Review

Medical Ultrasonography
2012, Vol. 14, no. 3, 225-230

Liver elastography for the diagnosis of portal hypertension in patients with liver cirrhosis

Roxana Şirli, Ioan Sporea, Simona Bota, Iulia Raţiu

Department of Gastroenterology and Hepatology, University of Medicine and Pharmacy "Victor Babeş" Timişoara, Romania

Abstract

Progressive hepatic fibrosis is a feature of almost all chronic liver diseases. In their final stage, advanced cirrhosis, the clinical signs are diagnostic, but compensated liver cirrhosis is not always easy to diagnose. Apart from liver biopsy, serologic and elastographic non invasive methods for the evaluation of fibrosis severity were developed in the last few years. Studies have been made in order to assess their value for predicting the occurrence of cirrhosis complications, particularly portal hypertension. Both Transient Elastography and ARFI elastography are valuable methods for the early diagnosis of cirrhosis. While TE is a promising method for predicting the presence of portal hypertension in cirrhotic patients, the diagnostic accuracy of ARFI in the liver seems to be poor. Probably the accuracy of ARFI elastography can be significantly increased if spleen stiffness is assessed, alone or in combination with liver stiffness and other parameters.

Keywords: liver stiffness, portal hypertension, transient elastography, ARFI elastography

Introduction

Chronic liver diseases impose a higher toll on public health systems since they are more and more frequent among general population, especially in areas with a high prevalence of infection with hepatitis viruses, but also due to the rising incidence of alcoholic steato-hepatitis (ASH) and non-alcoholic fatty liver disease (NAFLD) [1]. World Health Organization (WHO) estimates that 2.35% of the global population is infected with hepatitis C virus (HCV) (160 million chronically infected individuals), ranging from < 0.5% (eg, northern European countries) to approximately 20% in highly endemic areas, including urban centers in Western Europe and USA and the Nile Delta in Egypt [2]. Also according to WHO, more than 350 million individuals are chronically infected with hepatitis B virus (HBV), which is responsible for approximately 580,000 deaths from decompensated cirrhosis or hepatocellular carcinoma (HCC) each year [3, 4], the HBV prevalence rates ranging from less than 2% in Western Europe, North America, Australia to more than 8% in South-East Asia [3].

Progressive hepatic fibrosis is a feature of almost all chronic liver diseases. Its' final stage, cirrhosis, is characterized by a profound derangement of liver architecture caused by nodule formation. Approximately 20–30% of the patients with chronic HCV hepatitis will eventually develop cirrhosis and its complications within one or more decades after diagnosis [5]. If in advanced cirrhosis the clinical signs are diagnostic, compensated liver cirrhosis is not always easy to diagnose. Currently, liver biopsy is still considered to be the gold standard for fibrosis assessment [6], but it has its shortcomings: the intra- and interobserver variability [7, 8]; the sampling variability [9]; and, last, but not least, the fact that it is an invasive method, with morbidity and mortality greater than 0. Furthermore, liver biopsy (LB) can miss the diagnostic of cirrhosis in up to 20% of the cases [7].

Received 25.05.2012 Accepted 15.06.2012
Med Ultrason
2012, Vol. 14, No 3, 225-230
Corresponding author: Dr. Roxana Şirli
14/5, Sirius str,
300688 Timişoara, Romania
Phone: + 40-723-537039
Fax: + 40-256-488003
E-mail: roxanasirli@gmail.com

Considering all these facts, both serologic and elastographic non invasive methods for liver fibrosis assessment were developed in the last few years in order to replace LB. FibroTest – ActiTest [10], transient elastography (TE) [11, 12] and Acoustic Radiation Force Impulse elastography (ARFI) [13,14] have proven their value for the diagnosis of liver cirrhosis.

