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EDITORIAL

Liver ultrasound elastography: More than staging the disease

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Abstract

Ultrasound elastography is perhaps the most important breakthrough in the evolution of ultrasonography in the last 15 years. Since transient elastography was introduced, many other methods have been developed and became more and more widely available. The value of ultrasound elastography in staging a chronic liver disease has been established by numerous studies. There have been many studies that have shown that using liver elastography it is possible to predict the presence of the complications of cirrhosis: portal hypertension, presence of esophageal varices (and even their risk of bleeding) and hepatocellular carcinoma. It has been shown that liver elastography can predict the progression of liver fibrosis and also the survival (hepatic events - free) of the patients with chronic liver diseases. These are the real quests of the clinicians, this is the ultimate scope of any medical investigation - to predict the outcome of a patient and to help making therapeutic decisions. I brought together only a small amount of the data that has already been written on this subject to support my affirmation that liver ultrasound elastography is more than a tool for staging the liver disease, but it is also comparable to a crystal ball which in the hands of a skilled clinician can reveal the future of the patient and can help to improve this future.

Key words: Liver ultrasound elastography; Transient elastography; Fibrosis; Hepatitis; Survival; Cirrhosis

Core tip: In this editorial I brought together data from the literature in the support of the affirmation that liver ultrasound elastography is more than a tool for staging the disease, that it can also be used to predict the presence of the complications of cirrhosis: portal hypertension, presence of esophageal varices (and even their risk of bleeding), ascites and hepatocellular carcinoma. Studies shown that liver elastography can predict the progression of liver fibrosis and also the survival (hepatic events - free) of the patients with chronic liver diseases, being therefore a helpful tool in the hands of a skilled clinician.

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INTRODUCTION

Ultrasound elastography is perhaps the most important breakthrough in the evolution of ultrasonography in the last 15 years. Liver elastography in particular has seen an unprecedented development in the last 10 years since transient elastography (TE) was introduced in 2003 as a tool to assess the liver fibrosis. Since then, many approaches have been tried with the same purpose: to evaluate the stiffness of the liver tissue and thus to appreciate the extension of the liver damage, to correctly identify the stage of the fibrosis.

The main idea behind elastography is that the elasticity of the analyzed tissue can offer information on the health of that particular organ. A stiffer liver tissue usually indicates the presence of the consequence of any chronic liver disease: the fibrosis. There can be some interferences (inflammation, steatosis, meal consumption prior the examination)[1-5], but the increase of the stiffness of the liver is mostly due to fibrosis.

Liver ultrasound elastography techniques are based on the principle that the speed of a wave that propagates through the liver is influenced by the stiffness of the tissue. Basically, the stiffer the liver, the faster the wave passes through.

TE (Fibroscan/Echosens) uses a mechanical wave generated by a special transducer, while acoustic radiation force impulse imaging (ARFI, Siemens) and shear wave elastography (SWE, Supersonic Imaging) use sound waves. Other ultrasound elastography techniques have been also developed, but TE and ARFI are the subjects of most researches, these two techniques being the oldest in use.

The value of ultrasound elastography in staging a chronic liver disease has been established by numerous studies[6-14]. But staging the disease is just one step towards what the clinician actually wants to achieve: to glimpse into the future of the patient, to see how the disease is going to evolve, what complications and when are they going to occur.

Liver elastography has some limitations - TE cannot be performed or the results may be influenced in the presence of the obesity, ascites, narrow intercostal spaces. ARFI overcomes most of these limitations, the rate of unsuccessful or unreliable measurements being significantly lower than with TE.

The predictive value of the liver ultrasound elastography is the subject of this editorial. If not otherwise mentioned, the following information refers to TE.

USE OF LIVER ULTRASOUND ELASTOGRAPHY FOR THE PREDICTION OF THE PATIENT'S PROGNOSIS

There have been many studies that have shown that using liver elastography it is possible to predict the presence of the complications of cirrhosis: portal hypertension (PH), presence of esophageal varices (EV) and their risk of rupture, ascites and hepatocellular carcinoma (HCC). It has been shown that liver elastography can predict the progression of liver fibrosis and can also predict the survival of patients with chronic liver diseases.

