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## Role of liver stiffness in prediction of adverse outcomes in heart failure



Heart failure (HF) is a complex clinical scenario presenting with a constellation of manifestations such as dyspnea, fatigue, exercise intolerance, cough, and fluid retention. HF results in structural and functional dysfunction leading to impaired filling and ejection of heart chambers. Furthermore, heart failure can be divided into preserved ejection fraction (HFpEF) and reduced EF HF (HFrEF) considering the value of EF [1]. EF is a vital prognostic marker—numerous clinical decisions are related to left ventricular EF (LVEF) such as drugs for HF, primary prevention implantable cardiac defibrillator, left ventricular assist devices, the timing of interventions for valve repair or replacement, cardiac transplant, and others. Central venous pressure (CVP) changes in relation to the functional status of the heart and a change in CVP or systemic volume status is directly associated with a change in liver stiffness due to venous congestion, reduced perfusion of liver tissue, etc. Few studies in the literature reported the association between HF and liver stiffness with its usefulness for the predictive role in clinical outcomes.

HF has been classified into three subtypes on the basis of LVEF: HFrEF (<40%), HF with mid-range EF (40–49%) and HFpEF (>50%). HFpEF could be misleading since the process is silent. HFpEF at many occasions associated with underlying right-sided HF. We want to applaud Kitaoka and colleagues for putting light on the prognostic value of serum tenascin-C (TN-C) in HF patients with hypertrophic cardiomyopathy (HCM). TN-C is an extracellular matrix glycoprotein expressed during embryogenesis, but it might reappear during pathological circumstances such as myocardial infarction and dilated cardiomyopathy. Kitaoka et al. conducted a retrospective study involving 36 participants with especially HCM, and it illustrated that prevalence of HF was more often in the patients with high serum TN-C level than in those with low TN-C level. Therefore, in a HF patient with HCM, serum TN-C might be another important prognostic marker [2].

Liver stiffness (LS) measured by non-invasive ultrasound-based transient elastography using fibroScan® [Echosens™; Paris, France] has reformed the recognition of liver pathologies to be

specific liver fibrosis or cirrhosis. LS is a useful surrogate marker for advanced liver fibrosis (F3) and cirrhosis (F4) surpassing the past non-invasive approach to detect hepatic abnormalities. LS value below six kPa has been considered to be normal and excludes ongoing liver disease. LS of 8 and 12.5 kPa corresponds to cut-off values for F3 and F4 fibrosis respectively. More than 20 kPa LS strongly correlates to elevated portal pressure, and presence of esophageal varices. LS is reversibly associated with CVP with the direct strong relationship—increases exponentially with cardiac functional deterioration and improves dramatically after diuretic therapy (decongestion). So, LS could be used as a guiding tool for the optimal therapy during acute decompensated HF. Further, measuring LS may be helpful in identifying patients at risk of developing cardiac cirrhosis due to heart failure, as higher systemic venous pressure is well-recognized as a major risk factor of cardiac cirrhosis [3].

A recent study published in JACC by Taniguchi et al. illustrated that LS is a rewarding index for assessing the severity of HF and volume status. The study involved 171 participants diagnosed with HF with no signs of liver disease and disclosed a captivating fact—highest tertile LS (>6.9 kPa, corresponding to an estimated right filling pressure of >7.1 mmHg) had advanced New York Heart Association functional class, high prevalence of jugular venous distention, moderate/severe tricuspid regurgitation, and large inferior vena cava diameter. LS has remarkable predictive abilities for hospitalization, morbidity, and mortality as well [4].

Taniguchi and colleagues performed a study that included 31 participants in the test group and a validation group of 49 additional patients. They calculated LS using transient elastography in 31 patients without structural liver disease undergoing right-sided catheterization. They sought the relationship between LS and right atrial pressure (RAP), which proved to be correlated in the test group ( $r=0.95$ ,  $p<0.0001$ ). When the equation derived from test participants applied in the validation group, anticipated RAP was related with actual RAP ( $r=0.90$ ,  $p<0.0001$ ). As a matter of fact, measurement of LS for RAP assessment remains a reliable method even in the presence of severe tricuspid regurgitation or mechanical ventilation. It has been associated with greater accuracy compared to conventional echocardiography [5].

Some circumstances such as hepatitis, mechanical cholestasis, amyloid deposition, and cellular infiltration in the liver can affect the LS values. So, the usefulness of LS measurement in HF patients remains limited in patients with chronic liver diseases but the easier learning curve, reproducibility, rapidness, and non-invasiveness are favorable aspects for practical use of LS for selected HF populations. In the future, we need a larger dedicated study to establish other remarkable uses of LS in current medicine apart from HF, liver fibrosis, and cirrhosis subjects. And we look forward to using LS in our day-to-day medicine as an important prognostic marker and for making clinical decisions in various scenarios.

## Conflict of interest

There is no conflict of interest.

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### Author's reply



Thank you for being interested in our paper. Heart failure is a major public health problem worldwide and there are many problems to be solved. Heart failure is a complex clinical syndrome associated with multiple organs. The relation between the heart and the kidney is well known as cardiorenal syndrome. In recent years, the linkage between heart failure and the liver has been

drawing attention and the influence of the liver function on the severity and prognosis of heart failure has been studied [1]. Abnormalities in liver function are a cause of reduced perfusion or elevation of right-sided cardiac pressures and congestion leads to increased liver stiffness. Therefore, measurement of liver stiffness may be clinically useful in heart failure. Several methods such as measurement of biomarkers and non-invasive imaging are proposed to assess the liver stiffness or fibrosis and the usefulness has been reported in patients with heart failure [2–4]. As liver stiffness assessed by transient elastography is a hopeful tool to better management in patients with heart failure as Bandyopadhyay and colleagues mention in this letter to the editor, it is also a fact that transient elastography has some limitations [5]. I hope that the significance of transient elastography will be further investigated and contribute to the better management of patients with heart failure.

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