Among patients with cirrhosis, those with advanced disease, with complications such as significant (at least grade 2) esophageal varices (EV), hepatocellular carcinoma (HCC), ascites have a shorter survival. Thus it seems reasonable to find those at risk of developing such complications to start interventions such as screening for EV and HCC. Several published studies regarding the value of elastographic methods for predicting the occurrence of portal hypertension will be discussed in this review.

Transient Elastography (TE)

TE is an ultrasound-based method that evaluates liver stiffness (LS) as a marker for fibrosis. It was developed by Echosens starting from the principles of Hooke's law, which characterizes a material's strain response to external stress [15]. A FibroScan device is used, whose ultrasound transducer probe, mounted on the axis of a vibrator, transmits low-frequency vibrations which create elastic shear waves that propagate into the liver. A pulse-echo ultrasound acquisition is used to measure wave propagation velocity (proportional to tissue stiffness); faster wave progression occurring through stiffer material.

LS measurements by TE are performed in the right liver lobe with the patient laying in dorsal decubitus with the right arm in maximal abduction. The operator, assisted by ultrasound A-mode images, locates a portion of the liver free of large vessels, at least 6 cm thick. After the measurement area is located, the operator presses the probe button to begin acquisition. Measurements with an incorrect vibration shape or follow-up are automatically rejected by the software. In order to obtain reliable TE measurements, the manufacturer recommends that at least 10 valid shots should be obtained; with a success rate (SR: the ratio of valid shots to the total number of shots) at least 60%; and with interquartile range (IQR, the difference between the 75th percentile and the 25th percentile, essentially the range of the middle 50% of the data) less than 30% of the median LSM value. Thus, TE is considered failed if no valid shots can be obtained, and unreliable if fewer than 10 valid shots are obtained, with an IQR greater than 30%, and/or a SR less than 60% [16]. Values ranging from 2.5 to 75 kPa should be expected.

Different cut-off values for the diagnosis of cirrhosis were proposed for different etiologies: 12.5 kPa in HCV infection [17]; 13.4 kPa in HBV infection [18]; 10.3 kPa in NAFLD [19]; 22.4 kPa in ASH [20]; 17.3 kPa in cholestatic chronic diseases (primary biliary cirrhosis and primary sclerosing colangitis) [21].

Published meta-analyses proved that TE is a reliable method for the diagnosis of cirrhosis. Data from 9 studies were evaluated by Talwalkar et al [11] showing that TE has 87% pooled sensitivity [95% confidence interval (CI): 84–90%)] and 91% pooled specificity (95% CI: 89–92%) for the diagnosis of cirrhosis. Another meta-analysis from 2010 [22] evaluated 22 published papers. For a cut-off value of 15.08 kPa it showed a pooled sensitivity of 84.45% (95% CI: 84.2-84.7%) with pooled specificity of 94.69% (95% CI: 94.3%-95%). Finally, in a recently published meta-analysis which included 40 studies, the summary sensitivity and specificity of TE for diagnosing cirrhosis were 0.83 (95% CI: 0.79-0.86) and 0.89 (95% CI: 0.87-0.91), respectively [23]. The mean optimal cut-off was 15 ± 4.1 kPa.

Regarding the value of TE for predicting liver cirrhosis complications, published data are controversial.

Esophageal varices and their consequence, upper digestive hemorrhage, are one of the most feared complications of cirrhosis. The hemorrhage risk is related to varices' size so that primary prevention of variceal bleeding applies to patients with large EV (grade 2 or 3) diagnosed by periodical upper digestive endoscopy (Baveno V and AASLD Consensuses) [24, 25]. A program of periodical upper endoscopy in all cirrhotics would be very expensive, even for developed countries. Furthermore, repeated gastroscopies are often poorly accepted by patients. Some of the published studies stated that LS values < 19 kPa were highly predictive of the absence of significant EV (≥ grade 2) [26], the cut off values for the presence of grade 2 and 3 EV ranging from 27.5 [27] to 47.2 kPa [28], and the cut off value for esophageal bleeding being 62.7kPa [27]. In a study published in 2009 on 298 HCV patients, 70 of them with cirrhosis and 25 with EV, Castera concluded that TE predicted the presence of OV with 76% sensitivity and 78% specificity, but that TE cannot replace upper endoscopy for the diagnosis of EV [29].

