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Chapter

Ultrasound Based Elastography Techniques for the Evaluation of Nonalcoholic Liver Disease
Ioan Sporea, Raluca Lupușoru and Roxana Șirli

Abstract

The number of NAFLD patients is increasing in the developed world and non-invasive modalities for their evaluation are needed. Ultrasound-based methods are very useful for this approach, starting with standard ultrasound used for steatosis detection, and continuing with new modalities for steatosis, fibrosis, and inflammation quantification. Modern ultrasound systems can quantify all these parameters in NAFLD patients, thus making ultrasound a real Multiparameter Ultrasound (MPUS). The performance of ultrasound-based methods is very well documented with liver stiffness assessment as a marker of fibrosis, and more recently, for quantification of steatosis and viscoelastic properties as a marker of inflammation.

Keywords: nonalcoholic fatty liver disease (NAFLD), fatty liver, ultrasound, liver elastography, fat quantification

1. Introduction

Currently, at least in the developed world, the focus of hepatology changed, from chronic viral hepatitis (B or C), which is now well controlled with efficient drugs, to the problem of fatty liver. This disease occurs in both non-alcoholic patients with metabolic conditions as well as in alcoholic patients [1]. Nonalcoholic fatty liver disease (NAFLD) become more and more present in clinical practice, since it currently affects more than a quarter of the world population [2] and the prevalence is increasing [3]. Overweight and obesity, type 2 diabetes, dyslipidemia, and sedentariness are increasing at a global level, at least in the developed world [4, 5]. For a long time, the fatty liver was considered to be a “benign” entity, but in the last years, the potential evolution of this disease to severe fibrosis and cirrhosis has been proven. Furthermore, in the last years, NAFLD became an important indication for liver transplantation [6–8].

Recently, new terminology for NAFLD was proposed, to better reflect its clinical spectrum: Metabolic Associated Fatty Liver Disease (MAFLD) [9, 10]. This new terminology is used more and more, having the advantage to underline the role of metabolic factors and to not exclude the use of alcohol. Thus, we must be focused to screen for fatty liver in the population at risk: patients with obesity, metabolic syndrome, and type 2 diabetes mellitus (DM).
Recent data showed that 650 million people around the world are obese and 1.9 billion are overweight (39% of the adult population)! Type 2 diabetes mellitus (type 2 DM) become a frequent cause of morbidity in the last decade (1 in 11 people of the developed countries have type 2 DM) [11]. Furthermore, many of type 2 DM patients are overweight and obese. Association of obesity and type 2 DM increases the risk for fatty liver infiltration. Features of metabolic syndrome are frequent in the adult population; thus, all these conditions explain the increased incidence of fatty liver in daily practice.

These huge cohorts of patients should be evaluated, especially in regard to fibrosis severity, the main driver of fibrosis. Simple non-invasive biologic tests to predict significant fibrosis in patients with NAFLD are available, such as Fibrosis-4 (FIB-4) or APRI (which uses only transaminases serum levels, platelet count and age), with acceptable accuracy [12]. Other biologic tests are more accurate [Enhanced Liver Fibrosis (ELF™) Test, FibroMax, others], but also more complex and more expensive.

In the last 15 years numerous ultrasound (US) based elastography techniques have been developed [Transient Elastography (TE), point Shear Wave Elastography (pSWE) or 2D-SWE], which have demonstrated their practical value in many studies. International Guidelines classify these US elastography techniques into: Strain Elastography (used mostly for breast, thyroid and prostate nodules) and Shear Waves Elastography (SWE - in which external impulses generate shear waves inside the liver, whose speed is measured by ultrasound) [13, 14]. The faster the shear-waves speed are, the stiffer the tissue and the fibrosis are more severe. Based on the generation of the external impulse and the technology used to measure the shear-waves speed, SWE elastography is subdivided into: Transient Elastography (with a mechanic external impulse), Point SWE (pSWE) [in which an Acoustic Radiation Force Impulse (ARFI) is used and the shear-waves speed is measured in a point], and real-time elastography which includes 2D-SWE and 3D-SWE (in which ARFI is used, shear-waves speed is measured in an area of interest and in the same time a color-coded elastogram is generated) [13, 14].

