

Feasability, accuracy and reproducibility of transient elastography

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Abstract

Background: Transient elastography (TE) is a non-invasive method for the evaluation of liver diseases which is increasingly being accepted by patients and hepatologists. **Aim:** To evaluate the capacity of the TE (FibroScan) in estimating liver fibrosis in clinical practice. **Material and methods:** During 2 years 3459 examinations were performed. The time required for examination, the rate of valid determinations and the rate of uninterpretable results, taking into account the interquartile range (IQR) and the success rate (SR), were evaluated. The TE reproducibility (intra- and inter-observer reproducibility analyzed by 3 independent examiners) in 287 cases was evaluated using the intra-class correlation coefficient (ICC). A group of 167 healthy volunteers were examined to establish the average value of the liver stiffness. **Results:** The average time required for one examination was 4 min 15 s. In 94.7% of cases the determinations were valid. In 446 cases IQR was > 30% and SR < 60% resulting in 13.6% of cases without TE valid results, and 86.4% TE useful results for the evaluation of the chronic liver disease. Intra-observer reproducibility for the three operators were: 0.985, 0.949, and respectively 0.874 and the inter-observer reproducibility was analyzed with overall ICC 0.982. The average value of the liver stiffness in the control group was 4.8 - 1.9 kPa. **Conclusions:** TE is an easy and quick way to evaluate liver stiffness, user- and patient-friendly. Intra- and inter-observer reproducibility is excellent, TE being an operator-independent method.

Key-words: transient elastography, feasibility, accuracy, reproducibility

Rezumat

Introducere: Elastografia impulsională (EI) este o metodă tot mai utilizată în practica zilnică. Fiind noninvasivă, este agreată atât de medici, cât și de pacienți. **Scopul lucrării:** de a evalua capacitatea de estimare a fibrozei hepatice prin EI (FibroScan®) în practica clinică. **Material și metodă:** Într-o perioadă de 2 ani s-au efectuat 3459 de examinări, în care s-a evaluat durata de examinare, rata determinărilor valide și rata rezultatelor nedeterminabile ținând cont de intervalul intercvartilic (IQR) și rata de succes (SR). Reproducibilitatea intra- și interobservator a fost studiată utilizând coeficientul intra-clasă, în cazul a 287 de pacienți, la care s-a efectuat măsurători de către 3 operatori independenți. Valoarea medie a dunității hepatice a fost stabilită prin măsurătorile efectuate la un grup de 167 de voluntari sănătoși. **Rezultate:** Timpul mediu de examinare în cadrul lotului nostru a fost de 4 min 15 s. În 94,7% din cazuri determinările au fost considerate valide. În 446 din cazuri IQR a fost > 30% și SR < 60% rezultând 13,6% dintre cazuri la care valorile EI nu au putut fi utilizate și 86,4% în care a fost util pentru evaluarea bolii hepatice cronice. Reproducibilitatea intra-observator între cei trei examinatori a fost de: 0.985, 0.949, și respectiv 0.874 iar reproducibilitatea inter-observator a fost analizată cu un ICC pe ansamblu de 0.982. Valoarea medie a dunității hepatice la lotul martor a fost de 4.8 - 1.9 kPa. **Concluzie:** EI este o metodă facilă, rapidă de evaluare a fibrozei hepatice. Reproducibilitatea intra- and inter-observator este excelentă, EI fiind o metodă operator-independentă.

Cuvinte-cheie:

Introduction

Transient elastography (TE or FibroScan® - FS) had been used in clinical practice since 2003, first in France [1,2], then in other European countries [3,4] and on other continents [5,6,7,8], becoming increasingly popular, especially in ambulatory medicine.

Liver biopsy (LB) has led to remarkable progress in the field of hepatology. In current practice it was and is

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still widespread in establishing the diagnosis and therapy decision and to ascertain the efficacy of treatment [9].

Through its invasiveness, LB has its adverse side effects and potential complications. These have been evidenced in numerous retrospective and prospective studies [10-17]. Severe complications are rare but are still mentioned (0.3-0.5%), as well as a risk of mortality [9]. The main problems of liver biopsy as a diagnostic procedure are the sampling and observational errors [18].

Non-invasive methods, especially TE have become increasingly accepted. Using TE the volume of liver tissue explored corresponds to a cylinder with a diameter of 1 cm and a length of 4 cm (depth: 2.5 - 6.5 cm), corresponding to a volume 100 times greater than the fragment obtained by LB.

