Original papers

Med Ultrason 2014, Vol. 16, no. 2, 119-122
DOI: 10.11152/mu.2013.2066.162.rs1is2

Comparison between the M and XL probes for liver fibrosis assessment by Transient Elastography

Roxana Şirli, Ioan Sporea, Alexandra Deleanu, Laura Culcea, Milana Szilaski, Alina Popescu, Mirela Dănilă

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

Abstract

Objective: Liver stiffness measurement (LSM) using Transient Elastography (TE) for liver fibrosis assessment is difficult to be performed in obese and overweight patients by standard M probe, thus the XL probe was developed. The aim of our paper was to assess the usefulness of the XL probe in daily clinical practice. **Material and method:** Our study included 216 patients (mean BMI 30.1±4.1 kg/m2) with chronic hepatopathies, in which paired measurements were made using the M (3.5MHz) and XL (2.5 MHz) probes in the same session. In each patient 10 valid LSM were acquired with each probe, a median was calculated, expressed in kiloPascals (kPa). Unreliable TE measurements were considered: fewer than 10 valid shots; with a success rate (SR) <60% and/or interquartile range interval (IQR) ≥30%. **Results:** In 127 patients reliable LSM could not be obtained by standard M probe, 10 of them normal weight, 25 of them overweight, and 92 obese. By XL probe reliable measurements were obtained in 80/127(63%) of these patients: 8/10 (80%) of the normal weights, 17/25 (68%) of the overweight and 55/92 (59.8%) of the obese. In 98 patients with reliable M probe measurements, XL probe LSMs were also performed. XL LS values strongly and significantly correlated with those obtained by M probe (Spearman r=0.789, p<0.0001), but were significantly lower [median 6.4 kPa (range 3.1 – 53.8) vs 7.7 kPa (range 3.7–69.1), Wilcoxon paired t test p<0.001)]. **Conclusion:** By using the XL probe, reliable LSM by TE can be obtained in more than 60% of patients with unreliable measurements by M probe. LSM by XL probe are significantly correlated, but lower, than those obtained by M probe.

Keywords: liver stiffness, Transient Elastography, XL probe

Introduction

Fibrosis severity is an important prognostic factor in chronic hepatitis, either with viral or nonviral etiology. Also, it can be an important factor in the decision regarding treatment, especially in chronic hepatitis C patients. Currently, liver biopsy (LB) is considered to be the reference method to grade and stage the severity of liver lesions in chronic hepatitis [1]. But there are some drawbacks to consider regarding LB: it is an invasive procedure, poorly accepted by the patients, mild to severe complications occurring in up to 5% of cases [2]; there are also the issues of intra- and interobserver variability [3,4] and of sampling variability [5].

Considering these drawbacks, non invasive methods for the assessment of liver disease severity were developed. Serologic markers that aimed to evaluate activity and fibrosis [6] and also steatosis [7] were developed (like FibroMax), followed by an ultrasound based method, Transient Elastography (TE), able to assess liver stiffness (LS) as a marker of fibrosis [8].

Published meta-analyses confirmed the value of TE for fibrosis assessment in chronic hepatitis patients, proving it to be excellent for the diagnosis of cirrhosis and of moderate value for mild stages of fibrosis [9-12]. In some cases, however, reliable elasticity measurements by standard M probe are not obtained, especially in overweight (BMI≥25kg/m^2) and obese (BMI≥30kg/m^2) patients [13,14]. The introduction of the XL probe was

Received 12.03.2014 Accepted 2.04.2014
Med Ultrason
2014, Vol. 16, No 2, 119-122
Corresponding author: Dr. Roxana Şirli
14, Sirius str., ap.5
300688 Timişoara
Phone: +40-748331232
E-mail: roxanasirli@gmail.com

meant to improve the feasibility of TE in this category of patients [15,16].

The aim of our study was to assess the usefulness of the XL probe in daily clinical practice.