However, in patients with NAFLD, not only the evaluation of fibrosis is important, but also quantification of steatosis and inflammation is of practical value.

In this chapter, we aim to discuss the ultrasound-based methods for the evaluation of patients with NAFLD. In such patient’s evaluation and quantification of steatosis, fibrosis and inflammation are important. In practice, these methods are frequently used and more and more data are collected regarding their value.

2. Steatosis evaluation

In patients with NAFLD, the presence of steatosis is a common fact and then the evaluation of its severity is necessary. Ultrasoundography (US) is the simplest way to evaluate steatosis, and two signs are important: “bright” hyperechoic liver” with posterior attenuation (Figure 1) and increased hepatorenal index (Figure 2). Using these two signs, a semiquantitative assessment of steatosis severity can be performed. Many papers evaluated the performance of liver ultrasound for the assessment of the steatosis severity, some of them are quite old papers. Mathiesen et al. [15] compared the US with hepatic histology for steatosis assessment in a series of 165 patients. Steatosis was graded as none, mild, moderate or severe. In patients with increased echogenicity, 86.7% had at least moderate liver steatosis by histology. To detect steatosis, US had a sensitivity of 0.90, a specificity of 0.82, a positive predictive value of 0.87 and a negative predictive value of 0.87. In another study, Palmentieri et al. [16] compared the “bright liver” echo pattern to liver biopsy in 235 patients.
The study showed that the “bright liver” echo pattern was found in 67% of patients with steatosis of any degree and in 89% of patients with severe steatosis (≥30% of the hepatocytes involved). Among the subgroup of patients who had severe steatosis, the sensitivity and specificity of US were 91% and 93%, respectively.

Maybe the most important paper regarding the value of liver US for diagnosing fatty liver is a large meta-analysis [17], which included 49 studies and 4720 subjects. The sensitivity of US for moderate and severe steatosis was 84.8% (CI 95%: 79.5–88.9%), with a specificity of 93.6% (CI 95%: 87.2–97.0%).

Computer Assisted Diagnosis (CAD) was also evaluated as a tool to increase the accuracy of US for the detection and severity assessment of steatosis [18]. In a study including 120 patients [19], CAD was able to correctly classify the severity of steatosis with an accuracy of 82.2%. More recently, Artificial Intelligence (AI) has been used for the same purpose [20].
All these papers are in favor to use liver ultrasound for the detection of steatosis in patients with risk factors. The latest update of the European Association for the Study of the Liver (EASL) Guidelines regarding the non-invasive evaluation in chronic liver disease [12] states that: “Conventional ultrasound should be used as a first-line tool for the diagnosis of steatosis in clinical practice, despite its well-known limitations”. This method can be used for a semi-quantitative assessment of the severity of fatty infiltration.

For a quantitative evaluation of liver steatosis, the most used method in this moment is Controlled Attenuation Parameter (CAP). It is a module implemented on a FibroScan device (Echosens, Paris, France), which measures the attenuation of the ultrasound beams throughout the liver to assess steatosis severity. CAP was first used on the M probe and latter also on the XL probe (Figure 3).

Many papers have been published on the value of CAP for liver steatosis assessment, comparing it to liver biopsy. In the next table, we resumed the main published papers concerning the value of CAP (Table 1).

