LETTERS TO THE EDITOR

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Assessment of Liver Fibrosis With Elastography Point Quantification Versus Transient Elastography

Dear Editor:

We read the recent article by Conti et al[1] entitled "Assessment of Liver Fibrosis With Elastography Point Quantification vs Other Noninvasive Methods" with great interest. The authors evaluated the accuracy of elastography point quantification (ElastPQ) for the staging of liver fibrosis in patients with chronic liver disease (CLD) compared with aspartate transaminase to platelet ratio index, fibrosis-4 index, and transient elastography (TE), using liver biopsy (METAVIR scores) as the reference standard. They reported that ElastPQ has good to excellent performance for the noninvasive staging of liver fibrosis in patients with CLD. ElastPQ identified patients with fibrosis or cirrhosis with levels of accuracy that were not inferior to those of TE and outperformed serum fibrosis indexes in identifying each stage of liver fibrosis.

In 2018, we presented preliminary data from our study in which we compared the performance of ElastPQ (Epiq 7; Philips Healthcare, Amsterdam, the Netherlands) and TE (Fibroscan; Echosens, Paris, France) on 2 types of tissue equivalent phantoms (Computerized Imaging Reference Systems [CIRS], Inc, Norfolk, VA) and in a small cohort of patients with CLD. The 2 phantoms used (CIRS model SN LOT 12-693E1627-1 [Cablon] and CIRS model 040GSE [Cablon]) contain multiple hydrogel compartments with 4 reference stiffness values (6, 15, 24, and 30 kPa; attenuation, 0.5 dB/MHz/cm). We performed 20 stiffness measurements per reference stiffness value and elastography technique. Thus, a total of 160 measurements were performed. Data from the phantom measurements and the first 38 patients indicated that there might be differences between the 2 systems when using the cutoff values recommended by both manufacturers as being equivalent to the histologic fibrosis stage (METAVIR scores).[2] In the phantoms the ElastPQ measurements (medians) were closer to the phantom reference values than the TE measurements (medians). Nevertheless, no significant difference was observed between ElastPQ and TE ($P = .23$), ElastPQ and phantom reference values ($P = .69$), or TE and phantom reference values ($P = .14$). However, in patients a significant difference between ElastPQ and TE measurements ($P < .001$) was seen, although a moderate positive correlation was observed ($r = 0.59$, $P < .001$).

We have now completed this study and included a total of 93 patients with CLD between December 2017 and February 2019. Patients had the following CLD etiologies: 47 patients had chronic hepatitis B, 11 chronic hepatitis C, 1 chronic hepatitis E (on immunosuppressive therapy), 1 autoimmune hepatitis, 4 alcohol-related liver disease, 19 nonalcoholic fatty liver disease, 4 primary biliary cholangitis, 3 primary sclerosing cholangitis, and 3 had cryptogenic liver cirrhosis. Fifty-seven percent of the included patients were male. Median liver stiffness calculations were based on at least 10 measurements per patient for both techniques.

Using the cutoff values reported by Conti et al[1] (ElastPQ: ≥F2 6.0 kPa; ≥F3 6.2 kPa; = F4 9.5 kPa; TE: ≥F2 7.6 kPa; ≥F3 9.5k Pa; = F4 13.9 kPa), we observed an agreement between the 2 elastography systems that is similar to the agreement observed by Conti et al (Table 1). The small differences between the 2 patient cohorts might be explained by our small sample size and the clinical heterogeneity, for example, the low percentage of hepatitis C within our patient population. A subgroup analysis limited to hepatitis C was not possible because of the small sample size. Also, no recent liver biopsies were available from our cohort. There were no significant differences in the body mass index, waist circumference, transaminases, or transducer (used with TE) between patients where the 2 methods agreed versus those where they disagreed.

In conclusion, our results were similar to the findings of Conti et al[1] when their cutoff values were used. Nevertheless, caution is advised in extrapolating these findings to other clinical settings, especially when taking our observed differences using the manufacturer provided cutoff values (METAVIR-equivalent scores) into consideration.

Table 1. Concordance Between Elastography Point Quantification and Transient Elastography Including 95% Confidence Intervals

Group	Conti et al (n = 361)	Warringa et al (n = 93)
<F2 vs ≥F2	82.3% (77.9%–86.0%), n= 297	71.0% (60.5%–79.7%), n = 66
<F3 vs ≥F3	87.5% (83.6%–90.7%), n= 316	83.9% (74.5%–90.4%), n = 78
<F3 vs F4	93.9% (90.8%–96.1%), n = 339	88.2% (79.4%–93.7%), n = 82

Overall, our data and the results of Conti et al[1] have led us to replace TE measurements by ElastPQ in our standard CLD workup and surveillance. However, it is important to note that the logistical advantages of ElastPQ use in our clinical practice also contributed significantly to this decision.

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Acknowledgements
The authors thank Madelon Bruggemann-Gaasbeek, ultrasound technician, for having a crucial part in this project as being responsible for the ElastPQ measurements and all the logistics; Egbert Jan van der Wouden, Gastroenterologist, for his comments and the insightful suggestions; Ingrid M. Nijholt, Clinical epidemiologist in training, for her comments and contribution on methodology and statistics; and Jolande W. Bouwhuis, Internal medicine, for her contribution regarding the Fibroscan.

Conflicts of interest
The authors disclose no conflicts.

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https://doi.org/10.1016/j.cgh.2020.03.027

Reply. We thank Warringa et al for their comments regarding our article "Assessment of Liver Fibrosis With Elastography Point Quantification vs Other Noninvasive Methods."[1]

In their test using 2 types of tissue equivalent phantoms presented at 2018 European Congress of Radiology,[2] Elastography Point Quantification (ElastPQ) measurements were closer to the phantom values than transient elastography (TE) but no significant difference was described among TE, ElastPQ, and the reference values. Conversely, in a very small cohort of patients with chronic liver disease, no agreement was observed between the 2 systems when using the cutoff values recommended by manufacturers according METAVIR stage. However, these cutoffs seem to be much higher than those generally reported in the literature. For example, 22 kPa was used for identification of patients with severe fibrosis despite in a lot of papers the cutoff for cirrhosis was less than 15 kPa.[3-5] In fact, when the authors used cutoffs reported in our study (6.0 kPa, 6.2 kPa, and 9.5 kPa for classifying patients with F $\geq$2, F $\geq$3, and F4, respectively), agreement between the 2 elastography methods was confirmed. Further prospective studies and metanalyses are needed to establish disease-appropriate cut points for assessment of fibrosis stage.

In the study of Warringa et al,[1] ElastPQ was found to be an accurate noninvasive method for the staging of liver fibrosis in patients with chronic liver disease with similar diagnostic performance compared with TE for all stages of fibrosis as reported in other studies.[3-5] Although TE is a dedicated device available in all hepatologists' offices, it is not able to evaluate ultrasound morphologic characteristics of the liver. On the contrary, ElastPQ is implemented in conventional ultrasound systems and we fully share the observation of the authors about advantages of this tool in our clinical practice thanks to the fact that we can also perform a thorough examination in a specific area of interest of the liver. Despite the growing amount of evidence on the accuracy of new elastography techniques, all guidelines are still focused on the use of TE, which is considered the reference standard, and the use of ElastPQ is often overlooked. A new sensitivity toward ultrasound-based shear wave elastography is needed by the scientific community that gives much more consideration to the clinical applications of this tool in the noninvasive evaluation of liver fibrosis.

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Conflicts of interest
The authors disclose no conflicts.

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https://doi.org/10.1016/j.cgh.2020.04.072