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EFSUMB Guidelines and Recommendations on the Clinical Use of Liver Ultrasound Elastography, Update 2017 (Short Version)

EFSUMB-Leitlinien und Empfehlungen zur klinischen Anwendung der Leberelastographie, Update 2017 (short version)

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ABSTRACT

We present here the first update of the 2013 EFSUMB (European Federation of Societies for Ultrasound in Medicine and Biology) Guidelines and Recommendations on the clinical use of elastography with a focus on the assessment of diffuse liver disease. The short version provides clinical information about the practical use of elastography equipment and interpretation of results in the assessment of diffuse liver disease and analyzes the main findings based on published studies, stressing the evidence from meta-analyses. The role of elastography in different etiologies of liver disease and in several clinical scenarios is also discussed. All of the recommendations are judged with regard to their evidence-based strength according to the Oxford Centre for Evidence-Based Medicine Levels of Evidence. This updated document is intended to act as a reference and to provide a practical guide for both beginners and advanced clinical users.

ZUSAMMENFASSUNG

Dies ist die erste Überarbeitung der 2013 publizierten EFSUMB-Leitlinien zur klinischen Anwendung der Elastografie und konzentriert sich auf die diffusen Lebererkrankungen. Der klinische Teil dieser Leitlinien erläutert die praktische Anwendung der Elastografie bei der Beurteilung diffuser Lebererkrankungen unter Berücksichtigung der Geräteausstattung und Interpretation der Ergebnisse. Die aktuelle Literatur wurde analysiert unter besonderer Beachtung von Metaanalysen. Die klinische Anwendung der Elastografie wird unter Reflexion unterschiedlicher klinischer Szenarien und der unterschiedlichen Ätiologien diffuser Lebererkrankungen erläutert. Alle Empfehlungen erfolgten gemäß der Evidenz basierten Methodik der Oxford-Klassifikation. Das hier vorgestellte Update soll dem Anfänger und fortgeschrittenen Nutzer eine praktische Hilfe darstellen.

Introduction

The short version of this update of the 2013 EFSUMB (European Federation of Societies for Ultrasound in Medicine and Biology) Guidelines and Recommendations on the clinical use of shear wave elastography provides information about the practical use of elastography equipment and interpretation of results in the assessment of diffuse liver disease and analyzes the main findings based on published studies, stressing evidence from meta-analyses.

The long version also includes an update of the section on the basic principles of elastography, which now includes transient elastography (TE) as a shear wave elastography (SWE) method, and there are additional discussions of issues such as depth of penetration, whether to perform measurements in units of kilopascal (kPa) or ms^{-1}, and the comparability of data from different systems.

Investigator education

EFSUMB is working to promote high quality in ultrasound education and sustain excellent professional standards in elastography training and practice [1]. To ensure the lowest possible intraoperator variability, EFSUMB recommends that ultrasound elastography be performed by operators that have passed competence Level 1. However, it may also be possible to train dedicated personnel to perform elastographic measurements only [2].

The basic principles and technology for elastography were developed by the academic research community before commercial translation, and it remains a heavily researched and rapidly developing field. EFSUMB recommends that users maintain an awareness of this field.

RECOMMENDATION 1

The operator must acquire appropriate knowledge and training in ultrasound elastography (LoE 5, GoR C). Strong consensus (13/0/0, 100 %)

RECOMMENDATION 2

Data acquisition should be undertaken by dedicated and specially trained personnel. For pSWE and 2D-SWE, experience in B-mode ultrasound is mandatory (LoE 5, GoR C). Strong consensus (13/0/0, 100 %)

Shear wave elastography (TE, pSWE and 2D-SWE), general technical comments

Introduction

The liver is an important target organ for the use of elastography; stiffness correlates with the degree of fibrosis and indirectly with portal hypertension (see liver application).

Examination procedure

Subjects should be examined in a supine position with the right arm in maximal extension. The transducer is positioned in a right intercostal space to visualize the right liver lobe in A or B mode.

Artefacts and large vessels on the A-mode (TE) or B-mode image (pSWE and 2D-SWE) should be avoided. Optimal measurement quality of pSWE and 2D-SWE occurs with the ROI placed a minimum of 1 – 2 cm and a maximum of 6 cm beneath the liver capsule [3 – 6]. A transient breath hold in a neutral position is optimal.

RECOMMENDATION 3

Measurement of liver stiffness by SWE should be performed through a right intercostal space in supine position, with the right arm in extension, during breath hold, avoiding deep inspiration prior to the breath hold (LoE 2b, GoR B) [7, 8]. Strong consensus (18/0/0, 100 %)

RECOMMENDATION 4

Measurement of liver stiffness by SWE should be performed by experienced operators (LoE 2b, GoR B) [7, 8]. Strong consensus (18/0/0, 100 %)

RECOMMENDATION 5

Measurement of liver stiffness by pSWE and 2D-SWE should be performed at least 10 mm below the liver capsule (LoE 1b, GoR A) [3 – 6, 8 – 11]. Strong consensus (18/0/0, 100 %)

Fasting and resting

Food ingestion increases measurement readings (independent of fibrosis) for an estimated 120 – 180 minutes after the meal [12 – 14]. The examination should ideally be performed after an overnight fast, while abstaining from food/drinks (especially caffeine) and smoking. In addition, since exercise increases liver stiffness, subjects should be examined after a minimum of 10 – 20 minutes of rest [15].

RECOMMENDATION 6

Patients should fast for a minimum of 2 hours and rest for a minimum of 10 minutes before undergoing liver stiffness measurement with SWE (LoE 2b, GoR B) [7]. Majority consensus (13/2/3, 72 %)

Factors influencing liver stiffness independent of liver fibrosis (confounders)

Liver stiffness does not solely reflect liver fibrosis, but can reflect many other physiological or pathological conditions. Liver stiffness is increased with hepatic inflammation (often but not exclusively shown by an elevated transaminase level) [16 – 19], obstructive cholestasis [20] and hepatic congestion [21, 22]. For patients with falsely elevated liver stiffness measurements (LSMs) due to alcoholic hepatitis, liver stiffness decreases following 1 – 4 weeks of abstinence [23 – 25]. Other diseases, which cause increased liver stiffness, independent of liver fibrosis include amyloidosis, lymphomas and extramedullary hemopoiesis. Presently, it is uncertain whether hepatic steatosis modulates liver stiffness [26, 27] or does not [28, 29].