LIVER ELASTOGRAPHY IN THE PREDICTION OF PH

PH is traditionally evaluated by measuring (invasively) the hepatic vein portal gradient (HVPG) and is defined as the HVPG of over 5 mmHg. PH becomes clinically significant when HVPG value is over 10 mmHg as it is more often associated with the presence of the varices[15,16]. A value of over 12 mmHg predicts a high risk of variceal bleeding[15,16]. HVPG measurement is recommended to all patients newly diagnosed with cirrhosis for the evaluation of risk and establishment of prognosis[17] and is also a good tool to monitor the response to treatment and achievement of endpoints (over 20% HVPG decrease as compared to baseline and/or HVPG < 12 mmHg)[17].

Both liver stiffness and spleen stiffness have shown to be predictors for detecting PH[18-21]. Liver stiffness measurement (LSM) has a good correlation with HVPG $r = 0.81$, $P < 0.0001$ when using TE[18], and $r = 0.611$, $P < 0.0001$ with SWE[20]. One study that compared LS with spleen stiffness (SS) assessed both by SWE found that the diagnostic performance of LSM was significantly better than that of SS for the diagnosis of clinically significant PH (area under the receiver operating characteristic curve of 0.87 *vs* 0.64, $P = 0.003$).

LSM has also a good correlation with the stage of cirrhosis, increasing along with HVPG as the Child stage increases[22]. A meta analysis made on 18 studies which included 3644 patients found an overall specificity of 90% (95%CI: 0.81-0.95) and a sensitivity of 79% (95%CI: 0.58-0.91) for LSM by TE in the detection of significant PH[23]. The study of Zhang in 2014 showed that a value of over 13.6 kPa at TE predicts significant PH with a specificity of 72.53% and a sensitivity of 83.87%[21]. Another study comparing TE with ARFI found that both are well correlated with PH: $r = 0.765$; $P < 0.001$ for TE and $r = 0.646$; $P < 0.001$ for ARFI[24]. At the optimal cut-off (2.58 m/s), the sensitivity and specificity for ARFI (AUROC: 0.855) were 71.4% and 87.5%, respectively[24]. In the study by Carrión *et al*[25], there was a close correlation of TE with HVPG ($r = 0.84$, $P < 0.001$). The optimal liver stiffness cutoff value for diagnosis of PH (HVPG 6 mmHg) was 8.74 kPa, with a sensitivity of 90%, specificity 81%, positive predictive value 81%, and negative predictive value of 90%[25].

Predicting clinically significant PH is one step towards the prediction of the presence of EV and their risk of bleeding.

LIVER ELASTOGRAPHY IN THE PREDICTION OF THE PRESENCE OF EV AND THEIR RISK OF RUPTURE

Liver stiffness measured by TE showed good results in detecting the presence of EV, with AUROC's ranging between 0.76 and 0.88[18,26-28]. The cut-offs mentioned by the above studies were 17.6, 21.5, 19 kPa and respectively 19.2 kPa and for these cut-offs the sensitivities were 0.9, 0.76, 0.84 and 0.85 while the specificities were 0.43, 0.78, 0.7 and 0.87.

Studies have also shown a correlation between LSM and the size of the EV[27,29,30]. Thus, LSM may be of help in the selection of patients for endoscopic screening for EV and their complications.

Liver stiffness may also predict the risk of variceal bleeding by predicting large grade EV (Paquet grade higher or equal to 2), AUROC = 0.85 (95%CI: 0.75-0.94)[28]. Another study found an AUROC of 0.58 (95%CI: 0.48-0.67) for ARFI and 0.53 (95%CI: 0.44-0.63) for TE for predicting variceal bleeding[31] sowing that the two analyzed methods have similar value for this purpose. Elastography may be helpful to screen and identify patients who are at high risk of having large grade EV, which predict variceal bleeding and, therefore, need endoscopic screening.

Liver elastography can also be used in combination with other markers (such as spleen diameter and platelet count) to identify more precisely the patients with higher risk for EV bleeding[32].

LIVER ELASTOGRAPHY IN THE PREDICTION OF THE PRESENCE OF HCC

Prognosis of patients with chronic liver disease is determined by the extent and progression of liver fibrosis, which may lead to the development of HCC.