Nguyen-Khac et al demonstrated in a cohort of 183 cirrhotic patients that there are different cut-off LS values for predicting significant EV, according to the etiology of cirrhosis [28]. In patients with alcoholic cirrhosis, the cut-off for predicting significant EV was 47.2kPa with 84.6 % sensitivity, 63.6% specificity, 44% positive predictive value and 92.5% negative predictive value (AUROC=0.77), while in patients with viral etiology, the best cut-off was 19.8kPa, with 88.9% sensitivity, 55.1%

specificity, 26.7% positive predictive value, and 96.4% negative predictive value (AUROC=0.73).

Hepatic venous pressure gradient (HVPG) is the most sensitive tool for the assessment of portal hypertension. In an Italian study that evaluated 61 patients, the AUROCs of TE for predicting significant HVPG: ≥10 and ≥12 mm Hg were 0.99 and 0.92, respectively with 97% and 94% sensitivities for LSM cut off values of 13.6 kPa and 17.6 kPa, respectively. The AUROC for the prediction of EV was 0.76 and for a LSM cut off value of 17.6 kPa the sensitivity was 90% [30].

In a French study that included 150 patients, the correlation between LS by TE and HVPG was assessed [31]. For a cut off of 21 kPa, TE accurately predicted significant portal hypertension (HVPG > 10 mmHg), with an AUROC of 0.945.

Robic et al compared TE to HVPG as predictors of cirhhosis complications in 100 patients with chronic liver disease that were evaluated the same day by TE and HVPG measurements after which they were followed-up for 2 years. The performances of HVPG and LS for predicting the portal hypertension occurrence were similar: AUROCs 0.830 vs. 0.845. When patients were divided according to the 21.1kPa cut-off value, 100% of those with values lower than 21.1kPa remained free of portal hypertension complications, as compared to 47.5% of those with higher values. In the subgroup of cirrhotic patients, the performances of LS and HVPG were also similar [32].

Reiberger et al evaluated 122 cirrhotic patients with EV by means of TE and HVPG. In this study, the correlation of LS values assessed by TE and HVPG was stronger in controls with HVPG ≤ 12 mmHg (r=0.951) than in patients with HVPG > 12 mmHg (r=0.538). Also, the authors observed that an improvement in the correlation of LS with HVPG under beta-blockers was mainly noted in hemodynamic responders (r=0.864), but not in non-responders (r=0.535), whereas changes in LS, heart rate, and blood pressure were similar in responders and non-responders. For a cut-off value of 47.5 kPa, LS had 80.6% sensitivity and 47.7% specificity for discriminating cirrhotic patients with significant EV vs. those with grade 1 EV [33].

Finally, in a review published on line in 2011 that evaluated the available data, Castera concluded that "diagnostic performances of TE are acceptable for the prediction of clinically significant portal hypertension but far from satisfactory to confidently predict the presence of EV in clinical practice and to screen cirrhotic patients without endoscopy"[34]. But all the studies included in the review evaluated only small numbers of patients (ranging from 47 to 211), with contradicting results (cut-off values for significant EV ranging from 19.8 to 48 kPa, and AUROCs ranging from 0.73 to 0.87).

