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Shear wave elastography to evaluate hepatic damage in heart failure

Pieter van der Bijl, Victoria Delgado and Jeroen J. Bax

Department of Cardiology, Heart Lung Centre, Leiden University Medical Centre, Leiden, The Netherlands

Heart failure and liver disease commonly occur together due to (i) shared risk factors, for example, vascular disease, ethanol abuse, or autoimmune diseases (ii) hepatic damage secondary to heart failure (known as ‘cardiogenic liver injury’), which may be caused by elevated right-sided filling pressures (‘congestive hepatopathy’) and/or ischaemia due to left ventricular failure and hypoperfusion; and (iii) heart failure complicating primary liver disease (known as ‘cirrhotic cardiomyopathy’). Hepatic damage secondary to congestion is facilitated by the absence of valves in hepatic veins, allowing direct transmission of right ventricular pressure into the hepatic parenchyma. Ischaemia–reperfusion injury on the other hand occurs secondary to hypoperfusion of the liver when the left ventricle is unable to perfuse organs adequately; this mechanism is believed to be at play mostly in the setting of acute heart failure (‘acute cardiogenic liver injury’). Overlap of congestive hepatopathy and hypoperfusion may occur, since congestive hepatopathy leads to a decreased perfusion gradient across liver tissue, which also causes ischaemic damage. Chronic exposure of the liver to the above insults culminates in perivenular fibrosis, centrilobular necrosis, and eventually cirrhosis.

Cardiogenic liver injury worsens outcome in patients with heart failure,¹ and its diagnosis is currently based on (i) increased serum alanine aminotransferase and lactate dehydrogenase, (ii) inferior vena cava and hepatic venous congestion on abdominal ultrasound, and (iii) liver biopsy. The conventional diagnostic approach is limited by (i) the fact that it only detects hepatic involvement in heart failure at a fairly late stage, and (ii) liver biopsy is an invasive test and not amenable to frequent repetition. Shear wave elastography is a technique that has been applied to non-cardiac-related liver disease and which may be an earlier marker of cardiogenic liver injury. Its non-invasive nature and low cost also make it attractive. The term ‘elastography’ refers to the assessment of tissue elasticity: the ability to resist deformation caused by an applied force,² while a ‘shear wave’ represents particle motion perpendicular to the

direction of the force applied.² The speed of transmission of a shear wave can be measured and is based on the physical principle that a less elastic medium will propagate such a wave more rapidly. Applying shear wave elastography to liver disease requires an ultrasound transducer, which creates a high-intensity sound wave (much greater than with diagnostic ultrasonography) generating a shear wave in hepatic tissue. Non-elastic (‘stiff’) hepatic tissue will allow rapid shear wave propagation, the velocity of which can be quantified. Shear wave velocity can be related to elasticity with a simple formula incorporating tissue density (this only holds true if tissue viscosity is assumed to be zero). Tissue viscosity represents internal friction and is considered a separate physical property from elasticity.³ The velocity by which a shear wave propagates is impacted on by its frequency. The gradient of a shear wave velocity curve plotted against frequency is indicative of viscosity.³ This shear wave vs. frequency curve gradient is known as shear wave elasticity dispersion, and it has not been used to characterize cardiogenic liver injury before.

In the current issue of the journal, Nakayama *et al.*⁴ investigated 316 patients with heart failure who were classified into stages A–D of the American College of Cardiology (ACC)/American Heart Association (AHA) heart failure scheme.⁵ Patients with a history of liver disease or ethanol abuse, or with signs of liver disease, were excluded. Hepatic tissue elasticity and dispersion of the elasticity slope were evaluated with shear wave elastography ultrasound. Elasticity remained stable in stage A and B heart failure and only showed a significant increase from stage C to D heart failure. In contrast, the elasticity slope increased gradually from stages A to D, suggesting that it is already abnormal during the earlier stages of heart failure. Importantly, the dispersion slope demonstrated an increase prior to the detection of abnormal hepatic biochemistry.

Shear wave elastography has been investigated in heart failure to assess right-sided filling pressure⁶ and to identify cardiogenic liver injury.⁷ This technique has also been shown

to be of prognostic significance in acute cardiogenic liver injury.⁸ In a preclinical rodent model, shear wave elastography was correlated with liver fibrosis, while dispersion slope corresponded better to necroinflammation, raising the intriguing possibility that different histopathological substrates can be distinguished with ultrasound.⁹ Shear wave dispersion has been investigated in a limited number of human studies for characterizing non-cardiac liver disease, and two of these studies demonstrated only a weak association with histologically proven fibrosis.³ Sugimoto *et al.* evaluated the utility of shear wave dispersion in patients with non-alcoholic fatty liver disease and found it to correlate well with necroinflammation,¹⁰ which is in agreement with the above-mentioned preclinical study.⁹ While tissue necrosis is a prominent feature of cardiogenic liver injury, inflammation is usually not.¹¹ The exact histopathological correlates of shear wave dispersion in cardiogenic liver injury therefore remain to be elucidated, and unfortunately, no histological comparison was available for the current study.

A safe, low cost diagnostic technique to identify cardiogenic liver injury at its inception is potentially clinically useful. The progression of heart failure-related liver disease might be prevented or slowed down² by either (i) conventional heart failure therapy, or (ii) liver-directed treatments. Anti-failure (and other) drugs are metabolized by the liver, for example, many beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers, and knowing when hepatic function is impaired might allow appropriate dose adjustments. Shear wave elastography is already available as an application on some commercial cardiac ultrasound scanners, which facilitates its integration into a bedside echocardiography examination. Some technical issues have to be kept in mind when implementing shear wave elastography in daily practice: (i) it is affected by motion, for example, diaphragmatic (the patient has to stop breathing during the acquisition) and cardiac (only the right hepatic lobe is sampled); (ii) multiple measurements (up to 10) are required to improve test reliability; and (iii) the values obtained are affected

by subcutaneous adipose tissue and ascites (which may occur as part of the heart failure syndrome).³ Values from different vendors are not yet directly comparable and mandate follow-up on identical equipment.²

The current study is descriptive only⁴—the prognostic and therapeutic impact of using shear wave elastography in cardiogenic liver injury still has to be investigated. If shear wave elastography is abnormal in the early stages of heart failure, this might reflect only passive congestion, and it does not imply that (i) there are significant abnormalities of hepatic function that will impact clinically, for example, on pharmacokinetics, (ii) such early abnormalities necessarily imply irrevocable progression of liver damage, (iii) these early changes portend a worse outcome, or (iv) early changes reflected by shear wave elastography can be treated effectively. The application of this technology to cardiogenic liver injury is therefore in its infancy but holds considerable potential. More comprehensive characterization of cardiogenic liver injury interdigitates with an important contemporary concept in heart failure, that is, that it is a systemic disease and that many of its manifestations, prognostic factors, and therapeutic implications lie outside of the heart. Ultrasound has already proven its worth in assessing the heart failure syndrome more holistically, for example, by application to the liver, lungs, kidneys, and skeletal musculature.

Conflict of interest

The Department of Cardiology of Leiden University Medical Centre received research grants from Abbott Vascular, Bayer, Biotronik, BioVentrix, Boston Scientific, Edwards Lifesciences, GE Healthcare, and Medtronic. V.D. received speaker fees from Abbott Vascular, MSD, Medtronic, Edwards Lifesciences, and GE Healthcare. J.J.B. received speaker fees from Abbott Vascular. P.v.d.B. has nothing to disclose.

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