Published in final edited form as:

Hepatology. 2018 January ; 67(1): 13–15. doi:10.1002/hep.29417.

Role of 2D Shear Wave Elastography in the Assessment Of Chronic Liver Diseases

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Non-invasive imaging modalities for assessment of liver fibrosis are increasingly replacing liver biopsy for staging liver fibrosis and monitoring changes in liver stiffness over time. The two most commonly used modalities in the United States are vibration-controlled transient elastography (VCTE) and magnetic resonance elastography (MRE). MRE has been shown to have the highest accuracy in identifying fibrosis, particularly advanced fibrosis and cirrhosis.^{1–3} Besides MRE and VCTE, several other ultrasound-based elastographic modalities based on static strain-imaging or dynamic shear-wave imaging, have been developed.³ One such shear-wave imaging modality is 2-dimensional shear wave elastography (2D-SWE), developed by SuperSonic Imagine®. In contrast to VCTE in which shear waves are generated by a mechanical piston-like ultrasound transducer mounted on a vibrating actuator, 2D-SWE uses focused shear-wave speed imaging to generate shear waves of low amplitude. Then measurements are taken from sequential measurement points, and transformed to Young modulus and reported in kilopascals. 2D-SWE provides a large color-coded “elastogram”, that may be used by the operator to locate the best-suited place for high-quality measurements; additionally, 2D-SWE measures liver stiffness in a larger area than both point-SWE and VCTE.⁴ Some other techniques using shear-wave technology include ElastPQ (Philips Healthcare, Bothell, WA) and Virtual Touch Tissue Quantification (Siemens Medical Solutions, Mountain View, CA).

In this issue of *Hepatology*, Herrmann and colleagues performed an individual participant data pooled analysis combining data from 13 sites in 1134 patients with diverse etiologies of liver disease, to evaluate the performance of 2D-SWE for assessment of liver fibrosis, with liver biopsy as the gold standard. Using sophisticated analyses, clustered by site and using random-effects model to account for inter-site variability, they observed excellent discriminatory ability to distinguish cirrhosis (F4) vs. no cirrhosis (F3) in a cohort predominantly including patients with viral hepatitis (area under receiver operator curve

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Author Contributions: Both authors contributed to study concept, design, acquisition of data, data analysis and interpretation, writing and approval of manuscript

Disclosures: This work is supported in part by the American Gastroenterological Association (AGA) Foundation – Sucampo – ASP Designated Research Award in Geriatric Gastroenterology and by a T. Franklin Williams Scholarship Award; Funding provided by: Atlantic Philanthropies, Inc, the John A. Hartford Foundation, the Association of Specialty Professors, and P30CA23100-28, and R01DK106419 to Rohit Loomba. Siddharth Singh is supported by NIH/NLM training grant T15LM011271.

[AUROC], 0.92–0.96) and good discriminatory ability to detect significant fibrosis (>F1) (AUROC, 0.86–0.91). With a pooled prevalence of significant fibrosis (F2), severe fibrosis (F3) and cirrhosis (F4) of 22.1%, 15.9% and 16.2%, respectively in their cohort, the overall correct classification rate was 69.7%, 89.3% and 82.9%, respectively. At this prevalence, negative predictive value for ruling out advanced fibrosis (F3) was >95%. Age, elevated alanine aminotransferase and aspartate aminotransferase and low platelet count were associated with discordant results between liver biopsy and 2D-SWE. Valid VCTE measurements were available for a subset of patients (n=665). On comparison of diagnostic performance of 2D-SWE and VCTE, there were marginal differences in AUROC for diagnosis of cirrhosis (1.4–6.7%), severe fibrosis (1.4–12.8%) and significant fibrosis (4.2–11.2%), generally favoring 2D-SWE over VCTE. The performance of 2D-SWE was superior for hepatitis B and hepatitis C, as compared to other etiologies of liver disease.