RECOMMENDATION 7

The major potential confounding factors (liver inflammation indicated by AST and/or ALT elevation > 5 times the normal limits, obstructive cholestasis, liver congestion, acute hepatitis and infiltrative liver diseases) should be excluded before performing LSM with SWE, in order to avoid overestimation of liver fibrosis (LoE 2b, GoR B), and/or should be considered when interpreting the SWE results (LoE 1b, GoR B) [16 – 21, 23 – 25, 30 – 33]. Broad consensus (15/0/1, 94 %)

Normal values

TE measurements of Young's modulus in healthy people vary between 4.4 and 5.5 kPa (95th percentile 6.7 kPa) [34 – 37]. LSMs are generally higher in men than in women [34, 35] and may be affected by steatosis [34] but are not influenced by age [36, 37].

pSWE measurements using Virtual Touch Quantification (VTQ®) in healthy populations range between 1.01 and 1.59 m/s, but in most studies the range is 1.07 – 1.16 m/s [9, 10, 38 – 43]. Age has no apparent influence on the shear wave speed (SWS) assessed by VTQ® [38, 39, 43]. All but one study [9] similarly found no correlation between gender or body mass index (BMI) and SWS values. Depth as assessed by the skin-to-liver capsule distance may influence the SWS values assessed by VTQ® [38]. In healthy children, the mean SWS obtained in the right liver lobe was 1.07 ± 0.10 m/s in one study [44] and 1.12 m/s (range: 0.73 to 1.45 m/s) in another [45].

Values obtained with Elastography point quantification (ElastPQ®) in healthy people are comparable to those obtained with VTQ® [46 – 48], although in contrast to VTQ® findings, measurements using ElastPQ® were 8 % higher in healthy men than in healthy women [48].

2D-SWE measurements of Young's modulus using supersonic shear imaging (SSI) in healthy subjects cover the range 4.5 – 5.5 kPa (95th percentile 6.2 kPa) [49, 50]. Healthy men may have higher LSMs than healthy women, while BMI and age do not seem to influence LSM in subjects without liver disease [50].

For all equipment, a SWE measurement within the normal range, in a subject without other clinical or laboratory evidence of liver disease, may exclude significant liver fibrosis with a high degree of certainty.

The current literature has been recently summarized [51].

RECOMMENDATION 8

SWE within the normal range can rule out significant liver fibrosis when in agreement with the clinical and laboratory background (LoE 2A, GoR B) [34, 35]. Broad consensus (17/0/1, 94 %)

Transient elastography (TE)

Procedure

Transient elastography uses an ultrasound displacement M-mode and A-mode image produced by the system. The operator locates a portion of the liver at least 6 cm thick and free of large vascular structures. By pressing the acquisition button, the machine displays the median of the measured Young's modulus in kPa, the interquartile range (IQR) (the difference between the 75th and the 25th percentile), IQR/median (IQR/M), the value of the current measurement and, only in the old version of the system, the success rate (the ratio between valid and total number of acquisitions). The system displays a result only if the acquisition is valid, since the software automatically rejects acquisitions without correct vibration shape or a correct follow-up of the vibration propagation [7, 8, 52].

For children as well as in adults with a thoracic circumference ≤ 75 cm, the S probe is recommended, either S1 for a thoracic circumference < 45 cm or S2 for 45 – 75 cm [53].

How to measure?

Following the manufacturer's recommendation, assessment is reliable when 10 valid readings and an IQR ≤ 30 % of the median (IQR/M ≤ 30 %) are obtained. The majority of studies have used these reliability criteria as well as a success rate ≥ 60 %. However, these criteria have not been externally validated. A reliable TE assessment can be achieved in over 90 % of adults, when both the M and XL probes are used as required [54 – 57]. Because the M probe takes measurements between 25 and 65 mm from the probe, to increase viability, those patients with a skin-to-liver capsule distance (SCD) of > 25 mm should be assessed with the XL probe.

The diagnostic accuracy of the XL probe appears similar to that of the M probe but the Young's modulus values are lower than those obtained with the M probe by a mean of 1.5 kPa (range of 0.8 – 2.3 kPa) [54 – 58].

RECOMMENDATION 9

10 measurements should be obtained. An IQR/M ≤ 30 % of the 10 measurements is the most important reliability criterion (LoE 1b, GoR A) [59, 60]. Strong consensus (17/0/0, 100 %)

RECOMMENDATION 10

Values obtained with the XL probe are usually lower than with the M probe. Therefore, no recommendation on the cut-offs to be used can be given (LoE 2B, GoR B) [(54 – 57, 61)]. Broad consensus (13/1/3, 77 %)

Reproducibility

The intra- and interobserver agreements are excellent, with reported intraclass correlation coefficients (ICC) above 0.90 [62 – 64]. The agreement decreases in overweight patients or in early stages of fibrosis [62, 63]. Although the LSM seems to be reproducible at different examination sites, the best examination site is the median axillary line on the first intercostal space under the liver percussion dullness upper limit, with the patient lying in dorsal decubitus [63].

Point shear wave elastography (pSWE)

Experience with point shear wave elastography (pSWE) has been mainly acquired with the VTQ® product, because it was the first method available, subsequently followed by ElastPQ® and, more recently, by pSWE methods from many companies.

Procedure (how to measure?)

The operator can select the depth at which liver elasticity is evaluated by placing a "measuring box" (size depending on the manufacturer) in the right liver lobe (segment V, VIII or VII), via an intercostal approach and with the transducer at 90° in relation to the liver capsule, in an area free of large vessels. In a pSWE study using VTQ® to measure SWS [3], the best correlation with histological fibrosis was observed for measurements performed 1 – 2 cm and 2 – 3 cm beneath the liver capsule (0.675 and 0.714, respectively), but in up to 15 % of cases, measurements could not be obtained if performed 2 – 3 cm under the liver capsule.

RECOMMENDATION 11

Adequate B-mode liver image is a prerequisite for pSWE and 2D-SWE measurements (LoE 5, GoR D). Strong consensus (18/0/0, 100 %)

How many measurements?

Most studies perform 10 valid measurements by pSWE and report the median of these values. A few studies have used only 5 [65, 66] or 6 [67] valid measurements. Another study [68] calculated the mean and standard deviation (SD) of 10 valid measurements. A high SD correlated with misclassification of fibrosis. Additionally, higher stages of fibrosis were associated with a higher SD, indirectly indicating that "more" measurements should be obtained in patients with suspected fibrosis.

RECOMMENDATION 12

The median value of at least 10 measurements should be used for liver elastography by pSWE (LoE 2b, GoR B) [68]. Strong consensus (18/0/0, 100 %)

Reproducibility

pSWE has excellent intra- and interoperator reproducibility for liver elastography assessment in both healthy subjects and patients with chronic liver disease [42, 46, 48, 69 – 71].