Liver stiffness is significantly higher in patients with HCC than in patients without HCC[33-35]. However, most of the studies found that liver stiffness alone is insufficient to predict the presence or absence of HCC and that it should be associated in a score with other markers. A score developed by Wong *et al*[33] based on liver stiffness, age, serum albumin and hepatitis B virus DNA level was found to have AUROC's of 0.83 to 0.89 in the identification of the HCC patients and a very good negative (99.4%-100%) for the exclusion of HCC in patients. In the study conducted by Feier *et al*[34], LS was significantly higher (42 kPa *vs* 27 kPa, $P < 0.0001$) in the HCC group than in the non-HCC group, but other 3 parameters (alanine-aminotransferase, alpha-fetoprotein and interquartile range of the LSMs) were added to elastography in a score and the resulted model combining the four variables showed a good diagnostic performance in both training and validation groups, with AUROCs of 0.86 and 0.8, respectively[34].

Jung *et al*[36] has shown that liver stiffness is also useful as a part of a predictive model that identifies patients that are at risk for late recurrence after curative resection of HCC. On multivariate analysis, patients with older age, male sex, heavy alcohol consumption (> 80 g/d), lower serum albumin, HBe antigen positivity and LSM > 8 kPa were at a significantly greater risk of HCC development.

LIVER ELASTOGRAPHY IN THE PREDICTION OF THE SURVIVAL OF THE PATIENTS WITH CHRONIC LIVER DISEASES

Liver stiffness, expressing the severity of the liver damage, is correlated with hepatic events and death. It has been shown by many studies that measuring liver elasticity one can predict the survival of a patient[37-40].

In the study conducted by Wong *et al*[37], they found age, Hui index and liver stiffness to be independent predictors of hepatic event - free survival. The same study showed that the worsening of the liver stiffness and Hui index at a follow up visit compared to baseline predicted a hepatic event.

Pang *et al*[38] found that liver stiffness by TE was an independent predictor of complications (hazard ratio 1.05 per kPa; 95%CI: 1.03-1.06), with the 2-year incidence rates of death or hepatic complications of 2.6%, 9%, 19%, and 34% in patients with liver stiffness < 10 kPa, 10-19.9 kPa, 20-39.9 kPa, and ⩾ 40 kPa, respectively ($P < 0.00005$).

de Lédinghen *et al*[39] showed that survival in patients with chronic B hepatitis was significantly decreased in patients diagnosed with severe fibrosis, no matter if liver elastography was used ($P < 0.0001$) or liver biopsy ($P = 0.02$) for the staging of fibrosis.

The study conducted by Vergniol *et al*[40] also showed that in patients with chronic C hepatitis, noninvasive tests for liver fibrosis (measurement of liver stiffness or FibroTest) can predict 5-year survival.

The fact that liver stiffness can predict survival may help clinicians in their decision-making process for establishing therapeutic options for the patient and even liver transplantation indication.

CONCLUSION

In the past 10 years, liver ultrasound elastography struggled and succeeded to partially replace liver biopsy for the purpose of staging the liver diseases regardless of their etiology. However, as the method became more widely available and because the actual quest of the clinician is to evaluate as completely as possible the extent of the liver damage, its complications and if possible, even to predict an outcome, LSM was studied recently for these purposes also.

It is now known that cirrhosis has a complex and dynamic pathologic spectrum. The average risk of progressing from compensated to decompensated cirrhosis is 6%-9% per year[41]. Survival in the com-

Table 1 Use of ultrasound elastography to predict liver disease related complications