Having in mind that the CAP module is available both in M and XL probes, the next question is if the same cut-off values can be used in practice for both probes? Chan et al. evaluated a cohort of 180 patients by liver biopsy and CAP with both M and XL probes [36]. The group had a mean age of 53.7 ± 10.8 years and NAFLD was identified in 86.7% of them, the sensitivity, specificity, PPV, and NPV of CAP using the M/XL probe for the diagnosis of steatosis grade ≥ S1 was 93.9%/93.3%, 58.8%/58.8%, 95.6%/95.6%, and 50.0%/47.6%, respectively. Thus, the authors concluded that the same cut-off values for CAP may be used for the M and XL probes for the diagnosis of hepatic steatosis grade.

However, in another prospective study on 100 adults [37], which compared CAP with the M vs. the XL probe for quantification of hepatic fat content, using magnetic resonance imaging proton density fat fraction (MRI-PDFF) as the standard, the mean CAP values by M probe (310 ± 62 db/m) were significantly lower than by the XL probe (317 ± 63 db/m) \( (P = 0.007) \). The authors demonstrated that the M probe under-quantifies CAP values as compared with the XL probe and they proposed that the type of probe should be considered when interpreting CAP data from patients with fatty liver.

![Figure 3. FibroScan (Echosens, Paris, France) with M and XL probes (in light blue CAP values are shown, while in yellow the liver stiffness values).](image-url)
In the last years, ultrasound modules for the quantification of liver steatosis have been implemented in standard US machines, by several companies. The advantage of these systems is that when steatosis is seen by standard ultrasound, immediately a quantification can be performed. Several papers have been published in this area, with good results. In the following pages, we will present the most recent developments in this field.

**Ultrasound Guided Attenuation Parameter (UGAP)** from General Electric (**Figure 4**) was evaluated for the detection of hepatic steatosis as compared with CAP, using histopathology as the reference standard [38]. In a cohort of 163 chronic liver disease patients who underwent UGAP, CAP and liver biopsy on the same day, the AUROC’s of UGAP for identifying >S1, >S2 and S3 were 0.900, 0.953 and 0.959, respectively, which were significantly better than the results obtained with CAP.

**Attenuation imaging (ATI)** from Canon (**Figure 5**) has shown promising results for fatty quantification in several published papers. In a study performed on 114 subjects potentially at risk of steatosis and 15 healthy controls, ATI results were compared to the ones obtained with CAP, using MRI-PDFF as the reference method [39]. ATI showed a better correlation with MRI-PDFF (r = 0.81) than CAP (r = 0.65). Similar good results have been obtained by the same group in a later paper [39]. In this study, the correlation between ATI and PDFF was better than with CAP (0.83 vs. 0.58).

In another study, in which liver histology was used as a reference in a series of 108 subjects, it has been reported that the degree of steatosis was the only significant determinant factor for the ATI results and that the AUROCs for different grades of steatosis ranged from 0.84 to 0.93 [40].

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Cut-off values for each steatosis grade (dB/m)</th>
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<tr>
<td></td>
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<td>$S \geq 1$</td>
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<tr>
<td>Chan 2014 [21]</td>
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<td>263</td>
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<td>De Ledinghen 2016 [22]</td>
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<td>—</td>
</tr>
<tr>
<td>Imajo 2016 [23]</td>
<td>142</td>
<td>236</td>
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<tr>
<td>Park 2017 [24]</td>
<td>104</td>
<td>261</td>
</tr>
<tr>
<td>Naveau 2017 [25]</td>
<td>123</td>
<td>298</td>
</tr>
<tr>
<td>Sissiqui 2019 [26]</td>
<td>393</td>
<td>285</td>
</tr>
<tr>
<td>Shalimar 2020 [27]</td>
<td>219</td>
<td>285</td>
</tr>
<tr>
<td>Oeda 2019 [28]</td>
<td>137</td>
<td>—</td>
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<tr>
<td>Eddowes 2019 [29]</td>
<td>88</td>
<td>302</td>
</tr>
<tr>
<td>Petroff 2021 [30]</td>
<td>2346</td>
<td>294</td>
</tr>
<tr>
<td>Karlas 2017 [31]</td>
<td>2735</td>
<td>248</td>
</tr>
<tr>
<td>Zenovala 2021 [33]</td>
<td>204</td>
<td>245</td>
</tr>
<tr>
<td>Mikolasevic 2021 [34]</td>
<td>179</td>
<td>304</td>
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<tr>
<td>Gu 2021 [35]</td>
<td>1183/3295/2835</td>
<td>273,5</td>
</tr>
</tbody>
</table>