Quality criteria

One study [72] evaluated factors that influenced the correlation of SWS assessed by VTQ® with histological fibrosis in a cohort of 106 chronic hepatitis C (CHC) patients. In univariate and multivariate analysis, an IQR/M ≥ 30 % was associated with a discordance of at least 2 stages of fibrosis between SWS and histological fibrosis. Using ElastPQ®, a recent study has suggested that an IQR/M ≤ 30 % is the most important quality criterion, whereas the number of measurements seems not to affect the performance, provided that they are at least five [73]. Thus, the compliance with quality criteria may increase the diagnostic accuracy of pSWE [68, 72]. Quality parameters have been described for other manufacturers as well [74].

2D-SWE

Almost all 2D-SWE studies for liver applications have been carried out using SSI, because other companies have only recently introduced 2D-SWE products. This description is therefore limited to the SSI system, but the principles may be applied to other 2D-SWE products.

Procedure

Obtaining an elastogram

2D-SWE evaluation should be performed in a well-visualized area of the right liver lobe, free of large vessels, liver capsule, ligaments and the gallbladder [75]. Since movement greatly influences results, the subject is asked to suspend breathing.

With 2D-SWE working in continuous and not with single shot emissions, the SWE acquisition is continued for 4 – 5 seconds (can be longer for other scanning systems) once a stable SWE image is obtained. The operator should aim to achieve homogeneous color filling of the SWE ROI. Usually a Young's modulus scale of up to 30 kPa is sufficient, but a higher scale of up to 150 kPa can be adopted on a case-by-case basis. The operator freezes the image (and optionally saves the clip for further post-processing) and an analysis box (Q Box, for SSI) is placed on the most homogeneous, stable elastogram for a few seconds to measure Young's modulus (SWS, if the scanner is set to that mode).

How to measure?

Analysis box size and shape

For 2D-SWE measurements, the analysis box should be set to at least 10 mm, preferably 15 mm or more. A round shape is usually chosen [31, 32]. The ROI should be placed over an isoechoic area of liver parenchyma, as seen on the grayscale image (no vessel, no nodule, no other structure), in priority in the middle line of the elastogram (avoiding positioning the Q Box on the edges of the elastogram), while also avoiding SWS artefactual areas (reverberation, noisy areas from rib shadowing).

Valid and invalid measurements

There is no agreement on objective quality criteria. Some authors suggest that a minimal Young's modulus value of ≤ 0.2 kPa in the analyzed region is useful to identify invalid measurements as indicated by a lack of concordance with TE [76], while others use a minimal Young's modulus value of < 1 kPa. Furthermore, among valid measurements an IQR/M ≤ 30 % is recommended by other studies mimicking TE reliability criteria. For 2D-SWE with Logiq E9 (GE), the manufacturer recommends an IQR/M below 30 % as a quality criterion. Temporal stability of the elastogram for three seconds or more during breath hold in combination with placement of the analysis box in a homogeneous area with complete filling results in high accuracy, high reliability and low variance of measurements with SSI [77 – 79]. The new software version of the Aixplorer® system also shows the stability index (SI) and according to the manufacturer a reliable LSM should exclude measurements with an SI < 90 %. Aplio 500 (Toshiba) provides a display of shear waves travelling within the box, allowing selection of areas not affected by artefacts for analysis. For 2D-SWE with the Philips system, a confidence map guides the operator to perform measurements in areas where the signal-to-noise ratio of the SWS assessment is high.

How many measurements?

From 3 to 15 measurements are used in published studies, but data from several studies suggest that 3 measurements suffice to obtain consistent results for the assessment of liver fibrosis and portal hypertension, and for optimal correlation with TE [6, 32, 33, 79 – 81]. There is no convincing evidence to suggest superiority of the mean versus median of the SSI measurements. However, since the median and IQR are robust against non-normal distributed data, they should be preferred for reporting.

RECOMMENDATION 13

For 2D-SWE a minimum of three measurements should be obtained; the final result should be expressed as the median together with the interquartile range (LoE 2b, GoR B) [6, 82]. Strong consensus (18/0/0, 100 %)

Reproducibility

Reproducibility in healthy subjects

In three studies, the intraobserver reproducibility of SSI during the same session was excellent (ICC ranged from 0.92 to 0.95) [49, 83, 84]. The interobserver agreement on different days was affected by operator experience and ranged from 0.63 to 0.84 [83, 84].

Reproducibility in patients

The intraobserver reproducibility of 2D-SWE for liver stiffness assessment in liver fibrosis patients is excellent, with the ICC ranging from 0.90 to 0.95 in published studies [30, 31, 82]. The intra-subject reproducibility (evaluated over periods of 2 days to 4 weeks) ranges between 0.83 and 0.90 [85]. Interobserver reproducibility on the same day ranges from 0.83 [85] to 0.94 [77]. Intra- and interobserver variance may be inferior to pSWE using VTQ® [85].

Limitations

Failures

Common causes of failure are: depth below 4 – 5 cm [5], poor ultrasound window, reverberations, pulsatile movement, poor breath hold, large amounts of ascites [82], intercostal wall thickness ≥ 25 mm [86], BMI ≥ 30 kg/m^2, histological steatosis and waist circumference ≥ 102 cm [31, 33].

Unreliable assessments

The main factors limiting the applicability of 2D-SWE include obesity, poor acoustic window or presence of artefacts and inability of the subjects to hold their breath [5, 30, 31, 33, 82].

Comparison of results between systems

Introduction

Different US-based SWS technologies are available for the noninvasive assessment of liver fibrosis and the measurements produced can be slightly to moderately different between systems from different manufacturers. Even systems that use the same technique but were developed by different manufacturers can yield different values due to different and proprietary methods to measure the SWS.

Studies on phantoms

The Ultrasound Shear Wave Speed technical committee of the Radiological Society of North America, Quantitative Imaging Biomarker Alliance (QIBA) has quantified the differences between commercially available systems. Working on elastic phantoms, a statistically significant difference in the SWS estimates among systems and depth of measurement in the phantom was shown, whereas no statistically significant differences were found among operators using the same or equivalent systems under the same conditions [87]. Similar results were obtained using phantoms with viscoelastic properties similar to those observed in normal and fibrotic liver [88]. The measurements were performed at multiple focal depths (3.0, 4.5 and 7.0 cm). The deepest focal depth (7.0 cm) produced the greatest inter-system variability for each phantom (up to 17.7 %) as evaluated by the interquartile range. Inter-system variability was consistent across all phantoms and was not related to stiffness.

Sources of variability

Several sources of variability are detailed in published studies, including technical and patient-dependent factors that could affect comparability between systems.