Ref.	Method	Cut-off value	Sensitivity	Specificity	AUROC
Elastography to predict significant portal hypertension					
Zhang *et al*[21]	TE	13.6 kPa	83.87%	72.53%	0.83
Salzl *et al*[24]	TE	16.8 kPa	89.75%	75%	0.87
Salzl *et al*[24]	ARFI	2.58 m/s	71.4%	87.5%	0.85
Carrión *et al*[25]	TE	8.74 kPa	90%	81%	0.94
Elastography to predict the presence of esophageal varices					
Vizzutti *et al*[18]	TE	17.6 kPa	90%	43%	0.76
Castéra *et al*[26]	TE	21.5 kPa	76%	78%	0.86
Kazemi *et al*[27]	TE	19 kPa	84%	70%	0.84
Pár *et al*[28]	TE	19.2 kPa	85%	87%	0.88
Elastography to predict hepatocellular carcinoma					
Feier *et al*[34]	TE	38 kPa	51.7%	90.4%	0.68
Wong *et al*[33]	TE (part of a score)	-	-	-	0.83-0.89
Elastography to predict the liver related death of the patients with liver cirrhosis					
				Rate of death	
Pang *et al*[38]	TE	40 kPa		34%/3 yr	
de Lédinghen *et al*[39]	TE	< 9 kPa		2.9%/5 yr	
		> 20 kPa		38.5%/5 yr	

TE: Transient elastography (fibroscan); ARFI: Acoustic radiation force impulse imaging.

pensated state is of an average of 12 years, while in the decompensated state the median survival is of only 2 years[41]. Thus identifying patients in early stages of a liver disease (even in the compensated state of cirrhosis) is crucial for the outcome of the patient. Besides, identifying patients with complications and establishing their survival prognostic is of more help in the treatment decision and in the monitoring plan for the future.

We now have noninvasive means to precisely stage the fibrosis. Particularly, as shown above, liver ultrasound elastography (with many methods developed by now for the same purpose - TE, ARFI or SWE) is also a useful tool for identifying patients with a higher risk of having complications like PH, EV and even HCC. With the use of elastography the clinician can also appreciate the risk of the patient of having an unfavorable course and develop complications like EV rupture, decompensation of the cirrhosis and even death (Table 1).

Therefore, used rationally, liver ultrasound is more than a tool for staging the disease, is a kind of crystal ball that in the hand of a skilled clinician can reveal the future of the patient and contribute to the improvement of this future.

REFERENCES

1 **Chan HL**, Wong GL, Choi PC, Chan AW, Chim AM, Yiu KK, Chan FK, Sung JJ, Wong VW. Alanine aminotransferase-based algorithms of liver stiffness measurement by transient elastography (Fibroscan) for liver fibrosis in chronic hepatitis B. *J Viral Hepat* 2009; **16**: 36-44 [PMID: 18673426 DOI: 10.1111/j.1365-2893.2008.01037.x]

2 **Roulot D**, Czernichow S, Le Clésiau H, Costes JL, Vergnaud AC, Beaugrand M. Liver stiffness values in apparently healthy subjects: influence of gender and metabolic syndrome. *J Hepatol* 2008; **48**: 606-613 [PMID: 18222014 DOI: 10.1016/j.jhep.2007.11.020]

3 **Corpechot C**, El Naggar A, Poujol-Robert A, Ziol M, Wendum D, Chazouillères O, de Lédinghen V, Dhumeaux D, Marcellin P, Beaugrand M, Poupon R. Assessment of biliary fibrosis by transient elastography in patients with PBC and PSC. *Hepatology* 2006; **43**: 1118-1124 [PMID: 16628644 DOI: 10.1002/hep.21306]

4 **Arena U**, Lupsor Platon M, Stasi C, Moscarella S, Assarat A, Bedogni G, Piazzolla V, Badea R, Laffi G, Marra F, Mangia A, Pinzani M. Liver stiffness is influenced by a standardized meal in patients with chronic hepatitis C virus at different stages of fibrotic evolution. *Hepatology* 2013; **58**: 65-72 [PMID: 23447459 DOI: 10.1002/hep.26343]

5 **Berzigotti A**, De Gottardi A, Vukotic R, Siramolpiwat S, Abraldes JG, García-Pagan JC, Bosch J. Effect of meal ingestion on liver stiffness in patients with cirrhosis and portal hypertension. *PLoS One* 2013; **8**: e58742 [PMID: 23520531 DOI: 10.1371/journal.pone.0058742]

6 **Sandrin L**, Fourquet B, Hasquenoph JM, Yon S, Fournier C, Mal F, Christidis C, Ziol M, Poulet B, Kazemi F, Beaugrand M, Palau R. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. *Ultrasound Med Biol* 2003; **29**: 1705-1713 [PMID: 14698338 DOI: 10.1016/j.ultrasmedbio.2003.07.001]