Material and method

Patients and Liver Stiffness Measurements

Our prospective study included 216 difficult to evaluate patients (mean BMI 30.1±4.1 kg/m^2) with chronic hepatopathies (either HBV, HCV chronic hepatitis or with NASH/NAFLD), in which liver stiffness measurements (LSM) were made by Transient Elastography, using a FibroScan® device (EchoSens - Paris, France). After informed consent was obtained, in each patient paired measurements were made with the M (3.5MHz) and XL (2.5 MHz) probes in the same session. The measurements were made in the right liver lobe through the intercostal spaces, on patients in dorsal decubitus with the right arm in maximal abduction. The tip of the probe, covered with coupling gel, was placed on the skin between the ribs aiming at the right liver lobe. The operator, assisted by ultrasound time-motion and A-mode images provided by the system, located a portion of the liver at least 6 cm thick and free of large vascular structures. Once the area of measurement had been located, the operator pressed the probe button to begin an acquisition. Measurements which did not had a correct vibration shape or a correct follow up of the vibration propagation were automatically rejected by the software.

Ten valid LSM were acquired with each probe, a median was calculated expressed in kiloPascals (kPa). Reliable LS measurements were defined as median of 10 valid measurements with a success rate (SR = ratio of the number of successful acquisitions divided by the total number of acquisitions) ≥ 60% and an interquartile range (IQR=the range of the middle 50% of the data) <30%. Unreliable TE measurements were considered the following situations: fewer than 10 valid shots; SR<60% and/or IQR≥30%. Paired t test was used to compare LSM obtained with both probes.

Statistical analysis

The statistical analysis was performed using the MedCalc Software (MedCalc Program, version 12.3.0, Belgium). The distribution of numerical variables was first tested by the Kolmogrov-Smirnov test. For numerical variables with normal distribution, the mean value and standard deviation were calculated, while for non-normal distribution median values and range intervals were presented. Differences between numerical variables were analyzed by Wilcoxon paired t test. Qualitative variables were presented as numbers and percentages. A p-value less than 0.05 was regarded as significant for each statistic test. Spearman's rank correlation coefficient (r) was used to assess the correlation of LS measurements by means of M and XL probes.

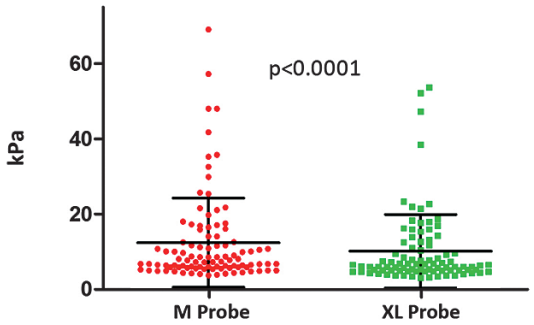

Fig 1. Mean LSM by M vs. XL probes

Results

In 127 patients (40.2% men, mean age 56.8±12.6 years, mean BMI 30.6±4.6 kg/m^2) reliable LSM could not be obtained by the standard M probe, 10 of them normal weight (BMI<25kg/m^2), 25 of them overweight, and 92 obese. By XL probe reliable measurements were obtained in 80/127 (63%) of these patients: 8/10 (80%) of the normal weight; 17/25 (68%) of the overweight; and 55/92 (59.8%) of the obese.

In 98 patients with reliable M probe measurements (58.2% men, mean age 53.3±10.6 years, mean BMI 29.4±3.3 kg/m^2), XL probe LSMs were also performed. LS values obtained by XL probe strongly and significantly correlated with those obtained by M probe (Spearman r=0.789, p<0.0001).

The median LS values by XL probe were significantly lower than those obtained by M probe [median 6.4 kPa (range 3.1 – 53.8) vs 7.7 kPa (range 3.7 – 69.1); Wilcoxon paired t test p<0.001] (fig 1).