Technical factors

Measurement depth

As shown by the studies on phantoms [87], the influence of depth on the estimation of elastic properties is not negligible. Furthermore, with curved transducers used in liver imaging, the angle affects the readings, with the best results being achieved when the ROI is straight ahead. Using VTQ®, it has been shown that the results with the lowest variability are obtained at a depth of 4 – 5 cm with a convex transducer (1 – 4 MHz; mean push pulse: 2.67 MHz) and at a depth of 2 – 3 cm with a linear transducer (4 – 9 MHz; mean push pulse: 4 MHz) [89]. The acoustic push pulse is progressively attenuated as it traverses the tissue. Attenuation is higher in a stiffer liver. Thus, measurements are more variable in cirrhotic patients [4].

Frequency of the transducer

In a prospective study on 89 patients with CHC, pSWE (based on VTQ®) was performed using both available transducers (4C1 and 9L4) [90]. The linear transducer gave higher values (1.91 ± 0.87 m/s vs. 1.70 ± 0.67 m/s). However, the results were correlated to each other (r = 0.70). Using the same method in a phantom and a series of eight volunteers, it was found that the convex transducer showed values that were significantly higher than those obtained with the linear transducer [89].

Position of the transducer

The highest intra- and interobserver agreement was obtained for the measurements performed through the intercostal space rather than the subcostal approach [48, 69, 91].

Operator experience

Methods using pSWE have shown excellent interobserver agreement, with concordance ranging from 0.80 to 0.97 for measurements performed via an intercostal approach, and independent of operator experience, suggesting that operators require only a short period of training to perform reliably LSMs [42, 46, 69, 92]. Using 2D-SWE (SSI) an expert operator had higher reproducibility of measurements over time than a novice operator [84]. It is suggested that at least 50 supervised 2D-SWE measurements should be performed by a novice operator in order to obtain consistent measurements. Echosens, the manufacturer of the FibroScan device, recommends that TE be performed by an experienced operator (> 100 examinations). Using liver biopsy as the reference standard, a recent study has shown that ElastPQ® matched TE for accuracy after the operator had performed at least 130 examinations [93].

Equipment

Proprietary elastographic technologies generally give different estimates of the SWS within the same liver. This translates into the need to define threshold values for fibrotic stages for each specific equipment model.

Clinical studies

Diagnostic accuracy

Some comparative studies show similar accuracy for different elastographic systems. Larger prospective studies are necessary to find if there are differences in accuracy between each different system for liver stiffness evaluation.

RECOMMENDATION 14

The results with the lowest variability in comparing different pSWE or 2D-SWE systems were obtained at a depth of 4 – 5 cm from the transducers (with convex transducers) (LoE 4, GoR C) [89]. Accordingly, this location is recommended if it is technically suitable. Broad consensus (17/0/1, 94 %)

Liver diseases

Introduction

The assessment of fibrosis in chronic liver diseases is pivotal for prognosis and guiding management, including whether to commence antiviral treatment. Liver biopsy is considered the "gold standard" for fibrosis assessment and stage classification and can also grade necro-inflammatory activity. However, liver biopsy is limited by its invasiveness, sampling error and the inter- and intraobserver variability in microscopic evaluation. Therefore, noninvasive methods for liver fibrosis assessment including ultrasound elastographic methods have been an intense field of research [7].

Due to the differences among elastography methods outlined in previous sections, cut-off values for fibrosis are system-specific and cannot be equated across machines.

It is becoming increasingly clear that the best cut-off values of the different elastography techniques used to evaluate the presence and severity of liver fibrosis depend upon the etiology of the underlying liver disease, and upon the prevalence of the condition under study in the target population. Differences between cut-offs may be simply related to differences in cirrhosis prevalence and severity in the studied populations, known as the spectrum bias. Therefore, elastography values should be interpreted by a liver specialist aware of the clinical aspects of the liver disease to be assessed and aware of the peculiarities of elastography in general and each elastography technique in particular.

Besides increasing evidence regarding liver stiffness measured by different techniques to detect liver fibrosis and cirrhosis (described in detail in the following paragraphs), other new applications of elastography are being tested in the field of liver diseases. They include spleen stiffness assessment for portal hypertension and the evaluation of the stiffness of focal liver lesions to differentiate between benign and malignant nodules. These applications appear promising, but remain under development and cannot yet be recommended in clinical practice.

Clinical needs

The ranges for intermediate fibrosis stages (F2-F3) are quite narrow, in the order of a Young's modulus of 2 – 3 kPa (over a total range spanning 2 to 75 kPa with the TE), so that small differences in outputs could shift the assessment of patients from one stage to another [94]. However, in "the real life" situation, attention should be focused on the patient and what is appropriate from a clinical point of view. Following the availability of novel antiviral agents, the European Association for the Study of the Liver (EASL) together with the Asociación Latinoamericana para el Estudio del Hígado (ALEH) have produced guidelines for the clinical use of noninvasive tests for the evaluation of liver disease severity and prognosis [52]. These guidelines have outlined that the two clinically relevant endpoints in patients with viral hepatitis are the detection of significant fibrosis (F≥ 2) and the detection of cirrhosis (F = 4), and the most important endpoint is the detection of cirrhosis, because it guides treatment (A1 recommendation). In patients with NAFLD and with chronic liver diseases of other etiologies, the detection of cirrhosis is also the most important clinical endpoint (A1 recommendation).

Chronic hepatitis C (CHC)

Fibrosis staging

Transient elastography

In patients with CHC, TE can differentiate absent and mild fibrosis from significant fibrosis and cirrhosis, but is not accurate enough to distinguish between separate stages of fibrosis (F1-F4) [95 – 97]. A Young's modulus greater than 6.8 – 7.6 kPa indicates a high probability of significant fibrosis (F ≥ 2) on biopsy. However, optimal cut-off values vary considerably depending on fibrosis prevalence and may range between 5.2 – 9.5 kPa as indicated in the clinical practice guidelines of the EASL [52]. Accordingly, the optimal cut-off values for predicting cirrhosis (F = 4) range between 11 and 15 kPa [52]. Therefore, the local fibrosis prevalence and the diagnostic aim (sensitive screening vs. secure exclusion strategies) must be considered when adapting cut-off values for clinical use. It should be emphasized that TE gives the best diagnostic performance in the context of cirrhosis diagnosis, and for this purpose it is better at ruling out than at ruling in cirrhosis.

In CHC patients with HIV co-infection, TE can be used with similar diagnostic accuracy as compared to HCV infection alone for fibrosis and cirrhosis detection [98]. TE can also be helpful in liver transplant recipients for the staging of recurrent fibrosis and cirrhosis [99].

