F1 (%)	55,7%	47%	92,3%	3%
F2 (%)	8,7%	11,8%	7,7%	17%
F3 (%)	14,4 %	15,7%	0%	38%
F4 (%)	21,1%	25,5%	0%	42%

Table 1 : Distribution of Patients by Fibrosis Stage in the main liver diseases of our study

The average CAP in our series is 231.5 dB/m, with extremes ranging from 100 to 400 dB/m. 56.1% of cases (n=420) had no steatosis, 11.4% of cases (n=86) had mild steatosis classified as S1, 12% of cases (n=90) had moderate steatosis classified as S2, and 20.5% of cases (n=154) had severe steatosis classified as S3. The average CAP value according to the different etiologies was as follows: 208.7 dB/m in HCV, 227.7 dB/m in HBV, 286.3 dB/m in MASLD, 274.6 dB/m in MASH, 215.4 dB/m in AIH, 209.4 dB/m in PSC, and 231.3 dB/m in PBC.

In our series, 49% of patients with viral hepatitis C had steatosis on Fibroscan®, 32% of those with viral hepatitis B, 40% of patients with autoimmune hepatitis, and 28.6% of patients with PBC.

	HBV	HCV	MASLD	MASH
CAP (db/m)	227,7	208,7	286,3	274,6
S0 (%)	55,7%	68,6%	23,8%	0%
S1 (%)	8,7%	9,8%	16,7%	20%
S2 (%)	14,4 %	11,8%	16,7%	30%
S3 (%)	21,1%	9,8%	42,8%	50%

Table 2: Distribution of patients by degree of steatosis in the main liver diseases of our study

Discussion:

The FibroScan® is a non-invasive diagnostic and quantification method for hepatic fibrosis. Developed by Echosens (Paris, France), the procedure relies on pulse elastography technology.

- Evaluation of fibrosis:

Initially validated in patients with chronic hepatitis C [1], FibroScan® revealed a strong correlation between liver elasticity and the degree of fibrosis assessed by the Metavir score. Several studies have reported excellent diagnostic performance for detecting advanced fibrosis and cirrhosis, with areas under the ROC curve (AUROC) ranging from 0.88 to 0.99 [2-4]. Thresholds have been established for each stage of fibrosis. The diagnosis of fibrosis $F \geq 2$, $F \geq 3$, and $F = 4$ was based on elasticity values ranging from 7.1 to 8.8, 9.5 to 9.6, and 12.5 to 14.6 kPa, respectively [4, 5]. These same thresholds were used in our study for patients with HCV. In various studies, 15 to 20% of patients with HCV have F4 fibrosis.

This figure was slightly higher in our study. However, our study had a larger number of patients without significant fibrosis. This could be related to the extensive screening campaigns conducted throughout the kingdom. Most studies on liver elasticity in HCV patients have revealed that liver stiffness decreases rapidly after HCV antiviral treatment due to the resolution of inflammation, with greater reduction in patients classified as F4 (25 kPa initially, 21.5 at 24 months) [6]. The retrospective nature of our study did not allow us to evaluate this factor. The results of FibroScan® in the context of HBV are similar to those already published for HCV [7]. In a study conducted by Ogawa [8] on 68 patients with HBV, the average values of the measurements were 3.5 kPa for F0, 6.4 kPa for F1, 9.5 kPa for F2, 11.4 kPa for F3, and 15.4 kPa for F4 in HBV patients [9]. These averages were similar in our study. In the study by Cardoso et al. [10], 50% of patients had no fibrosis (F0-F1), 42% of patients had fibrosis classified as F2 or higher, and 8% had F4 fibrosis. In our study, the ratio of F0-F1 patients was similar (55.1%). However, the percentage of F4 patients, 21.4%, is significantly higher. This may be explained by the diagnostic delay in some patients. Several studies have reported that patients with chronic B AgHBe-infection with preserved hepatic parenchyma had liver elasticity values comparable to healthy subjects. In a prospective study conducted by Oliveri et al. [11], the average liver elasticity value of patients with chronic B AgHBe- infection was 4.3 ± 1.0 kPa, while that of healthy subjects was 4.6 ± 1.2 kPa. The same results were found in the study by Sporea et al. [9] as well as in our study, where the average elasticity for these same patients was similar, at 5.6 kPa. Liver elasticity as defined by the Ludwig classification, both in primary biliary cholangitis and primary sclerosing cholangitis, is correlated. The areas under the ROC curve for diagnosing different stages of fibrosis (significant fibrosis, severe fibrosis, and cirrhosis) are 0.92, 0.86 to 0.95, and 0.96, respectively [7]. The threshold values for each stage of fibrosis are slightly higher than those observed in chronic viral hepatitis. In PBC, the measurement of liver elasticity by FibroScan® is currently recommended by the European Association for the Study of the Liver (EASL) clinical practice guidelines for disease staging at diagnosis and during follow-up [12, 13]. The threshold of 9.6 kPa was retained to differentiate early PBC (≤ 9.6 kPa) from advanced PBC (> 9.6 kPa) [13]. A landmark French study on PBC conducted by Corpechot et al. (n = 150) demonstrated the high specificity and sensitivity (>90%) of FibroScan® in distinguishing fibrotic stages [14]. In his study, he found 55% of patients were F0-F1, 20% F2, 17% F3, and 8% F4. This distribution is similar in our study. In PSC, FibroScan® is a valuable tool for assessing fibrosis. The thresholds used by various studies to classify the severity of mild to moderate and moderate to severe fibrosis were as follows: F0—F1/F2: <11.1 kPa; F2/F3—F4: ≥11.1 kPa [15, 16]. These same thresholds were used in our study.

Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the most common liver disease worldwide. Its prevalence is high: from 16 to 31% in the general population of wealthy countries [17,18], up to 46% in heavy drinkers [19], and from 50 to 80% in the obese population [20, 21]. In our study, 44% of patients, regardless of etiology, had steatosis.The measurement of liver elasticity by FibroScan® is a method recommended in thecurrent clinical guidelines on MASLD by the EASL, the European Association for the Study of Diabetes (EASD), and the European Association for the Study of Obesity (EASO) as a non-invasive procedure for assessing hepatic fibrosis in patients with MASLD [6, 22]. According to Ozercan et al., the measurement of liver elasticity by FibroScan® has a sensitivity of

95% and a specificity of 77% in detecting hepatic fibrosis in patients with MASLD. In the new EASL-EASD-EASO clinical practice guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD), threshold values of 8 kPa and 12 kPa are recommended to exclude advanced fibrosis.

Regarding the use of M and XL probes, Oeda et al. showed no differences in accuracy between the two probes [23]. However, the introduction of the XL probe has led to more reliable results than the M probe in overweight or obese patients [3]. Indeed, in our study, the use of the XL probe allowed us to optimize the FibroScan results in 23.2% of cases in these patients.

- Measurement of CAP:

The assessment of ultrasonic attenuation has been implemented on the FibroScan® and constitutes the CAP or controlled attenuation parameter function. It has been shown that CAP effectively detects steatosis at a level of ≥ 10%, which is more sensitive than other imaging modalities [20,24,25]. In fact, its performance in detecting any steatosis (S ≥ 1) is generally excellent, with an area under the ROC curve (AUROC) often greater than 0.8. Indeed, in our study, steatosis was detected in 44% of patients of all etiologies combined. Additionally, 35% of patients with steatosis on FibroScan® did not have steatosis on ultrasound. Metabolic factors are so significantly related to the presence of steatosis in the general population that non-alcoholic fatty liver disease has been proposed as an outcome of metabolic syndrome [26]. Obesity is associated with insulin resistance and can also lead to type 2 diabetes and contribute to steatosis [27, 28]. Previous studies have reported a high BMI as a factor associated with hepatic steatosis [27, 29, 30]. Machado's meta-analysis demonstrated that the most significant correlations with steatosis were diabetes and obesity, respectively. Furthermore, a definitive positive correlation was found between the presence of steatosis and high BMI, dyslipidemia, hypertriglyceridemia, and hypercholesterolemia [26]. The issue of screening for MASLD continues to spark debate. Nevertheless, there is growing alignment among international medical societies in favor of non-invasive screening of diabetic individuals for hepatic fibrosis, regardless of the pre-existence of MASLD [22, 31].

Conclusion:

Impulse elastography by FibroScan® is now widely used in clinical hepatology. Through this study, we explored its indications and examined its results for various liver diseases. Our research revealed that FibroScan® has high sensitivity and specificity in detecting liver fibrosis as well as hepatic steatosis through its CAP function. This makes it an essential tool for the early screening and follow-up of patients with chronic liver diseases.

REFERENCES :

[1] Castera L, Vergniol J, Foucher J, Le Bail B, Chanteloup E, Haaser M, et al. Prospective comparison of transient elastography, Fibrotest®, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. Gastroenterology 2005;128:343–50.

[2] Sandrin L, Fourquet B, Hasquenoph JM, Yon S, Fournier C, Mal F, Christidis C, Ziol M, Poulet B, Kazemi F, Beaugrand M, Palau R. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. Ultrasound Med Biol 2003Dec;29(12):1705-13. doi: 10.1016/j.ultrasmedbio.2003.07.001. PMID: 14698338.