Discussions

TE is a validated method for liver fibrosis assessment, especially in chronic viral hepatitis, a fact proven by its inclusion in the EASL Guidelines for fibrosis assessment in chronic B and C hepatitis [17]. This technique is integrated into a FibroScan® device (EchoSens, Paris, France). The liver tissue is mechanically stimulated by the device's ultrasound transducer mounted on the axis of a vibrator. The vibrator generates a completely painless vibration (with 50Hz frequency and 2 mm amplitude for

the M probe and 50 Hz frequency and 3 mm amplitude for the XL probe) [18], which induces an elastic shear wave that propagates through the skin and the subcutaneous tissue to the liver. The shear wave is tracked using the coaxial ultrasound transducer, its velocity is directly related to the tissue stiffness, which is calculated by the device and expressed in kilopascals (kPa) [18,19]. Beside the standard M-probe (3.5 MHz), an S-probe (5 MHz) for pediatric use and an XL-probe (2.5 MHz) for overweight and obese patients are available.

As mentioned in the introduction, we cannot always obtain reliable measurements by TE. In a previously published study by our group, the rate of failed and unreliable measurements by standard M probe was 29.2% from 8218 patients [14], while in the Castera study it was 18.9% from 13,369 measurements [13]. In both studies, as well as in a Chinese study [20], the most important predictor factor for failed an unreliable measurements was the Body Mass Index (BMI). In the Romanian study, the rate of failed and unreliable measurements increased from 14.9% in normal weight patients to 49.5% in obese ones [14], results similar with those observed in the Castera study [13].

In order to overcome this drawback of TE, a special probe for obese patients was developed. The XL probe has a frequency of 2.5 MHz, as opposed to the M probe (3.5 MHz), in order to increase penetrability, and also the amplitude of the vibrator is higher: 3 mm [18]. In the original study that evaluated the XL probe [21], which included 99 patients with a mean BMI of 40.5 kg/m^2, reliable LSM with XL-probe were obtained in 59% of cases, in whom LSM by M probe were unreliable. In a German study performed in 50 NASH and NAFLD patients (a rather small number of patients), reliable XL LSM were obtained in 83%, in whom M probe was inefficient [22]. In the Myers et al study [15], which included 276 patients with BMI $\geq$ 28 kg/m^2, reliable LSM with XL-probe were obtained in 61% of cases, in whom LSM by the M probe were unreliable, while in the de Lédinghen study on 286 cases, the rate of reliable XL LSM was 56.9% [16]. The results of our study are in line with the above mentioned data, since we obtained reliable LSM by XL probe in 63% of patients in whom TE was not feasible by M probe.

As expected, in our study the rate of reliable XL measurements decreased with the increase of BMI, from 80% in normal weights, to 68% in over weights and to 59.8% in obese. Similar results were observed in de Lédinghen study [16], and in the Wong study, in which reliable measurements by XL probe were obtained 65% of obese patients (BMI > 30 kg/m^2) vs. 75% overall [17].

In our study the LS values obtained by XL probe strongly correlated with those obtained by M probe: Spearman r=0.789, p<0.0001. The result was similar to the de Lédinghen study (r = 0.74, p <0.0001) [16], but lower than in the Myers study (r = 0.86; P < 0.0005) [15] and than in a Spanish study, on 254 chronic hepatitis patients, in which Spearman r was 0.897, p<0.001 [24], while in the Wong study, in 517 patients, Spearman r was 0.89, p < 0.001 [23].

Even if strong correlations between LSM by XL and M probes were found in the above mentioned studies, the values obtained by XL probe were lower than those obtained by M probe: median liver stiffness 6.8 vs. 7.8 kPa (p<0.00005 in the Myers study) [15], 9.5 vs. 11.3kPa, (p<0.001 in the Spanish study) [24] and 6.4 vs 7.7 kPa (p<0.001) in our current study.

A limitation of our study is that liver biopsy was not performed in all our patients, so that cut-offs for different stages of fibrosis by M and XL probe could be compared. In the study performed by Wong et al, in which LSM by XL and M probes were compared to liver biopsy, XL cut-offs at 4.8 kPa and 10.7 kPa were the best estimates of 6.0 kPa and 12.0 kPa of M probe in overweight patients (BMI=25-30 kg/m^2), while in obese (BMI>30 kg/m^2) the M probe cut-offs may be used also for the XL probe [23].