The use of TE for the diagnosis of cirrhosis and the estimation of fibrosis severity in CHC has been endorsed in the recommendations for the management of viral hepatitis by the EASL and the ALEH, ideally in combination with an alternative and unrelated noninvasive approach such as laboratory tests/serum markers of fibrosis [100]. In the case of TE failure or inconclusive noninvasive test results, biopsy is still recommended when fibrosis staging is relevant for clinical decisions, although a preliminary attempt with an alternative SWE method could be considered.

RECOMMENDATION 15

TE can be used as the first-line assessment for the severity of liver fibrosis in patients with chronic viral hepatitis C. It performs best with regard to the ruling out of cirrhosis (LoE 1b, GoR A) [4, 98, 100]. Broad consensus (17/0/1, 94 %)

Point shear wave elastography (pSWE)

As with TE, VTQ® SWS quantification has been studied extensively in patients with CHC. Cut-offs of 1.21 – 1.34 m/s predict significant fibrosis (F ≥ 2) (AUROC 0.85 – 0.89), while VTQ® cut-offs between 1.55 and 2 m/s (AUROC 0.89 – 0.93) predict cirrhosis [70, 101]. The diagnostic performance of VTQ® is comparable to TE [102] with high accuracy for predicting significant (F ≥ 2, AUROC 0.87) and severe fibrosis (F ≥ 3, AUROC 0.91) as well as cirrhosis (AUROC 0.93) [103]. However, discordance (>one fibrosis stage) between VTQ® and histology occurred in > 30 % in a study including 106 patients infected with HCV. The discordance was associated with female gender and a high interquartile range (IQR/M ≥ 30 %) of Young's modulus [72]. Therefore, pSWE results require cautious interpretation. Evidence regarding ElastPQ® is limited [46, 104]. The results in the pilot study [46] for fibrosis staging are similar to those reported for VTQ®, but more data are needed. Fibrosis biomarkers may help to clarify indistinct cases [105].

RECOMMENDATION 16

pSWE as demonstrated with VTQ® can be used as the first-line assessment for the severity of liver fibrosis in patients with chronic hepatitis C. It performs best with regard to the ruling out of cirrhosis (LoE 2a, GoR B) [103]. Broad consensus (17/0/1, 94 %)

2 D shear wave elastography (2D-SWE)

2D-SWE using SSI was reported in several studies in patients with CHC [106, 107]. Diagnostic accuracy was high for the detection of significant and advanced fibrosis and cirrhosis (AUC> 0.90). In these studies the diagnostic performance for 2D-SWE was better than for TE [106, 108] and serum fibrosis markers (FIB-4 index, APRI and Forns' index) [108]. In one study including 102 obese CHC patients, 2D-SWE had excellent diagnostic accuracy for the detection of severe fibrosis and cirrhosis (AUROC > 0.90 for both) [109].

RECOMMENDATION 17

2D-SWE as demonstrated with SSI can be used as a first-line assessment for the severity of liver fibrosis in patients with chronic hepatitis C. It performs best with regard to the ruling out of cirrhosis (LoE 1b, GoR A) [106 – 108]. Broad consensus (17/0/1, 94 %)

Prediction of hepatic complications

Growing evidence supports the use of TE for risk stratification and the prediction of clinical endpoints. Liver stiffness predicts 5-year mortality with better accuracy than histological fibrosis staging (METAVIR) for HCV mono-infected (TE > 9.5 kPa) [110] and HIV co-infected patients (TE > 9.0 kPa) [111]. Furthermore, an elevated Young's modulus indicates an increased risk of hepatocellular carcinoma (HCC) development (TE > 10 kPa) [112], hepatic decompensation and variceal bleeding [113]. Especially for patients with an established diagnosis of cirrhosis, TE can be used for grouping patients into different risk classes [112]. The combination of liver stiffness (Young's modulus of > 14 kPa) with platelet count (< 141 × 10^3/µL) and response to antiviral treatment may increase the predictive value of TE for HCC development [114]. In patients with compensated liver cirrhosis, liver stiffness helps to identify patients with portal hypertension (see section recommendations on portal hypertension). Data regarding firm endpoint prediction using pSWE and 2D-SWE are lacking and no evidence-based recommendation can be specified. Two groups evaluated the predictive value of TE in transplant patients with a recurrence of HCV infection [115, 116]. A Young's modulus > 8.7 kPa at 12 months after liver transplantation was associated with a significantly reduced five-year graft and cumulative patient survival [115].

Role of elastography in the setting of anti-HCV treatments

Role of SWE to identify patients to be treated

In the absence of universal access to direct-acting antiviral agents (DAA) as a consequence of high cost, different countries have implemented strategies to prioritize patients for treatment. TE is used as the first-line investigation for the prioritization of HCV patients for DAA (e. g., Young's modulus values ≥ 7.1 kPa are considered equivalent to fibrosis ≥F2, and values ≥ 9.5 kPa are considered equivalent to fibrosis ≥F3). In countries using interferon-based strategies, TE can help to identify patients with cirrhosis who have a lower likelihood of achieving a sustained virological response (SVR: undetectable HCV-RNA, 24 weeks after completion of antiviral therapy).

Role of SWE during treatment (monitoring)

Limited evidence in the setting of interferon-based therapy postulated that increasing liver stiffness as measured by TE during the treatment period might indicate a reduced possibility of achieving a sustained virological response [117, 118]. Data in patients undergoing IFN-free antiviral therapies suggest that liver stiffness rapidly declines during treatment, even in patients with advanced fibrosis and cirrhosis. This decline appears to reflect the reduction in liver inflammation, restoration of liver function and the decrease in portal pressure, like an effect of HCV eradication [119, 120].

Role of SWE after treatment (monitoring in follow-up)

Data regarding the usefulness of liver stiffness monitoring during antiviral therapy are scant. In the largest prospective study published (n = 91), a significant liver stiffness decrease was observed during therapy with peg-interferon and ribavirin; the decrease in liver stiffness continued after treatment only in patients who achieved SVR [121]. In the era of DAAs, it is important to remark that after successful HCV eradication, the use of pre-treatment cut-off values can impair the accuracy of TE [122, 123], and it might lead to erroneous conclusions if the SVR status is not carefully taken into account [120]. Several studies have evaluated the use of VTQ® for monitoring IFN-based antiviral therapy in

HCV patients: SWE decrease or increase reflects response or no response to treatment, respectively [124 – 126]. For IFN-free antiviral therapies, no data are available.