In a study from our group [35] that included 1000 consecutive cirrhotic patients, not available for the Castera review, we found out that for a cut-off value of 31 kPa negative and positive predictive values for at least grade 2 EV were 76.2% and 71.3%, respectively. For >31 kPa criterion, the cut off value was chosen to maximize the sum of sensitivity and specificity, whereas for >40 kPa criterion we chose a cut off value to have a PPV of more than 85%: with 77.8% sensitivity, 68.3% specificity, 86% PPV and 55% NPV (95%CI: 49.60–60.23). For a cut-off value of 17.1 kPa, chosen to have a NPV close to 90%, we found the NPV to be 89.3%, with 43.2% PPV, 92.6% sensitivity and 33.5% specificity (AUROC 0.7807). Thus, according to our data, in patients with TE values >40 kPa at least 8/10 cases will have significant portal hypertension. Therefore it is reasonable to recommend prophylactic beta-blocker therapy without endoscopy. On the other hand, in patients with TE values <40 kPa, 5/10 cases will have significant esophageal varices (NPV 54.9%), thus we recommend endoscopic evaluation. Below the cut-off value of 17.1 kPa we do not recommend endoscopic evaluation, since the chance of those patients having significant EV is only 1 in 10 (NPV 89.3%).

Acoustic Radiation Force Impulse Elastography (ARFI)

ARFI is a new elastographic method that assesses LS as a marker of fibrosis. It is performed with a Siemens Acuson S2000TM ultrasound system and it involves targeting an anatomical region to be investigated for elastic properties with the use of a ROI cursor, with a predefined size, provided by the system, while performing real-time B-mode imaging. The ultrasound probe automatically produces an acoustic "push" pulse (262μs), with a fixed transmit frequency of 2.67 MHz, that generates shear-waves which propagate into the liver, tracked using ultrasound correlation-based methods [36]. Using image-based localization and a proprietary implementation of ARFI technology, shear wave speed may be quantified. Measurement value and depth are also reported and the results of the elasticity are in m/s.

Scanning is performed between the ribs in the right liver lobe (e.g. segment 8) (in order to avoid cardiac motion), approximately in the place where liver biopsy is usually performed, 1 cm under the capsule, with minimal scanning pressure applied by the operator, while the patient is asked to stop breathing for a moment, in order to minimize breathing motion [37-39].

In the study performed by Lupşor et al [40], 112 patients with chronic hepatitis C were evaluated by means of liver biopsy (fibrosis stage assessed according to the Metavir scoring system), ARFI and TE. The mean ARFI values in F4 patients were significantly higher than in F3: 2.552 ± 0.782 m/s vs. 1.520 ± 0.575 m/s. A cut-off value of 2 m/s was proposed to differentiate patients with cirrhosis (AUROC 0.911).

In a paper published by our group [41], we compared ARFI to liver biopsy in a multicentre study that included 274 subjects with HCV chronic hepatitis. We found a direct, strong, correlation (Spearman r=0.707) between ARFI measurements and the fibrosis stage (p<0.0001). For predicting cirrhosis (F=4), for a cut-off value of 1.82 m/s, LS measurements by ARFI had 91% sensitivity, 90% specificity; with AUROC 0.937.

The experience accumulated with ARFI in the last years was followed by a meta-analysis by Friedrich-Rust et al [13] which evaluated 9 full papers assessing ARFI as compared to liver biopsy as reference method. The original patient data were available from 8 studies including 518 patients. The mean diagnostic accuracy of ARFI for cirrhosis, expressed as AUROC was 0.93. In the subgroup of patients undergoing both ARFI and TE, the diagnostic accuracy of ARFI was comparable to TE for the diagnosis of significant and severe fibrosis, with a trend to be inferior for the diagnosis of cirrhosis.

In a paper from our group [42] that compared ARFI to TE as predictors of fibrosis severity, with biopsy as gold standard, 223 subjects were included. We found a significant correlation (Spearman rho = 0.870) between TE and fibrosis stage (p < 0.0001) and a weaker one between ARFI and fibrosis stage (Spearman rho = 0.646; p < 0.0001). TE measurements were also correlated with ARFI measurements (Spearman rho = 0.733, p < 0.0001). For predicting cirrhosis (F = 4), the optimum cut-off values were 14.4 kPa for TE (AUROC: 0.985) and 1.7 m/s for ARFI (AUROC: 0.931). The conclusion of this paper was that fibrosis evaluation by means of ARFI is not superior to TE for the assessment of liver fibrosis and that ARFI is an accurate test for the diagnosis of cirrhosis.