7 **Castéra L**, Vergniol J, Foucher J, Le Bail B, Chanteloup E, Haaser M, Darriet M, Couzigou P, De Lédinghen V. Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. *Gastroenterology* 2005; **128**: 343-350 [PMID: 15685546 DOI: 10.1053/j.gastro.2004.11.018]

8 **Friedrich-Rust M**, Ong MF, Martens S, Sarrazin C, Bojunga J, Zeuzem S, Herrmann E. Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. *Gastroenterology* 2008; **134**: 960-974 [PMID: 18395077 DOI: 10.1053/j.gastro.2008.01.034]

9 **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 [PMID: 21146892 DOI: 10.1016/j.jhep.2010.07.033]

10 **Cardoso AC**, Carvalho-Filho RJ, Stern C, Dipumpo A, Giuily N, Ripault MP, Asselah T, Boyer N, Lada O, Castelnau C, Martinot-Peignoux M, Valla DC, Bedossa P, Marcellin P. Direct comparison of diagnostic performance of transient elastography in patients with chronic hepatitis B and chronic hepatitis C. *Liver Int* 2012; **32**: 612-621 [PMID: 22103765 DOI: 10.1111/j.1478-3231.2011.02660.x]

11 **Sporea I**, Sirli R, Deleanu A, Tudora A, Popescu A, Curescu M, Bota S. Liver stiffness measurements in patients with HBV vs HCV chronic hepatitis: a comparative study. *World J Gastroenterol* 2010; **16**: 4832-4837 [PMID: 20939112 DOI: 10.3748/wjg.v16.i38.4832]

12 **Chon YE**, Choi EH, Song KJ, Park JY, Kim do Y, Han KH, Chon

CY, Ahn SH, Kim SU. Performance of transient elastography for the staging of liver fibrosis in patients with chronic hepatitis B: a meta-analysis. *PLoS One* 2012; **7**: e44930 [PMID: 23049764 DOI: 10.1371/journal.pone.0044930]

13 **Mahadeva S**, Mahfudz AS, Vijayanathan A, Goh KL, Kulenthran A, Cheah PL. Performance of transient elastography (TE) and factors associated with discordance in non-alcoholic fatty liver disease. *J Dig Dis* 2013; **14**: 604-610 [PMID: 23859493 DOI: 10.1111/1751-2980.12088]

14 **Kumar R**, Rastogi A, Sharma MK, Bhatia V, Tyagi P, Sharma P, Garg H, Chandan Kumar KN, Bihari C, Sarin SK. Liver stiffness measurements in patients with different stages of nonalcoholic fatty liver disease: diagnostic performance and clinicopathological correlation. *Dig Dis Sci* 2013; **58**: 265-274 [PMID: 22790906 DOI: 10.1007/s10620-012-2306-1]

15 **Bosch J**, Garcia-Pagán JC, Berzigotti A, Abraldes JG. Measurement of portal pressure and its role in the management of chronic liver disease. *Semin Liver Dis* 2006; **26**: 348-362 [PMID: 17051449]

16 **Groszmann RJ**, Garcia-Tsao G, Bosch J, Grace ND, Burroughs AK, Planas R, Escorsell A, Garcia-Pagan JC, Patch D, Matloff DS, Gao H, Makuch R. Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. *N Engl J Med* 2005; **353**: 2254-2261 [PMID: 16306522 DOI: 10.1056/NEJMoa044456]

17 **de Franchis R**. 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 [PMID: 20638742 DOI: 10.1016/j.jhep.2010.06.004]

18 **Vizzutti F**, Arena U, Romanelli RG, Rega L, Foschi M, Colagrande S, Petrarca A, Moscarella S, Belli G, Zignego AL, Marra F, Laffi G, Pinzani M. Liver stiffness measurement predicts severe portal hypertension in patients with HCV-related cirrhosis. *Hepatology* 2007; **45**: 1290-1297 [PMID: 17464971 DOI: 10.1002/hep.21665]

19 **Elkrief L**, Rautou PE, Ronot M, Lambert S, Dioguardi Burgio M, Francoz C, Plessier A, Durand F, Valla D, Lebrec D, Vilgrain V, Castéra L. Prospective comparison of spleen and liver stiffness by using shear-wave and transient elastography for detection of portal hypertension in cirrhosis. *Radiology* 2015; **275**: 589-598 [PMID: 25469784]