The monitoring of cirrhotic patients after SVR will become the new standard in the era of DAAs. Although it is tempting to use SWE in this setting to observe the dynamics of liver stiffness over time, no recommendation can be made at this stage on cut-offs and the time interval to identify cirrhosis regression.

RECOMMENDATION 18

SWE is not recommended to monitor fibrosis changes during anti-HCV treatment (LoE 3, GOR D) [122, 123]]. Strong consensus (18/0/0, 100 %)

RECOMMENDATION 19

LSM changes after successful anti-HCV treatment should not affect the management strategy (e. g. surveillance for HCC occurrence in patients at risk) (LoE 3, GOR D) [52]. Broad consensus (16/0/1, 94 %)

Chronic hepatitis B (CHB)

Introduction

A large amount of evidence regarding elastography in CHB is available. There are > 50 published studies. The majority of them use TE but also validate the elastographic methods of pSWE and 2D-SWE.

Fibrosis staging

The most important goal of noninvasive diagnostic tools is diagnosis of compensated cirrhosis that would benefit from treatment regardless of the transaminase level [127].

Transient elastography

Transient elastography is the most validated elastographic method for staging CHB and has similar accuracy in this clinical scenario compared to CHC [52]. Three meta-analyses confirmed the good performance of TE in CHB staging [128 – 130]. Despite LSMs showing a substantial overlap among adjacent stages of fibrosis (particularly at lower fibrosis stages), LSM may effectively identify patients with ≥F2 and F4. Recent publications confirmed previous evidence, suggesting that the AUROCs for ≥F2 vary between 0.80 and 0.90 [131, 132] with Young's modulus cut-off values between 6.6 kPa and 8.8 kPa [132, 133]. Regarding the identification of cirrhosis (F4), recent data confirm previous evidence, with AUROCs ranging between 0.81 and 0.97 [132] and cut-off values between 9.4 and 13.4 kPa [134, 135]. A recent meta-analysis suggested that a value > 11.7 kPa should raise suspicion of cirrhosis [128]. It has been suggested that LSM cut-offs should be adapted to transaminase levels [135] since transaminase levels tend to influence LSM in CHB, and hepatitis flares are often observed in CHB. However, recent studies showed that ALT-adapted cut-offs do not influence TE diagnostic performance [136] and that the only variable associated with overestimation of F4 stage in CHB is moderate/severe necro-inflammatory activity without any direct correlation with transaminase levels [137]. Interestingly, a Young's modulus of < 5 kPa in patients with normal ALT and low serum HBV DNA levels (< 2000 IU/ml) characterize inactive HBV carriers [138, 139]. TE can be used to rule out significant fibrosis and cirrhosis in HBV inactive carriers, which is the best indication for TE in HBV.

RECOMMENDATION 20

TE is useful in patients with CHB to identify those with cirrhosis. Concomitant assessment of transaminases is required to exclude flare up (elevation > 5 times upper limit of normal). (LoE 1b, GoR A) [128 – 130]. Broad consensus (17/1/0, 94 %)

RECOMMENDATION 21

TE is useful in inactive HBV carriers to rule out fibrosis (LoE 2, GOR B) [138, 139]. Strong consensus (18/0/0, 100 %)

Point shear wave elastography (pSWE)

VTQ® has the advantage of a lower failure rate and has a similar diagnostic performance as TE. The discriminative ability for staging fibrosis in CHB is good, with AUROCs for ≥F2 and F4 of 0.76 – 0.91 [134, 140] and 0.72 – 0.97 [103, 134], respectively. These findings were confirmed in a meta-analysis that included patients with several etiologies of liver disease. The analysis of data of patients with CHB showed an AUROC for ≥F2 of 0.88 and the best cut-off was 1.35 m/s and the AUROC for F4 was 0.93 and the best cut-off was 1.87 m/s [141, 142]. There is limited data about other pSWE methods. ElastPQ® has been used for staging CHB patients in four studies, with good performance for staging liver fibrosis. Further validation is required [92, 142 – 144].

2 D shear wave elastography (2D-SWE)

Recently, 2D-SWE (SSI) was tested in patients with CHB and proved to have a lower failure rate than TE and at least similar performance for fibrosis staging [145]. The AUROC for ≥F2 varies between 0.85 and 0.91 [32, 146], with Young's modulus cut-offs between 7.1 and 8.0 kPa [145, 146], while the AUROC for F4 varies between 0.92 and 0.98 [147, 145], with optimal cut-offs between 10.1 and 11.7 kPa [32, 145]. The best indications of 2D-SWE in HBV are inactive carriers to rule out significant fibrosis and cirrhosis diagnosis.

RECOMMENDATION 22

pSWE as demonstrated with VTQ® is useful in patients with CHB to identify those with cirrhosis (LoE 2a, GoR B) [141]. Strong consensus (18/0/0, 100 %)

RECOMMENDATION 23

2D-SWE as demonstrated with SSI is useful in patients with CHB to identify those with cirrhosis (LoE 3a, GoR C) [146, 147]. Broad consensus (17/0/1, 94 %)

Monitoring (evaluation of) response to treatment

Under nucleoside/nucleotide analogs, liver stiffness measured by TE significantly decreases regardless of the baseline values of ALT [148, 149]. The only factors associated with decline of LSM are higher baseline LSM and HBV DNA levels [148]. The diagnostic accuracy and thresholds of liver stiffness using TE may differ in untreated and treated patients with chronic hepatitis B and C. This aspect should be taken into account when interpreting the results of elastography. Moreover, even if liver stiffness declines with antiviral treatment, it is unknown if this reflects disease regression and LSM changes should not affect management.

RECOMMENDATION 24

LSM changes under HBV treatment should not affect the management strategy (e. g. surveillance for HCC occurrence in patients at risk) (LoE 2b, GOR B) [148, 149]. Strong consensus (16/0/0, 100 %)

Prognostic relevance

Baseline LSM by TE has modest prognostic relevance with an AUROC between 0.70 and 0.73 for liver-related events [150, 151], which may be increased by adding spleen diameter and platelet count as a prediction model called LSPS (= LSM × spleen diameter/platelet count) up to a level of 0.83 [152]. TE is a good prognostic marker for HCC development that may occur without cirrhosis. A Young's modulus of > 8 kPa might be a value indicating the need to start screening for HCC, even if a complete virological response was achieved [153, 154]. The risk of HCC is even higher if the Young's modulus by TE is > 12 – 13 kPa, which also implies an increased risk of decompensation [131, 153 – 155].

Non-alcoholic fatty liver disease (NAFLD)

In NAFLD patients, noninvasive markers should aim at the following: a) identify the risk of NAFLD/NASH among individuals with metabolic syndrome; b) identify those with a worse prognosis; c) monitor disease progression; d) predict response to treatment.