Conclusion

By using the XL probe, reliable LSM by TE can be obtained in more than 60% of patients with unreliable measurements by M probe. LSM by XL probe are significantly correlated, but lower, than those obtained by M probe.

Conflict of interest: none

Acknowledgements: Isabel Dan, Nadia Cornu, Melania Ardelean

References

1. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD; American Association for the Study of Liver Diseases. Liver biopsy. Hepatology 2009; 49: 1017-1044.
2. Mueller M, Kratzer W, Oeztuerk S, et al. Percutaneous ultrasonographically guided liver punctures: an analysis of 1961 patients over a period of ten years. BMC Gastroenterol 2012; 12: 173.
3. 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.

4. Persico M, Palmentieri B, Vecchione R, Torella R, de SI. Diagnosis of chronic liver disease: reproducibility and validation of liver biopsy. Am J Gastroenterol 2002; 97: 491-492.
5. Ratziu V, Charlotte F, Heurtier A, et al. Sampling variability of liver biopsy in nonalcoholic fatty liver disease. Gastroenterology 2005; 128: 1898-1906.
6. Poynard T, Imbert-Bismut F, Munteanu M, et al. Overview of the diagnostic value of biochemical markers of liver fibrosis (FibroTest, HCV FibroSure) and necrosis (ActiTest) in patients with chronic hepatitis C. Comp Hepatol 2004; 3: 8.
7. Poynard T, Ratziu V, Charlotte F, et al; LIDO Study Group; CYTOL study group. Diagnostic value of biochemical markers (NashTest) for the prediction of non alcoholo steato hepatitis in patients with non-alcoholic fatty liver disease. BMC Gastroenterol 2006; 6: 34.
8. 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.
9. 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.
10. 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.
11. 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.
12. 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.
13. 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.
14. Sirli R, Sporea I, Bota S, Jurchiş A. Factors influencing reliability of liver stiffness measurements using transient elastography (M-probe)-monocentric experience. Eur J Radiol 2013; 82: e313-e316.
15. Myers RP, Pomier-Layrargues G, Kirsch R, et al. Feasibility and diagnostic performance of the FibroScan XL probe for liver stiffness measurement in overweight and obese patients. Hepatology 2012; 55: 199-208.
16. de Lédinghen V, Wong VW, Vergniol J, et al. Diagnosis of liver fibrosis and cirrhosis using liver stiffness measurement: comparison between M and XL probe of FibroScan®. J Hepatol 2012; 56: 833-839.
17. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatitis C virus infection. J Hepatology 2011; 55: 245–264.
18. Bamber J, Cosgrove D, Dietrich CF, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 1: Basic principles and technology. Ultraschall Med 2013; 34: 169-184.
19. 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.
20. Wong GL, Wong VW, Chim AM, et al. Factors associated with unreliable liver stiffness measurement and its failure with transient elastography in the Chinese population. J Gastroenterol Hepatol 2011; 26: 300-305.
21. de Lédinghen V, Vergniol J, Foucher J, El-Hajbi F, Merrouche W, Rigalleau V. Feasibility of liver transient elastography with FibroScan using a new probe for obese patients. Liver Int 2010; 30: 1043-1048.
22. Friedrich-Rust M, Hadji-Hosseini H, Kriener S, et al. Transient elastography with a new probe for obese patients for non-invasive staging of non-alcoholic steatohepatitis. Eur Radiol 2010; 20: 2390-2396.
23. Wong VW, Vergniol J, Wong GL, et al. Liver stiffness measurement using XL probe in patients with nonalcoholic fatty liver disease. Am J Gastroenterol 2012; 107: 1862-1871.
24. Herrero JI, Iñarrairaegui M, D'Avola D, Sangro B, Prieto J, Quiroga J. Comparison of the M and XL FibroScan® probes to estimate liver stiffness by transient elastography. Gastroenterol Hepatol 2014 Jan 10. pii: S0210-5705(13)00284-7. doi: 10.1016/j.gastrohep.2013.10.009.