In another paper that compared ARFI to TE for fibrosis assessment in 139 HCV patients, the best cutoff values for cirrhosis were ≥11 kPa (AUROC: 0.80) for TE and ≥2.0 m/s (AUROC: 0.89) for ARFI. By pair wise comparison of AUROC, ARFI was marginally more accurate than TE for the diagnosis of cirrhosis (p=0.09) and significantly more accurate for significant fibrosis (F≥2) and severe fibrosis (F≥3), p=0.024 and p=0.002, respectively. By partial AUROC analysis, ARFI performance results were significantly higher for all three stages of fibrosis. The average concordance rates of TE and ARFI vs. liver biopsy were 45.4 and 54.7%, respectively [43].

Regarding the value of ARFI elastography in the liver as a predictor of portal hypertension, there are several published studies with controversial results. The first one, published by our group in 2010 [44] evaluated 157 cirrhotic patients, from which 129 had recent gastroscopies. In our study, the mean value of ARFI measurements in patients with large EV (at least grade 2 - 57p.) was not significantly different from the one in patients with no or small EV (72p.): 2.73±0.71 vs. 2.8±0.71m/s (p=0.49). Also, in patients with at least grade 2 EV, the mean value of ARFI measurements in those with a history of variceal bleeding (21p.) was not significantly different than the one in patients with no history of bleeding: 2.78±0.81 vs. 2.77±0.7m/s (p=0.99).

The first data regarding the correlation of ARFI measurements with HVPG were presented at the EASL meeting from 2010 by Salzl et al. They evaluated 36 cirrhotic and 12 non-cirrhotic patients and obtained a good correlation of LS measurements assessed by ARFI with HVPG measurements (r=0.709), while the AUROC for predicting clinically significant portal hypertension was 0.874 [45].

Rifai et al evaluated spleen stiffness (SS) and LS in 125 subjects (25 healthy controls, 70 patients with chronic hepatopathies without portal hypertension and 30 cirrhotics with portal hypertension). In this study, LS performed significantly better than SS for predicting significant portal hypertension (AUROC 0.90 vs. 0.68), but the LS cut-off value obtained in this study for predicting significant portal hypertension (1.67 m/s) was lower than the ones proposed by most published studies for diagnosing liver cirrhosis [37-43]. The best SS cut-off value for predicting portal hypertension was 3.29 m/s, with 47% sensitivity and 73% specificity [46].

The study of Vermehren et al, published on-line in 2011, showed quite different results. It included 166 cirrhotics evaluated by ARFI in the liver, ARFI in the spleen, TE and FibroTest [47]. ARFI liver was significantly correlated with ARFI spleen (r=0.48, p<0.001), TE (r=0.75, p<0.001) and FibroTest (r=0.21, p=0.006). The diagnostic accuracies (AUROC) for the diagnosis of large EV were 0.58 (95% CI: 0.48-0.67), 0.58 (0.49-0.67), 0.53 (0.44-0.63) and 0.50 (0.41-0.59) for ARFI liver, spleen, TE and FibroTest respectively (p>0.20). Multiple logistic regression analysis showed that ARFI spleen was better than ARFI liver for the prediction of large EV.

Recently, Gao et al published data regarding the correlation of LS and spleen stiffness (SS) values assessed by ARFI with HVPG measurements in 10 cirrhotic patients, before and after transjugular intrahepatic portosystemic

shunt (TIPS) placement. There was no significant difference between mean LS values by ARFI pre and post TIPS placement, but the mean SS values before TIPS placement were significantly higher than after TIPS was installed (3.65±0.32 m/s vs. 3.27±0.30 m/s, p<0.001) [48].