**Table 1.**

*Value of CAP for liver steatosis assessment.*
In a study that used once again MRI-PDFF as reference [41], in a cohort of 87 patients, the AUROCs of ATI for detection of hepatic steatosis ≥5% and ≥10%, were 0.76 and 0.88, respectively (95% CI: 0.66–0.85 and 0.79–0.94) and the correlation of ATI with MRI-PDFF was moderate ($p = 0.66$).

The Attenuation coefficient (ATT) from Hitachi was used in a multicenter prospective study including patients who underwent liver biopsy and ATT measurements on the same day [42]. Correlations between ATT and steatosis grade were evaluated. In a total of 351 patients that were enrolled in this study, the median
values of ATT for steatosis grades S0, S1, S2, and S3 were 0.55, 0.63, 0.69, and 0.85 dB/cm/MHz, respectively, and ATT increased with the increase in steatosis grade \((P < 0.001)\). The AUROC's corresponding to \(S \geq 1\), \(S \geq 2\), and \(S \geq 3\) were 0.79, 0.87, and 0.96, respectively.

**Speed of sound estimation (SSE)** (Figure 6) implemented in the Aixplorer US system - MACH 30 was compared with MRI-PDFF in a pilot study including 100 patients [43]. The technique's reproducibility was excellent, with an intraclass correlation coefficient (ICC) of 0.93. An SSE cutoff \(\leq 1.537 \text{mm/}\mu\text{s}\) showed 80% sensitivity and 85.7% specificity in detecting any steatosis (S1–S3). In a multivariate regression analysis, only MRI-PDFF and BMI were associated with SSE values.

In another study in a cohort of 215 NAFLD patients using Aixplorer MACH 30 system [44] for the evaluation of steatosis, Sound Speed Plane-wave Ultrasound (SSp. PLUS) and Attenuation Plane-wave Ultrasound (Att. PLUS) were used in comparison with CAP. In this study, SSp.PLUS correlated better than Att.PLUS with CAP values: \((r = -0.74\) vs. \(r = 0.45)\) and the best SSp.PLUS cut-off value for predicting the presence significant steatosis by CAP was 1524 m/s.

**Quantification of steatosis (AC-TAI and SC-TAI)** using the Samsung ultrasound system (Figures 7 and 8) was evaluated in a cohort of 120 subjects suspected of having NAFLD [45]. The participants underwent US examination for radiofrequency (RF) data acquisition. Using RF data analysis, the attenuation coefficient (AC) based on tissue attenuation imaging (TAI) (AC-TAI) as well as a scatter-distribution coefficient (SC) based on tissue scatter-distribution imaging (TSI) (SC-TSI) were measured and compared with MRI-PDFF. In this study, AC-TAI and SC-TSI were significantly correlated with MRI-PDFF \((r = 0.659\) and 0.727, \(p < 0.001\) for both). For detecting hepatic fat contents of \(\geq 5%\) and \(\geq 10\%\), the areas under the AUROC of AC-TAI were 0.861 (95% CI: 0.786–0.918) and 0.835 (95% CI: 0.757–0.897), while those of SC-TSI were 0.964 (95% CI: 0.913–0.989) and 0.935 (95% CI: 0.875–0.972), respectively.