20 **Procopet B**, Berzigotti A, Abraldes JG, Turon F, Hernandez-Gea V, García-Pagán JC, Bosch J. Real-time shear-wave elastography: Applicability, reliability and accuracy for clinically significant portal hypertension. *J Hepatol* 2015; **62**: 1068-1075 [PMID: 25514554 DOI: 10.1016/j.jhep.2014.12.007]

21 **Zhang W**, Wang L, Wang L, Li G, Huang A, Yin P, Yang Z, Ling C, Wang L. Liver stiffness measurement, better than APRI, Fibroindex, Fib-4, and NBI gastroscopy, predicts portal hypertension in patients with cirrhosis. *Cell Biochem Biophys* 2015; **71**: 865-873 [PMID: 25417057 DOI: 10.1007/s12013-014-0275-z]

22 **Reiberger T**, Ferlitsch A, Payer BA, Pinter M, Homoncik M, Peck-Radosavljevic M. Non-selective β-blockers improve the correlation of liver stiffness and portal pressure in advanced cirrhosis. *J Gastroenterol* 2012; **47**: 561-568 [PMID: 22170417 DOI: 10.1007/s00535-011-0517-4]

23 **Shi KQ**, Fan YC, Pan ZZ, Lin XF, Liu WY, Chen YP, Zheng MH. Transient elastography: a meta-analysis of diagnostic accuracy in evaluation of portal hypertension in chronic liver disease. *Liver Int* 2013; **33**: 62-71 [PMID: 22973991 DOI: 10.1111/liv.12003]

24 **Salzl P**, Reiberger T, Ferlitsch M, Payer BA, Schwengerer B, Trauner M, Peck-Radosavljevic M, Ferlitsch A. Evaluation of portal hypertension and varices by acoustic radiation force impulse imaging of the liver compared to transient elastography and AST to platelet ratio index. *Ultraschall Med* 2014; **35**: 528-533 [PMID: 24871695 DOI: 10.1055/s-0034-1366506]

25 **Carrión JA**, Navasa M, Bosch J, Bruguera M, Gilabert R, Forns X. Transient elastography for diagnosis of advanced fibrosis and portal hypertension in patients with hepatitis C recurrence after liver transplantation. *Liver Transpl* 2006; **12**: 1791-1798 [PMID: 16823833 DOI: 10.1002/lt.20857]

26 **Castéra L**, Le Bail B, Roudot-Thoraval F, Bernard PH, Foucher J, Merrouche W, Couzigou P, de Lédinghen V. 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 [PMID: 19013661 DOI: 10.1016/j.jhep.2008.08.018]

27 **Kazemi F**, Kettaneh A, N'kontchou G, Pinto E, Ganne-Carrie N, Trinchet JC, Beaugrand M. Liver stiffness measurement selects patients with cirrhosis at risk of bearing large oesophageal varices. *J Hepatol* 2006; **45**: 230-235 [PMID: 16797100 DOI: 10.1016/j.jhep.2006.04.006]

28 **Pár G**, Trosits A, Pakodi F, Szabó I, Czimmer J, Illés A, Gódi S, Bajor J, Sarlós P, Kenyeres P, Miseta A, Vincze A, Pár A. [Transient elastography as a predictor of oesophageal varices in patients with liver cirrhosis]. *Orv Hetil* 2014; **155**: 270-276 [PMID: 24509356 DOI: 10.1556/OH.2014.29824]

29 **Bureau C**, Metivier S, Peron JM, Selves J, Robic MA, Gourraud PA, Rouquet O, Dupuis E, Alric L, Vinel JP. Transient elastography accurately predicts presence of significant portal hypertension in patients with chronic liver disease. *Aliment Pharmacol Ther* 2008; **27**: 1261-1268 [PMID: 18397389 DOI: 10.1111/j.1365-2036.2008.03701.x]

30 **Li F**, Yan T, Shao Q, Ji D, Li B, Li Z, Chen G. [Clinical study of FibroScan efficiency for diagnosing size of oesophageal varices in liver cirrhosis patients]. *Zhonghua Gan Zang Bing Za Zhi* 2014; **22**: 600-603 [PMID: 25243961 DOI: 10.3760/cma.j.issn.1007-3418.2014.08.010]