[3] Zougmoré HT, Cadranel JFD, Fantognon G, Azzi B, Smadhi R, Ngele Efole JR, Mrabti S, Heng R, Ntsama MA, Medmoun M, Kazerouni F, Le Magoarou T. Fibroscan® and Shear Wave correlated well in hepatic fibrosis evaluation of patients with chronic liver diseases "in real life situation". Medicine (Baltimore). 2022 Aug 12;101(32):e30025. doi: 10.1097/MD.0000000000030025. PMID: 35960072; PMCID: PMC9371580.

[4]Ziol M, Handra-Luca A, Kettaneh A, et al.. Noninvasive assessment of liver fibro sis by measurement of stiffness in patients with chronic hepatitis C. Hepatology. 2005;41:48–54.

[5] Ziol M, Barget N, Bourcier V, Garnier T, Beaugrand M. Amount and type of liver fibrosis detected by stiffness measurements (abstract). Hepatology 2005;42(Suppl 1):A368.

[6] Rinaldi L, Giorgione C, Mormone A, Esposito F, Rinaldi M, Berretta M, Marfella R, Romano C. Non-Invasive Measurement of Hepatic Fibrosis by Transient Elastography: A Narrative Review. Viruses. 2023 Aug13;15(8):1730. doi: 10.3390/v15081730. PMID: 37632072; PMCID: PMC10459581.

[7] Vergniol, J., & de Lédinghen, V. L'élastométrie impulsionnelle (FibroScan®) : un nouvel outil diagnostique en hépatologie. La Presse Médicale, 2009;38(10), 1516–1525. doi:10.1016/j.lpm.2008.08.018

[8] Ogawa E, Furusyo N, Toyoda K et al. Transient elastography for patients with chronic hepatitis B and C virus infection: Non-invasive, quantitative assessment of liver fibrosis. Hepatol Res 2007; 37: 1002–1010

[9] Sporea, I., Sirli, R., Deleanu, A., Iulia, R., Tudora, A., Dan, I., & Popescu, A. What Did We Learn from the First 3,459 Cases of Liver Stiffness Measurement by Transient Elastography (FibroScan®)? Ultraschall in Der Medizin - European Journal of Ultrasound 2010;32(01), 40–45. doi:10.1055/s-0029-1245525

[10] Cardoso AC, Carvalho-Filho RJ, Stern C, et al.. Direct comparison of diagnostic per formance of transient elastography in pa tients with chronic hepatitis B and chronic hepatitis C. Liver Int. 2012;32:612–21.

[11] Oliveri F, Coco B, Ciccorossi P, et al.. Liver stiffness in the hepatitis B virus carrier: a non-invasive marker of liver disease influenced by the pattern of transaminases. World J Gastroenterol. 2008;14:6154–62.

[12] Cristoferi L, Calvaruso V, Overi D, Viganò M, Rigamonti C, Degasperi E, Cardinale V, Labanca S, Zucchini N, Fichera A, Di Marco V, Leutner M, Venere R, Picciotto A, Lucà M, Mulinacci G, Palermo A, Gerussi A, D'Amato D, Elisabeth O'Donnell S, Cerini F, De Benedittis C, Malinverno F, Ronca V, Mancuso C, Cazzagon N, Ciaccio A, Barisani D, Marzioni M, Floreani A, Alvaro D, Gaudio E, Invernizzi P, Carpino G, Nardi A, Carbone M; Italian PBC Registry. Accuracy of Transient Elastography in Assessing Fibrosis at Diagnosis in Naïve Patients With Primary Biliary Cholangitis: A Dual Cut-Off Approach. Hepatology. 2021 Sep;74(3):1496-1508. doi: 10.1002/hep.31810.

[13] Hirschfield GM, Beuers U, Corpechot C, Invernizzi P, Jones D, Marzioni M, et al. EASL Clinical Practice Guidelines: the diagnosis and management of patients with primary biliary cholangitis. J Hepatol 2017;67:145□172.

[14] Corpechot C, Carrat F, Poujol□Robert A, Gaouar F, Wendum D, Chazouillères O, et al. Noninvasive elastography□based assessment of liver fibrosis progression and prognosis in primary biliary cirrhosis. Hepatology 2012;56:198□208.

[15] Tafur M., Cheung A., Menezes R.J., Feld J., Janssen H., Hirschfield G.M., Jhaveri K.S. Risk stratification in primary sclerosing cholangitis: Comparison of biliary stricture severity on MRCP versus liver stiffness by MR elastography and vibration-controlled transient elastography. Eur. Radiol. 2020;30:3735–3747. doi: 10.1007/s00330-020-06728-6.

[16] Corpechot C., Gaouar F., El Naggar A., Kemgang A., Wendum D., Poupon R., Carrat F., Chazouillères O. Baseline values and changes in liver stiffness measured by transient elastography are associated with severity of fibrosis and outcomes of patients with primary sclerosing cholangitis. Gastroenterology. 2014;146:970–979. doi: 10.1053/j.gastro.2013.12.030.