All these results concerning the quantification of liver steatosis using ultrasound are very promising and every day new papers are published in well-known medical journals considering the rapid development of this field.
3. Evaluation of fibrosis

In the early times of non-invasive assessment of patients with chronic liver disease, the main field of research was liver fibrosis. Replacing in many cases liver biopsy, this assessment is essential for the prognosis of patients [46, 47]. Early papers in this field evaluated Transient Elastography (TE) as a predictor of fibrosis in NAFLD [48]. Later, ARFI technologies (Acoustic Radiation Force Impulse) with pSWE and 2D-SWE became fields of research [49]. In Table 2 we presented the main papers evaluating TE and SWE methods for the assessment of liver fibrosis in NAFLD patients.

Considering the practical value of different systems, TE is the oldest system, a semi-blind method of evaluation, it can assess fibrosis severity as well as steatosis (with CAP) in the same machine, is not possible to be performed in patients with ascites and in some areas TE and CAP measurements are made by technicians. ARFI technologies (pSWE and 2D-SWE) are included in standard ultrasound systems and fibrosis assessment (and others parameters) can be performed immediately after B-mode examination and can evaluate to the patients with ascites.
### Ultrasound Based Elastography Techniques for the Evaluation of Nonalcoholic Liver Disease

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<table>
<thead>
<tr>
<th>Study</th>
<th>No of patients</th>
<th>Elastography</th>
<th>Cut-off values for each fibrosis stage</th>
</tr>
</thead>
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<td></td>
<td></td>
<td></td>
<td>F1</td>
</tr>
<tr>
<td>Petta 2016 [50]</td>
<td>324</td>
<td>TE</td>
<td>—</td>
</tr>
<tr>
<td>Yoneda 2007 [51]</td>
<td>67</td>
<td>TE</td>
<td>&gt;5.6 kPa</td>
</tr>
<tr>
<td>Gaia 2011 [52]</td>
<td>72</td>
<td>TE</td>
<td>&gt;5.5 kPa</td>
</tr>
<tr>
<td>Kumar 2013 [53]</td>
<td>205</td>
<td>TE</td>
<td>&gt;6.1 kPa</td>
</tr>
<tr>
<td>Lupsor 2010 [54]</td>
<td>72</td>
<td>TE</td>
<td>—</td>
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<tr>
<td>Petta 2011 [55]</td>
<td>169</td>
<td>TE</td>
<td>—</td>
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<td>Ratziu 2010 [56]</td>
<td>53</td>
<td>TE</td>
<td>&gt;5.1 kPa</td>
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<td>Yoneda 2008 [57]</td>
<td>50</td>
<td>TE</td>
<td>—</td>
</tr>
<tr>
<td>Nobili 2008 [58]</td>
<td>52</td>
<td>TE</td>
<td>—</td>
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<tr>
<td>Wong 2010 [48]</td>
<td>146</td>
<td>TE</td>
<td>—</td>
</tr>
<tr>
<td>Wong 2012 [59]</td>
<td>193</td>
<td>TE</td>
<td>—</td>
</tr>
<tr>
<td>Musso 2011 [60]</td>
<td>60</td>
<td>TE</td>
<td>—</td>
</tr>
<tr>
<td>Yoneda 2010 [61]</td>
<td>54</td>
<td>TE</td>
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<td>Mahadeva 2013 [62]</td>
<td>131</td>
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<td>Imajo 2016 [23]</td>
<td>152</td>
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<tr>
<td>Pathik 2015 [63]</td>
<td>89</td>
<td>TE</td>
<td>—</td>
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<tr>
<td>Kumar 2013 [53]</td>
<td>207</td>
<td>TE</td>
<td>—</td>
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<tr>
<td>Cassinotto 2016 [49]</td>
<td>291</td>
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<td>—</td>
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<tr>
<td>Kamali 2019 [32]</td>
<td>77</td>
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<td>Eddowes 2019 [29]</td>
<td>88</td>
<td>TE</td>
<td>—</td>
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<tr>
<td>Seki 2017 [64]</td>
<td>171</td>
<td>TE</td>
<td>&gt;7.2 kPa</td>
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<td>Lee 2017 [65]</td>
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<td>Hsu 2018 [66]</td>
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<td>Myers 2012 [69]</td>
<td>276</td>
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<td>Furlan 2020 [70]</td>
<td>59</td>
<td>TE</td>
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<td>Leong 2020 [71]</td>
<td>100</td>
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<td>&gt;6.95 kPa</td>
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<td>pSWE</td>
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<td>pSWE</td>
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<td>Cassinotto 2013 [74]</td>
<td>165</td>
<td>pSWE</td>
<td>—</td>
</tr>
<tr>
<td>Friedrich-Rust 2012 [75]</td>
<td>50</td>
<td>pSWE</td>
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### Table 2. Value of TE, pSWE and 2D-SWE for liver fibrosis assessment in NAFLD patients.