Recently, in a paper accepted for presentation at the EASL meeting 2012 we tried to combine several parameters in order to increase the accuracy of ARFI elastography for predicting significant EV. We evaluated LS and SS by means of ARFI in 223 cirrhotic patients, 58.8% having significant EV. The following parameters were significantly higher in patients with significant EV as compared with those without EV or grade 1 EV: the mean SS assessed by ARFI (m/s) (3.35±0.52 vs. 3.09±0.57, p=0.0005), the mean spleen size (mm) (143.5±27 vs. 132.4±25.9, p=0.002) and the percentage of patients with ascites (61.8% vs. 34%,p=0.0001). LS was similar in the 2 groups of patients. By multiple regression analysis we obtained the following formula for predicting significant EV: Prediction of significant EV (Pred EV_{2-3}) score = -1.141 + 0.454 x spleen size (1- if spleen size ≤ 126mm and 2- if > 126mm) + 0.488 x ascites (1-absent, 2-present) + 0.187 x SS (1 -if SS ≤ 3.44 m/s and 2- if > 3.44 m/s). For cut-off values > 0.476 Pred EV_{2-3} had 68.2% sensitivity, 78% specificity and 72.2% accuracy (AUROC=0.809) for predicting significant EV. The mean LS and SS values and also the mean Pred EV_{2-3} value were not useful for predicting variceal bleeding.

Probably further studies are needed to assess the real value of ARFI measurements in the liver and spleen, alone and/or in combination, for predicting portal hypertension in cirrhotic patients.

Conclusion

As a conclusion to our review we can say that both TE and ARFI elastography are valuable methods for the early diagnosis of cirrhosis. While TE is a promising method for predicting the presence of portal hypertension in cirrhotic patients, the diagnostic accuracy of ARFI in the liver seems to be poor. Probably the accuracy of ARFI elastography can be significantly increased if spleen stiffness is assessed, alone or in combination with liver stiffness and other parameters.

References

1. Portincasa P. Non-alcoholic steatohepatitis (NASH): approaching more tailored and effective therapies. J Gastrointestin Liver Dis 2007; 16: 167-169.
2. Lavanchy D. Evolving epidemiology of hepatitis C virus. Clin Microbiol Infect 2011; 17: 107-115.
3. World Health Organization. Hepatitis B. World Health Organization Fact Sheet 204 (Revised August 2008). Available at: http://www.who.int/mediacentre/factsheets/fs204/en/index.html Accessed February 25, 2012.
4. Goldstein ST, Zhou F, Hadler SC, Bell BP, Mast EE, Margolis HS. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. Int J Epidemiol 2005; 34: 1329-1339.
5. Benvegnu L, Gios M, Boccato S, Alberti A. Natural history of compensated viral cirrhosis: a prospective study on the incidence and hierarchy of major complications. Gut 2004; 53: 744–749.
6. McHutchison J, Poynard T, Afdhal N; International Fibrosis Group Meeting Participants. Fibrosis as an end point for clinical trials in liver disease: a report of the international fibrosis group. Clin Gastroenterol Hepatol 2006; 4: 1214-1220.
7. Regev A, Berho M, Jeffers LJ, et al. Sampling error and intraobserver variation in liver biopsy in patients with chronic HCV infection. Am J Gastroenterol 2002; 97: 2614-2618.
8. Persico M, Palmentieri B, Vecchione R, Torella R, de Sio I. Diagnosis of chronic liver disease: reproducibility and validation of liver biopsy. Am J Gastroenterol 2002; 97: 491-492.
9. Ratziu V, Charlotte F, Heurtier A, et al; LIDO Study Group. Sampling variability of liver biopsy in nonalcoholic fatty liver disease. Gastroenterology 2005; 128: 1898-1906.
10. Munteanu M. Non-invasive biomarkers FibroTest-ActiTest for replacing invasive liver biopsy: the need for change and action. J Gastrointestin Liver Dis 2007; 2: 173-174.
11. Talwalkar JA, Kurtz DM, Schoenleber SJ, West CP, Montori VM. Ultrasound-based transient elastography for the detection of hepatic fibrosis: systematic review and meta-analysis. Clin Gastroenterol Hepatol 2007; 5: 1214-1220.
12. Friedrich-Rust M, Ong MF, Martens S, et al. Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. Gastroenterology 2008; 134: 960-974.
13. Friedrich-Rust M, Nierhoff J, Lupsor M, et al. Performance of Acoustic Radiation Force Impulse-Imaging for the staging of liver fibrosis: a pooled meta-analysis. J Viral Hepat 2012; 19: e212-219.
14. Sporea I, Sirli R, Deleanu A, et al. Acoustic radiation force impulse elastography as compared to transient elastography and liver biopsy in patients with chronic hepatopathies. Ultraschall Med 2011; 32 Suppl 1: S46-52.
15. Sandrin L, Fourquet B, Hasquenoph JM, et al. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. Ultrasound Med Biol 2003; 29: 1705-1713.
16. Castera L, Foucher J, Bernard PH, et al. Pitfalls of Liver Stiffness Measurement: A 5-Year Prospective Study of 13,369 Examinations. Hepatology 2010; 51: 828-835.
17. Castera L, Vergniol J, Foucher J, et al. Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. Gastroenterology 2005; 128: 343–350.
18. Marcellin P, Ziol M, Bedossa P, et al. Non-invasive assessment of liver fibrosis by stiffness measurement in patients with chronic hepatitis B. Liver Int 2009; 29: 242–247.