After a period of enthusiasm in using the method, a proper analysis is required to determine the exact benefits not only with its positive results, but also with its limits, in evaluating various chronic liver diseases.

Material and method

During May 2007 – February 2009, 3459 patient were examined by TE. The duration of examination, the rate of valid determinations and the rate of uninterpretable results, taking into account the interquartile range (IQR) and the success rate (SR), which proved to be very important parameters regarding the accuracy of the results obtained by FibroScan, were evaluated. It had been showed by the provider that an IQR > 30% and a SR < 60% does not provide an accurate assessment of liver fibrosis.

The intra- and inter-observer reproducibility using the intra-class correlation coefficient (ICC) was calculated. The TE reproducibility in 287 cases was analyzed by 3 independent examiners.

In a group of 176 apparently healthy volunteers, i.e. without known liver disease, the average value of the liver stiffness was determined.

Results

For the 3459 examinations performed in the above-mentioned period, the average rating in our batch was 4 min and 15 s (minimum 1 min 55 sec - maximum 35 min 20 sec).

Of the 3459 examinations, in 183 cases we could not obtain 10 valid measurements, the failure rate being 5.3%. 3276 cases with valid examinations (**valid determinations in 94.7% of cases**) remained in the study.

In 446 cases IQR was more than 30% and SR less than 60%. So in 13.6% of cases the result of TE could

not be used, and in **86.4% it could be used to evaluate a chronic liver disease correctly.**

Reproducibility intra-observer was studied in 183 cases and the ICC for the three operators were: 0.985, 0.949, and respectively 0.874 (confidence interval - CI 0.977-0.990, 0.849-0.983 respectively 0.794-0.923) (fig 1).

Reproducibility inter-observer was analyzed in 104 cases. Overall ICC was 0.982 (CI 0.974 to 0.988) (fig 2).

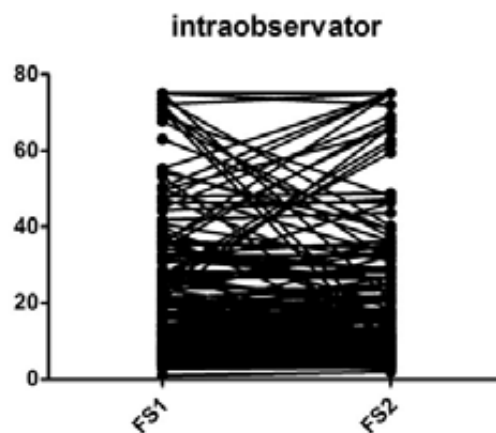


Fig 1. Intra-observer reproducibility of the FibroScan® measurements.

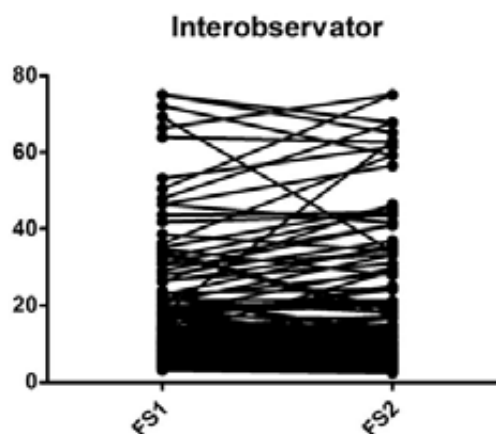


Fig 2. Inter-observer reproducibility of FibroScan® measurements.

Taking in account the batch of 176 volunteers without known liver pathology, in 11 cases we could not obtain valid measurements (6.2%). In the remaining 165 subjects, the mean value obtained was 4.8 ± 1.9 kPa (2.3 – 8.8 kPa). We did not find different levels of TE according to different age groups.

Discussion

Transient elastography is a method driven by a rapid learning curve, 50-100 examinations are required in order to make performance measurements [18,19]. Castera *et al.* shows in a recent study comprising 13369 patients, that operator experience of over 500 examinations has a significant influence on the final result [20].

Time evaluation is short, the average in our study was 4 minutes and 15 seconds.

From the 3459 examinations performed in our center, in 183 cases we could not obtain 10 valid measurements, the failure rate being 5.3%. Regarding the determination of the valid rate, the percentage of indeterminate results (inability to obtain 10 valid measurements) varies in literature between 2.4 and 9.4% in different studies [1,2,10,19-25], therefore our results are somewhere between this limits. The main reasons mentioned [20,27] for the impossibility of determining fibrosis by TE are BMI > 28, presence of steatosis and age. In our study, the main cause which led to undeterminable results was obesity (98%).