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<tr>
<td>Osaki 2010 [76]</td>
<td>101</td>
<td>pSWE</td>
<td>&gt;1.34 m/s &gt;1.79 m/s &gt;2.2 m/s &gt;2.9 m/s</td>
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<td>Lee 2017 [65]</td>
<td>94</td>
<td>pSWE</td>
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<td>pSWE</td>
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<td>pSWE</td>
<td>— — — &gt;1.49 m/s — —</td>
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<td>Cui 2016 [78]</td>
<td>114</td>
<td>pSWE</td>
<td>— &gt;1.29 m/s &gt;1.34 m/s &gt;2.48 m/s</td>
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<tr>
<td>Li 2016 [79]</td>
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<td>pSWE</td>
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<td>100</td>
<td>pSWE</td>
<td>&gt;6.83 kPa &gt;6.98 kPa &gt;7.02 kPa &gt;11.5 kPa</td>
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<tr>
<td>Sharpton 2021 [80]</td>
<td>114</td>
<td>pSWE</td>
<td>&gt;7.8 kPa &gt;6.8 kPa &gt;8.7 kPa &gt;10.6 kPa</td>
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<td>Cassinotto 2016 [49]</td>
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<td>2D-SWE</td>
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<td>2D-SWE</td>
<td>&gt;6.65 kPa &gt;8.04 kPa &gt;10.6 kPa &gt;12.37 kPa</td>
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published guidelines regarding the practical values of all these techniques have been published [13, 14]. Barr et al. [84] showed the advantages and disadvantages of each method. The most recent guideline (from 2021) is the EASL Guideline for the use of the main non-invasive tests, with the important recommendations in this field [12].

### 4. Evaluation of inflammation

In patients with NAFLD, it is of crucial importance to differentiate between simple steatosis and steatohepatitis (NASH: non-alcoholic steatohepatitis). The best method for this is liver biopsy. However, having in mind the huge number of subjects with NAFLD (1/4 of the population in the developed countries), this invasive technique is not feasible in practice for all the patients. It has been demonstrated that using only biologic tests (such as aminotransferases or Cytokeratin 18) is not enough, thus new methods that accurately assess inflammation are necessary [85].

The newest high-end US machines include modules that evaluate the viscoelastic properties of the liver. This parameter is considered to be an expression of inflammation in the fatty liver, useful for the diagnosis of steatohepatitis (NASH).
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Such a paper was published recently. Detection of steatosis, fibrosis and inflammation in 102 patients with NAFLD in comparison with liver biopsy was performed using a high-end US machine [86]. Attenuation coefficient (dB/cm/MHz) from attenuation imaging, liver stiffness measurements, and shear wave dispersion slope (SWDS, [m/s]/kHz) from 2D-SWE were evaluated. The AUROC values for steatosis grades S1, S2 or S3, were 0.93, 0.88, and 0.83, respectively, while for lobular inflammatory activity (SWDS) the system detected inflammation grades 1, 2 and 3 with an AUROCs of 0.89, 0.85, and 0.78, respectively.