Fibrosis staging (NAFLD)

Transient elastography

TE performance is better for cirrhosis than for significant fibrosis [156, 157]. TE has a higher rate of false-positive than false-negative results and a higher negative predictive value (NPV) than positive predictive value (PPV). Therefore, the ability to diagnose bridging fibrosis or cirrhosis is insufficient for clinical decision-making [158, 159]. A systematic review of TE in patients with NAFLD involved 9 studies and 1047 patients [160]. TE was excellent in diagnosing F3 fibrosis (85 % sensitivity, 82 % specificity) and cirrhosis (92 % sensitivity, 92 % specificity), but had only moderate accuracy for F2 fibrosis (79 % sensitivity, 75 % specificity).

With the M probe, patients with steatosis > 66 % at liver biopsy had higher LSM values, which led to higher false-positive LSM results [26]. Thus, in obese patients with a high degree of steatosis, TE (using the M probe) may be less accurate in diagnosing severe fibrosis in NAFLD, and additional evaluation may be warranted to avoid overestimation of fibrosis. However, additional studies on the effects of steatosis on LSM measured with an XL probe are needed. The XL probe produces lower stiffness values than the M probe. Different cut-offs should be used [57]. With the M probe, at a Young's modulus cut-off value of 7.9 kPa, the sensitivity, specificity, PPV and NPV for F3 or greater disease are 91 %, 75 %, 52 %, and 97 %, respectively [29].

In NAFLD patients, the best cut-off for F3 or greater disease is 7.2 kPa. With this cut-off, the NPV to exclude F3 or greater disease is 89 % (95 % CI 84 – 95 %). Cut-off values of 5.7 kPa and 9.3 kPa have 90 % sensitivity and specificity to rule out and rule in F3 disease, respectively [29].

RECOMMENDATION 25

TE can be used to exclude cirrhosis in NAFLD patients (LoE 2a, GoR B) [52, 160]. Broad consensus (13/0/3, 81 %)

Point shear wave elastography (pSWE)

A systematic review of 7 studies for a total of 723 patients who underwent SWS measurements with VTQ® technique to evaluate the diagnostic efficacy of pSWE in patients with NAFLD was recently published [161]. The summary sensitivity was 80.2 % for detecting significant fibrosis, which is not an appropriate endpoint.

2 D shear wave elastography (2D-SWE)

There are only two studies that evaluate the performance of 2D-SWE (SSI) [31, 162]. The results are too limited to make recommendations.

Comparison of different elastographic methods for NAFLD

One study recently compared TE (using the M probe), pSWE (VTQ®) and 2D-SWE (SSI) in 291 patients with NAFLD enrolled in two different hospitals [31]. All methods showed AUROCs ≥ 0.84 for severe fibrosis and cirrhosis and had a similar performance for the diagnosis of these endpoints. The diagnostic performance of 2D-SWE was superior to that of VTQ® for the diagnosis of significant fibrosis.

Follow-up of patients

Monitoring of the progression of fibrosis is also necessary in the follow-up of these patients. Patients who achieved a ≥ 5 % weight loss at the 6-month follow-up showed a decrease in LSM by TE, independent of the changes in aminotransferase levels [158]. No data are available for pSWE and 2D-SWE.

Prediction of liver-related complications

A recent study supports the use of TE for risk stratification and prediction of clinical endpoints [163]. For pSWE and 2D-SWE data on this aspect are lacking and no evidence-based recommendation can be given.

Alcoholic liver disease (ALD)

Fibrosis staging

Transient elastography in patients with prior or current chronic alcohol overuse can distinguish absent and mild fibrosis (F0 – 1) from severe fibrosis and cirrhosis, but similar to other etiologies, there is no evidence to suggest that it can differentiate absent and mild fibrosis from significant fibrosis. [164] Additionally, in the eight published single etiology studies on TE for staging liver fibrosis, there is no consensus regarding optimal Young's modulus cut-off values for significant fibrosis (≥F2), severe fibrosis (≥F3) or cirrhosis (= F4) [23, 30, 165 – 170]. The optimal cut-off values range from 7.8 [166] to 9.6 [30] kPa for significant fibrosis, from 8.0 [23] to 17.0 [168] kPa for severe fibrosis and from 12.5 [23] to 22.7 [165] kPa for cirrhosis. The considerable discrepancy between cut-off values in individual studies is likely a consequence of differences in fibrosis stage prevalence with overrepresentation of cirrhotic patients, place of recruitment, and whether patients with alcoholic hepatitis or decompensated disease were excluded.

TE is more suited to rule out than rule in cirrhosis. At a Young's modulus of 12.5 kPa, TE may rule out cirrhosis with a negative likelihood ratio of 0.07 if the disease prevalence is 50 % or lower [164].

RECOMMENDATION 26

TE can be used to exclude cirrhosis in patients with alcoholic liver disease, provided that acute alcoholic hepatitis is not present (LoE 2b, GoR B) [30, 164, 169, 170]. Strong consensus (15/0/0, 100 %)

Prognostication of alcoholic liver cirrhosis

There is scant evidence to suggest a role for ultrasound elastography for determining the prognosis and for the monitoring of patients with alcoholic liver disease [171], or for TE to predict esophageal varices [172] and the hepatic venous pressure gradient in patients with alcoholic cirrhosis [171].

Timing of liver stiffness measurements with regard to alcohol abstinence

In patients undergoing alcohol detoxification, 0.5 to 4 weeks of abstinence causes a clinically significant decrease in TE [23 – 25, 173]. However, the decrease is associated with a normalization of transaminases, bilirubin, alkaline phosphatase and/or gamma-glutamyltransferase. It is, therefore, unclear whether alcohol alone or alcohol-induced hepatitis and cholangiocyte damage cause the increase in liver stiffness. [170]. One study suggests that TE is accurate for staging in patients with ongoing alcohol abuse but normal gamma-glutamyltransferase [30], while another study suggests that AUROC for the diagnosis of cirrhosis in alcoholic patients diminishes when AST is above 100 – 150 U/L [170].

Screening the general population or high-risk groups in primary care

Ultrasound elastography for systematic screening of high-risk populations in primary care for alcoholic liver disease was performed in one study. TE was offered to primary care patients with an AST:ALT ratio ≥ 0.8 [174]. However, this study did not include biopsy confirmation in patients with elevated TE. In a diagnostic study, TE had excellent diagnostic accuracy for significant fibrosis and cirrhosis in a subgroup of 71 patients recruited from primary alcohol rehabilitation centers [30].