The problem concerning the obese patients appears to have been resolved by the appearance on the market earlier this year of a new type of probe (XL) specially designed by EchoSens for these cases.

In addition, the validity of the final result, as recommended by the producing company, depends on two important parameters:

- “interquartile range” (IQR), which shows the variability between the 10 valid determinations obtained and which is shown not to exceed 30% of the mean, ie the final result
- “success rate” (SR), represented by the ratio of the number of valid measurements and total shots and which has to be at least 60%.

The importance of these parameters has been discussed in many papers published to date [9,19,20-24].

In our study, in 446 cases (13.6%), IQR was > 30% and SR < 60%, so in only 86.4% of cases we could use TE to assess liver fibrosis. Data from our study do not differ from those in the literature, the unusable results (which cannot be obtained and the results which cannot be interpreted) range between 14.9% and 18.9% [10,20]. As a result we must consider that only approx. 85% of cases that are evaluated through TE are able to offer a valid measurement (and not approx. 95%).

Castera *et al.* stresses that it is important to take into consideration guidelines recommended by the manufacturer as well as the expertise of the examiner when conducting elastography (. Thus, in their study, they found

a highly significant statistical difference between operators with less or more than 500 examinations performed [20].

Reproducibility of TE is also important in the applicability of the method in the clinical practice. Reproducibility intra-observer has been studied in 183 cases and the ICC for the three operators were evaluated: 0.985, 0.949, and respectively 0.874 (confidence interval - CI 0.977-0.990; 0849 - 0983 and respectively 0794 to 0923). Reproducibility inter-observer was analyzed in 104 cases. Overall ICC was 0982 (CI 0974 to 0988).

These data overlap with data from the initial study conducted by Sandrin *et al.* where reproducibility was extremely good (the intra-operator standardized CV was 3.2% over the studied population and varied from 2% to 18%). No significant difference was noted between the three successive series of measurements made by the three different operators (Kruskal–Wallis test) and the corresponding CV was 3.3%. But it has also to be noted that the batch was very small (15 patients) and therefore clear conclusions on the parameters pertaining to the subjects and the basic etiology of liver disease that may interfere with EI performance were unable to be established.

There are two recent studies that answered this question [19,31] and show that the method is highly reproducible, both intra- and inter-observer. Fraquelli *et al.* showed in their study [19] that the intra-class correlation index (CCI) was 0.98 in both cases. It is been shown that the reproducibility of the method may be influenced by the expertise of the operator, and by the BMI (and hence the SR), and also Fraquelli *et al.* stresses in this connection that the examiner’s experience could make ICC increase to almost an absolute value.

TE average value obtained on volunteers without known liver pathology (in our group of 165 cases with valid determinations) was 4.8 + 1.9 kPa (2.3-8.8 kPa) and we did not find different values by TE in different age groups. The same has been evidenced by other authors (Roulot *et al.*) for 429 healthy subjects without known liver disease and normal transaminases [30, 31]. Prati *et al.* obtained similar results in a study of 1001 cases [31]. The mean value in these subjects was 5.5 + 1.6 kPa. Age appears not to influence the outcome. However, as stated in a previous study by Corpechot *et al.* [30] values are influenced by gender, men having higher values, 5.8 - 1.5 kPa in comparison to woman: 5.2 - 1.6 kPa (p = ES). Other factors that influence the result obtained by FibroScan are BMI over 28 kg/m² and presence of a metabolic syndrome, situations where values are higher by about 1 kPa.

Conclusions

TE is an easy way to evaluate liver stiffness, requiring a short time to gain expertise and is highly appreciated by patients, being noninvasive, in comparison with the liver biopsy.

Intra- and inter-observer reproducibility is excellent, TE being an operator-independent method.

It should be noted, that that is very important that the examiner should give maximum attention to the manufacturer's recommendations so that the results are applicable in the highest diagnostic accuracy, with an IQR of less than 30% and a SR of 60%. Using these criteria, we could obtain valid measurement only in about 85% of cases of FS evaluation. In performing a study regarding the value of FS in comparison with liver biopsy, we must use only this valid measurement.

Regarding the undeterminable results (inability to obtain 10 valid measurements) mostly in overweight patients, this shortcoming will perhaps remain largely on the past due to the appearance of the new probe "XL" (EchoSens, Paris, France) on the market specifically designed for obese patients.

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