31 **Vermehren J**, Polta A, Zimmermann O, Herrmann E, Poynard T, Hofmann WP, Bojunga J, Sarrazin C, Zeuzem S, Friedrich-Rust M. 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 [PMID: 22222050 DOI: 10.1111/j.1478-3231.2011.02736.x]

32 **Kim BK**, Kim do Y, Han KH, Park JY, Kim JK, Paik YH, Lee KS, Chon CY, Ahn SH. Risk assessment of esophageal variceal bleeding in B-viral liver cirrhosis by a liver stiffness measurement-based model. *Am J Gastroenterol* 2011; **106**: 1654-1652, 1730 [PMID: 21691339 DOI: 10.1038/ajg.2011.160]

33 **Wong GL**, Chan HL, Wong CK, Leung C, Chan CY, Ho PP, Chung VC, Chan ZC, Tse YK, Chim AM, Lau TK, Wong VW. Liver stiffness-based optimization of hepatocellular carcinoma risk score in patients with chronic hepatitis B. *J Hepatol* 2014; **60**: 339-345 [PMID: 24128413 DOI: 10.1016/j.jhep.2013.09.029]

34 **Feier D**, Lupsor Platon M, Stefanescu H, Badea R. Transient elastography for the detection of hepatocellular carcinoma in viral C liver cirrhosis. Is there something else than increased liver stiffness? *J Gastrointestin Liver Dis* 2013; **22**: 283-289 [PMID: 24078985]

35 **Wong GL**. Transient elastography: Kill two birds with one stone? *World J Hepatol* 2013; **5**: 264-274 [PMID: 23717737 DOI: 10.4254/wjh.v5.i5.264]

36 **Jung KS**, Kim JH, Kim SU, Song K, Kim BK, Park JY, Kim do Y, Ahn SH, Moon do C, Song IJ, Choi GH, Park YN, Han KH. Liver stiffness value-based risk estimation of late recurrence after curative resection of hepatocellular carcinoma: development and validation of a predictive model. *PLoS One* 2014; **9**: e99167 [PMID: 24910997 DOI: 10.1371/journal.pone.0099167]

37 **Wong GL**, Chan HL, Yu Z, Wong CK, Leung C, Ho PP, Chan CY, Chung VC, Chan ZC, Tse YK, Chim AM, Lau TK, Chan HY, Tse CH, Wong VW. Noninvasive assessments of liver fibrosis with transient elastography and Hui index predict survival in patients with chronic hepatitis B. *J Gastroenterol Hepatol* 2015; **30**: 582-590 [PMID: 25252074 DOI: 10.1111/jgh.12779]

38 **Pang JX**, Zimmer S, Niu S, Crotty P, Tracey J, Pradhan F, Shaheen AA, Coffin CS, Heitman SJ, Kaplan GG, Swain MG, Myers RP. Liver stiffness by transient elastography predicts liver-related complications and mortality in patients with chronic liver disease. *PLoS One* 2014; **9**: e95776 [PMID: 24755824 DOI: 10.1371/journal.pone.0095776]

39 **de Lédinghen V**, Vergniol J, Barthe C, Foucher J, Chermak F, Le Bail B, Merrouche W, Bernard PH. Non-invasive tests for fibrosis and liver stiffness predict 5-year survival of patients chronically infected with hepatitis B virus. *Aliment Pharmacol Ther* 2013; **37**: 979-988 [PMID: 23557139 DOI: 10.1111/apt.12307]

40 **Vergniol J**, Foucher J, Terrebonne E, Bernard PH, le Bail B, Merrouche W, Couzigou P, de Ledinghen V. Noninvasive tests for fibrosis and liver stiffness predict 5-year outcomes of patients with chronic hepatitis C. *Gastroenterology* 2011; **140**: 1970-1979, 1979.e1-3 [PMID: 21376047 DOI: 10.1053/j.gastro.2011.02.058]

41 **D'Amico G**, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol* 2006; **44**: 217-231 [PMID: 16298014 DOI: 10.1016/j.jhep.2005.10.013]

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