In a prospective study performed in a cohort of 120 consecutive adults who underwent liver biopsy for suspected NAFLD, Multiparametric US was used for liver assessment [87]. Three US parameters: dispersion slope [(m/s)/kHz], attenuation coefficient [dB/cm/MHz], and shear-wave speed (m/s), were evaluated with a 2D-SWE system, immediately before biopsy. This study has shown that dispersion slope identified lobular inflammation with an AUC of 0.95 (95% CI: 0.91, 0.10) for an inflammation grade ≥ A1 (mild), of 0.81 (95% CI: 0.72, 0.89) for an inflammation grade ≥ A2 (moderate), and of 0.85 (95% CI: 0.74, 0.97) for an inflammation grade A3 (marked). Considering the attenuation coefficient, it identified steatosis with an AUC of 0.88 (95% CI: 0.80, 0.97) for S ≥ 1 (mild), 0.86 (95% CI: 0.79, 0.93) for S ≥ 2 (moderate), and 0.79 (95% CI: 0.68, 0.89) for S ≥ 3 (severe). Shear-wave speed identified fibrosis with an AUC of 0.79 (95% CI: 0.69, 0.88) for fibrosis stage F ≥ 1, of 0.88 (95% CI: 0.82, 0.94) for F ≥ 2, of 0.90 (95% CI: 0.84, 0.96) for F ≥ 3 and of 0.95 (95% CI: 0.91, 0.99) for F4 (cirrhosis). Probably the most important fact is that this combination of dispersion slope, attenuation coefficient, and shear-wave speed showed an AUC of 0.81 (95% CI: 0.71, 0.91) for the diagnosis of NASH.

Although, there are still many steps to go to reach an accurate software for the detection of inflammation using US waves, these early papers are encouraging for the noninvasive assessment of patients with NAFLD. All necessary information can be obtained using the Multiparametric Ultrasound (MPUS), and this is an ideal technique for NAFLD patients (quantification of fibrosis, steatosis and inflammation in less than 5 minutes) (Figure 9).

Figure 9. Multiparameter ultrasound: 2D-SWE, Vi PLUS (viscosity index) and AttPLUS and SSpPLUS quantification.
In this moment, the main challenge in this field is to start the screening of the population at risk (MAFLD patients) for all the parameters of NAFLD [88]. Using simple biological tests [89] or maybe more sophisticated systems, such as ultrasound based or maybe MRI-based elastography, we can identify patients with advanced disease. Then intensive measures for such patients must be implemented.

5. Conclusion

Ultrasound methods are very useful for the evaluation of NAFLD patients. Identification of steatosis can be performed with standard ultrasound. Quantification of steatosis, fibrosis and inflammation can be assessed quickly with new high-tech ultrasound machines. Screening of patients at risk for the fatty liver with these modern tools is a challenge for the near future.

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References


Magnetic resonance imaging more accurately classifies steatosis and fibrosis in patients with nonalcoholic fatty liver disease than transient Elastography. Gastroenterology. 2016;150(3):626-637. DOI: 10.1053/j.gastro.2015.11.048


with nonalcoholic fatty liver disease. Diagnostics (Basel). 2021;11(5):787. DOI: 10.3390/diagnostics11050787


Ultrasound Based Elastography Techniques for the Evaluation of Nonalcoholic Liver Disease
DOI: http://dx.doi.org/10.5772/intechopen.102363


[51] Yoneda M et al. Transient elastography in patients with non-alcoholic fatty liver disease (NAFLD). Gut. 2007;56:1330-1331. DOI: 10.1136/gut.2007.126417


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[79] Li Y, Dong C. Diagnostic value of acoustic radiation force impulse imaging and APRI ratio index for quantitative for evaluating the degree of liver fibrosis in non-alcoholic fatty liver disease patients. Chinese Journal of Ultrasound in Medicine. 2017;(12):544-548


[88] Sporea I. To screen or not to screen for NAFLD? Medical Ultrasonography. 2021;23(2):133-134. DOI: 10.11152/mu-3251