This multi-center, collaborative study adds valuable information on the diagnostic performance of a newer non-invasive elastographic modality. With the use of individual participant level pooled analysis, more accurate cut-offs for classifying fibrosis stages were ascertained. There are certain limitations as acknowledged by the investigators. First, this was not a systematic literature review, but rather information on eligible participating sites was provided by the SuperSonic Imagine® and other study investigators; however, the results were compared with published reports of non-participating sites, and were generally comparable. Second, liver biopsies and histopathological analyses were performed locally, and not centrally read. Centralized reading, while definitely preferred, is challenging and resource intensive; importantly, the pathologists at local sites were blinded to results of 2D-SWE. Third, there were some protocol deviations from what was originally proposed (definition of acceptable liver biopsy, exclusion of ‘other’ etiologies of chronic liver diseases, etc.). Overall, these limitations are unlikely to bias findings from this study, which are generally representative of real-world practice. Finally, the number of patients with NAFLD were limited to draw firm conclusions regarding the true diagnostic accuracy of 2D-SWE in patients with NAFLD.

As compared to VCTE, 2D-SWE has the advantage of allowing operators to select a region of interest in a representative area of the liver and in principle, it could be saved and followed over time with repeated measurements, decreasing sampling variability.⁶ Additionally, since shear waves are generated inside the liver, body habitus and ascites should not theoretically be limitations in performing and interpreting results of this study. Unfortunately, this study was not able to provide information on quality of 2D-SWE measurements and failure rate of 2D-SWE (though this was originally one of the proposed secondary outcomes in the published protocol), since data was pooled only for successful 2D-SWE readings. Since the authors collected data on body mass index, it would have been useful to stratify the diagnostic performance of 2D-SWE in obese and non-obese at least in a subset of patients with successful readings. Point shear-wave elastographic technique, which is very similar to 2D-SWE, at least seems to have lower failure rate as compared to VCTE.⁴ In contrast to VCTE, 2D-SWE requires more technical expertise, though intra- and inter-observed reproducibility is reasonable; it is unlikely to be a tool used at point-of-care for liver stiffness assessment, where VCTE has shown promise.

Since the data reported in this manuscript does not allow direct comparison of sensitivity and specificity of 2D-SWE and VCTE (only AUROCs are reported), we used pooled data on diagnostic performance of VCTE from the recent American Gastroenterological Association Guidelines on the role of VCTE in chronic liver diseases.⁵ In an illustrative scenario where there is high risk or prevalence of cirrhosis (for example, 30%), there was no meaningful difference in the rate of false positives (2D SWE vs. VCTE: 8.5% vs. 6.3%) and false negatives (4.3% vs. 4.2%) with 2D-SWE and VCTE in adults with HCV. In contrast, in patients with hepatitis B, while rates of false negative results were comparable between 2D-SWE (6.0%) and VCTE (5.7%), rates of false positives were significantly lower with 2D-SWE (4.9% vs. 11.9%). These results, however, should be interpreted with caution since the majority of patients with HBV, and the corresponding estimates of diagnostic performance of 2D-SWE in this population, was derived from a single center in Asia. Since VCTE, particularly M-mode, is associated with high failure rates in obese patients with NAFLD, it is difficult to truly assess its overall and comparative diagnostic performance in this setting since most studies do not present intention-to-diagnose analyses. However, on indirectly comparing 2D-SWE to MRE for detection of cirrhosis, while the specificity is comparable (MRE vs. 2D-SWE, 0.87 vs. 0.88), sensitivity of MRE is higher (MRE vs. 2D-SWE, 0.88 vs. 0.75) based on results from a pooled analysis on the performance of MRE in patients with NAFLD.⁵ Hence, expected rates of false negatives would be lower with MRE especially in a high prevalence population (2D-SWE vs. MRE: 7.5% vs. 3.6%).⁶ Additionally, in a prospective comparative study in patients with NAFLD, MRE was superior to ARFI, particularly in obese patients.⁷

2D-SWE is a promising alternative that is comparable to VCTE for most indications, with limited data in NAFLD. It may be inferior to MRE for detection of cirrhosis in patients with NAFLD, albeit based on indirect comparisons and small number of patients. Further, multicenter, pragmatic, larger randomized controlled trials are needed to perform a head to head comparison between various non-invasive imaging modalities to determine their clinical utility in clinical practice.

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