19. Wong VW, Vergniol J, Wong GL, et al. Diagnosis of fibrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease. Hepatology 2010; 51: 454–462.
20. Nahon P, Kettaneh A, Tengher-Barna I, et al. Assessment of liver fibrosis using transient elastography in patients with alcoholic liver disease. J Hepatol 2008; 49: 1062–1068.
21 Corpechot C, El Naggar A, Poujol-Robert A, et al. Assessment of biliary fibrosis by transient elastography in patients with PBC and PSC. Hepatology 2006; 43: 1118–1124.
22. Stebbing J, Farouk L, Panos G, et al. A meta-analysis of transient elastography for the detection of hepatic fibrosis. J Clin Gastroenterol 2010; 44: 214-219.
23. Tsochatzis EA, Gurusamy KS, Ntaoula S, Cholongitas E, Davidson BR, Burroughs AK. Elastography for the diagnosis of severity of fibrosis in chronic liver disease: a meta-analysis of diagnostic accuracy. J Hepatol 2011; 54: 650-659.
24. de Franchis R; Baveno V Faculty. Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol 2010; 53: 762-768.
25. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W; Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology 2007; 46: 922-938.
26. Kazemi F, Kettaneh A, N'kontchou G, et al. Liver stiffness measurement selects patients with cirrhosis at risk of bearing large oesophageal varices. J Hepatol 2006; 45: 230-235.
27. Foucher J, Chanteloup E, Vergniol J, et al. Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. Gut 2006; 55: 403–408.
28. Nguyen-Khac E, Saint-Leger P, Tramier B, Coevoet H, Capron D, Dupas JL. Noninvasive diagnosis of large esophageal varices by Fibroscan: strong influence of the cirrhosis etiology. Alcohol Clin Exp Res 2010; 34: 1146-1153.
29. Castéra L, Le Bail B, Roudot-Thoraval F, et al. Early detection in routine clinical practice of cirrhosis and oesophageal varices in chronic hepatitis C: comparison of transient elastography (FibroScan) with standard laboratory tests and non-invasive scores. J Hepatol 2009; 50: 59–68.
30. Vizzutti F, Arena U, Romanelli RG, et al. Liver stiffness measurement predicts severe portal hypertension in patients with HCV-related cirrhosis. Hepatology 2007; 45: 1290-1297.
31. Bureau C, Metivier S, Peron JM, et al. Transient elastography accurately predicts presence of significant portal hypertension in patients with chronic liver disease. Aliment Pharmacol Ther 2008; 27: 1261-1268.
32. Robic MA, Procopet B, Métivier S, et al. Liver stiffness accurately predicts portal hypertension related complications in patients with chronic liver disease: a prospective study. J Hepatol 2011; 55: 1017-1024.
33. Reiberger T, Ferlitsch A, Payer BA, Pinter M, Homoncik M, Peck-Radosavljevic M; Vienna Hepatic Hemodynamic Lab. Non-selective β-blockers improve the correlation of liver stiffness and portal pressure in advanced cirrhosis. J Gastroenterol 2012; 47: 561-568.
34. Castera L, Pinzani M, Bosch J. Non invasive evaluation of portal hypertension using transient elastography. J Hepatol 2012; 56: 696–703.