With a prevalence of cirrhosis of 2 – 4 % in a background population of at-risk individuals [175], the positive predictive value of TE should be considered low regardless of cut-off values.

Point shear wave elastography (pSWE) and 2D-SWE

There is only one study to support the use of 2D-SWE (SSI) for assessing alcoholic liver fibrosis [30]. There are three small studies on the use of pSWE [176 – 178], two of which report diagnostic accuracies and test probabilities. The results are consistent regarding diagnostic accuracy, which suggests that VTQ® may be used to rule out severe fibrosis and cirrhosis. The results regarding cut-off values are, however, inconsistent. Therefore, there is insufficient evidence to make recommendations for using VTQ® to distinguish absent and mild fibrosis (F0 – 1) from significant or severe fibrosis and cirrhosis. Thus, there is still insufficient evidence to evaluate the role of pSWE or 2D-SWE in alcoholic liver disease.

Cholestatic liver disease and autoimmune hepatitis (AIH)

Risk stratification is a major need in patients with chronic cholestatic diseases in order to allow personalized management and the selection of candidates for clinical trials of new drugs. Studies of liver stiffness as a surrogate of liver fibrosis and prognosis focusing on cholestatic liver disease (primary biliary cholangitis-PBC, primary sclerosing cholangitis-PSC) or AIH are scarce. Most available data focus on TE [179 – 181].

Transient elastography

Transient elastography is currently considered one of the best surrogates of fibrosis in PBC. High baseline or increasing values over time indicate a worse outcome in this population [141, 179]. Liver stiffness was investigated in 73 patients with PSC, regularly undergoing clinical and elastographic follow-up [182]. LSMs were able to differentiate severe vs. non-severe fibrosis with a high discriminative accuracy for cirrhosis (AUROC 0.88). There was high reproducibility between two operators. Higher baseline LSM and an increase of LSM over time were associated with adverse outcome such as death, liver transplantation, ascites, hepatic encephalopathy, gastrointestinal bleeding, or HCC [182]. Dilatation of the intrahepatic biliary system due to a dominant

stricture should be excluded in PSC before interpreting the LSMs. Cholestasis increases liver stiffness independent of liver fibrosis.

Data regarding the pediatric population with biliary atresia suggest that liver (and spleen) elastography could be a valuable tool to predict outcomes before surgery, and might be used after the Kasai operation to monitor liver disease and portal hypertension [183].

Due to the limited evidence, no recommendation can be given.

Point shear wave elastography (pSWE)

VTQ® was initially performed in 9 patients with AIH, PBC and PSC having higher shear wave velocities than healthy volunteers [184]. In total, two studies dealt with VTQ® in AIH and primary biliary cholangitis. In 15 patients with treated AIH, VTQ® could differentiate between the absence of fibrosis and significant fibrosis [185]. SWS assessed by VTQ® showed good diagnostic accuracy for detecting cirrhosis (AUROC 0.91) in 61 patients with primary biliary cholangitis [186].

2 D shear wave elastography (2D-SWE)

Data regarding 2D-SWE in AIH, PBC and PSC are not available. Liver stiffness assessment helped in differentiating between biliary atresia and neonatal hepatitis in one study [187].

Due to the paucity of data, no recommendation can be given.

Portal hypertension

Transient elastography

In patients with compensated advanced chronic liver disease/cirrhosis, LSM correlates with the hepatic venous pressure gradient (HVPG). Even though the correlation between the two does not allow for an accurate estimate of the exact HVPG value (range: 0.59 – 0.70), the discriminative ability of liver stiffness for the presence of clinically significant portal hypertension (CSPH, defined as HVPG ≥ 10 mmHg, threshold for the appearance of complications) is very high, with a summary AUROC of 0.93 in a recent meta-analysis [188]. However, it should be emphasized that most of the patients included in the studies concerning HVPG had viral or alcoholic cirrhosis, and evidence regarding other etiologies is limited. In viral cirrhosis, Young's modulus values of > 20 – 25 kPa are highly specific for CSPH, and values of > 21 kPa predict the onset of a first clinical decompensation with an accuracy similar to that of HVPG > 10 mmHg [189].

RECOMMENDATION 27

LSM with TE is useful to identify patients with a high likelihood of having clinically significant portal hypertension (HVPG ≥ 10 mmHg) (LoE 2b, GoR B) [188, 189]. Strong consensus (15/0/0, 100 %)

The accuracy of LSM in predicting the presence and size of gastroesophageal varices has been the subject of several studies. Despite the fact that it is currently the best single noninvasive predictor in this field with summary AUROCs of 0.84 for esophageal varices (EV) and 0.78 for large EV in a recent meta-analysis [188], the cut-offs vary widely among the studies, and the accuracy is not sufficient to replace endoscopy. The accuracy of LSM for the diagnosis of CSPH and varices improves if it is combined with platelet count and spleen size [190, 191]. Recent data indicates that if a combination of a Young's modulus value of < 20 kPa and a platelet count of > 150 G/L is used, varices needing treatment can be ruled out with a high accuracy (< 5 % of patients missed) [192, 193], and endoscopy can be safely avoided [194].

Point shear wave elastography (pSWE)

Point SWE (VTQ®) has been used in three studies addressing the diagnosis of CSPH [195 – 197] and showed excellent applicability and very good diagnostic accuracy (AUROC 0.82 – 0.90). VTQ® has been used in a few studies addressing the diagnosis and severity of esophageal varices. SWS was higher in patients with esophageal varices of any size, and was even higher in patients with large varices [195, 196]. However, reliable cut-offs are not available yet. No strong recommendation regarding the cut-offs to be used can be made due to the limited evidence.

2 D shear wave elastography (2D-SWE)

2D-SWE (SSI) has been tested for the diagnosis of CSPH in 4 studies and a further small series [6, 198 – 201]. The accuracy of the method was reliable in all of the published studies (AUROC 0.80 – 0.92).

Two studies performed a head-to-head comparison between LSM by TE and 2D-SWE [6, 198]. TE was less applicable, and both techniques showed similar accuracy for the diagnosis of CSPH.

LSM by 2D-SWE is higher in patients with esophageal varices of any size and is further increased in patients with large varices. However, reliable cut-offs are not available yet. No strong recommendation regarding the cut-offs for 2D-SWE can be given, and further evidence is needed.

RECOMMENDATION 28

Liver stiffness using TE combined with platelet count is useful to rule out varices requiring treatment (LoE 2b, GoR B) [194]. Although preliminary results are encouraging, there is insufficient evidence to recommend pSWE and 2D-SWE in this setting. Broad consensus (13/0/1, 93 %)

Conflict of interest

Some authors declare conflicts of interest, which are available from the publisher.

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