[17] Poynard, T., P. Ingiliz, et al. "Concordance in a world without a gold standard: a new non-invasive methodology for improving accuracy of fibrosis markers." PLoS One 2008;3(12): e3857.

[18] Castera, L., J. Foucher, et al. "Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 examinations." Hepatology 2010;51(3): 828-835.

[19] Castera, L., N. Goutte, et al. "How does transient elastography applicability impact on diagnostic accuracy? Results in 1044 patients with viral hepatitis and liver biopsies > 20 mm from a multicenter prospective cohort (Fibrostic)." Hepatology 2012;56: 224A224A.

[20] Sasso, M., V. Miette, et al. "The controlled attenuation parameter (CAP): a novel tool for the non-invasive evaluation of steatosis using Fibroscan." Clin Res Hepatol Gastroenterol 2012;36(1): 13-20

[21] Sasso M, Audiere S, Kemgang A, Gaouar F, Corpechot C, Chazouilleres O, et al. Liver steatosis assessed by controlled attenuation parameter (CAP) measured with the XL probe of the FibroScan: a pilot study assessing diagnostic accuracy. Ultrasound Med Biol. 2016;42:92–103.

[22] European Association for the Study of the Liver (EASL) European Association for the Study of Diabetes (EASD) European Association for the Study of Obesity (EASO) EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J. Hepatol. 2016;64:1388–1402. doi: 10.1016/j.jhep.2015.11.004.

[23] Oeda S., Takahashi H., Imajo K., Seko Y., Ogawa Y., Moriguchi M., Yoneda M., Anzai K., Aishima S., Kage M., et al. Accuracy of liver stiffness measurement and controlled attenuation parameter using FibroScan® M/XL probes to diagnose liver fibrosis and steatosis in patients with non-alcoholic fatty liver disease: A multicentre prospective study. J. Gastroenterol. 2020;55:428–440. doi: 10.1007/s00535-019-01635-0.

[24] Sasso, M., M. Beaugrand, et al. "Controlled attenuation parameter (CAP): a novel VCTE guided ultrasonic attenuation measurement for the evaluation of hepatic steatosis: preliminary study and validation in a cohort of patients with chronic liver disease from various causes." Ultrasound Med Biol 2010;36(11): 1825-1835.

[25] Fraquelli, M., C. Rigamonti, et al. "Reproducibility of transient elastography in the evaluation of liver fibrosis in patients with chronic liver disease." Gut 2007;56(7): 968-973.

[26] Machado, M. V., Oliveira, A. G., & Cortez-Pinto, H. Hepatic steatosis in hepatitis b virus infected patients - meta-analysis of risk factors and comparison with hepatitis c infected patients. Journal of Gastroenterology and Hepatology, 2011. doi:10.1111/j.1440-1746.2011.06801.x

[27] Sirinawasatien A, Techasirioangkun T. The Prevalence and Determinants of Hepatic Steatosis Assessed by Controlled Attenuation Parameter in Thai Chronic Hepatitis C Patients. Gastroenterol Res Pract. 2020 Nov 2;2020:8814135. doi: 10.1155/2020/8814135. PMID: 33204256; PMCID: PMC7655258.

[28] Shoelson S. E., Herrero L., Naaz A. Obesity, inflammation, and insulin resistance. Gastroenterology. 2007;132(6):2169–2180. doi: 10.1053/j.gastro.2007.03.059.

[29] Bedossa P. Pathology of non -alcoholic fatty liver disease. Liver Int. 2017 Jan;37 Suppl 1:85 - 89. doi: 10.1111/liv.13301.

[30] Zarski JP, Sturm N, Guechot J, Paris A, Zafrani ES, Asselah T, Boisson RC, Bosson JL, Guyader D, Renversez JC, Bronowicki JP, Gelineau MC, Tran A, Trocme C, De Ledinghen V, Lasnier E, Poujol-Robert A, Ziegler F, Bourliere M, Voitot H, Larrey D, Rosenthal-Allieri MA, Fouchard Hubert I, Bailly F, Vaubourdolle M; ANRS HCEP 23 Fibrostar Group. Comparison of nine blood tests and transient elastography for liver fibrosis in chronic hepatitis C: the ANRS HCEP-23 study. J Hepatol. 2012 Jan;56(1):55-62. doi: 10.1016/j.jhep.2011.05.024.

[31] Chalasani N., Younossi Z., Lavine J.E., Charlton M., Cusi K., Rinella M., Harrison S.A., Brunt E.M., Sanyal A.J. The diagnosis and management of non-alcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67:328–357. doi: 10.1002/hep.29367.