35. Sporea I, Rațiu I, Sirli R, Popescu A, Bota S. Value of transient elastography for the prediction of variceal bleeding. World J Gastroenterol 2011; 17: 2206-2210.
36. Nightingale K, Soo MS, Nightingale R, Trahey G. Acoustic radiation force impulse imaging: in vivo demonstration of clinical feasibility. Ultrasound Med Biol 2002; 28: 227–235.
37. Friedrich-Rust M, Wunder K, Kriener S, et al. Liver fibrosis in viral hepatitis: noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography. Radiology 2009; 252: 595-604.
38. Goertz RS, Zopf Y, Jugl V, et al. Measurement of Liver elasticity with acoustic radiation force impulse (ARFI) technology: an alternative noninvasive method for staging liver fibrosis in viral hepatitis. Ultraschall Med 2010; 31: 151–155.
39. Sporea I, Sirli R, Deleanu A, et al. Acoustic radiation force impulse elastography as compared to transient elastography and liver biopsy in patients with chronic hepatopathies. Ultraschall Med 2011; 32 Suppl 1: S46-52.
40. Lupsor M, Badea R, Stefanescu H, et al. Performance of a new elastographic method (ARFI technology) compared to unidimensional transient elastography in the noninvasive assessment of chronic hepatitis C. Preliminary results. J Gastrointestin Liver Dis 2009; 18: 303-310.
41. Sporea I, Şirli R, Bota S, et al. Is ARFI elastography reliable for predicting fibrosis severity in chronic HCV hepatitis? World J Radiol 2011; 3: 188-193.
42. Sporea I, Badea R, Sirli R, et al. How efficient is acoustic radiation force impulse elastography for the evaluation of liver stiffness? Hepat Mon 2011; 11: 532-538.
43. Rizzo L, Calvaruso V, Cacopardo B, et al. Comparison of transient elastography and acoustic radiation force impulse for non-invasive staging of liver fibrosis in patients with chronic hepatitis C. Am J Gastroenterol 2011; 106: 2112-2120.
44. Sirli R, Sporea I, Bota S, Ciof O, Popescu A, Danilă M. Can Acoustic Radiation Force Impulse Elastography (ARFI) predict the complications of liver cirrhosis? Medicina Interna 2010; 7:15-20.
45. Salzl P, Reiberger T, Homoncik M, et al. A Hepatic Hemodynamic Lab. Comparison of liver stiffness assessment by Fibroscan and Acoustic Radiation Force Impulse imaging for the evaluation of liver fibrosis and cirrhosis. J Hepatol 2010; 52 (Suppl 1): S171.
46. Rifai K, Cornberg J, Bahr M, et al. ARFI elastography of the spleen is inferior to liver elastography for the detection of portal hypertension. Ultraschall Med 2011;32 Suppl 2:E24-30.
47. Vermehren J, Polta A, Zimmermann O, et al. Comparison of acoustic radiation force impulse imaging with transient elastography for the detection of complications in patients with cirrhosis. Liver Int 2012; 32: 852-858.
48. Gao J, Ran HT, Ye XP, Zheng YY, Zhang DZ, Wang ZG. The stiffness of the liver and spleen on ARFI Imaging pre and post TIPS placement: a preliminary observation. Clin Imaging 2012; 36: 135-141.