

Focusing on Cardio-Hepatic Syndrome in Heart Failure and Cardiovascular Interventions: Is it Time to Update the Prognostic Risk Scores?

Heart failure (HF) is a multifactorial, heterogeneous disease characterized by congestion and/or reduced cardiac output, leading to unmet metabolic demands of vital organs. Regardless of the etiology or phenotypic features (ischemic vs. non-ischemic, reduced or preserved ejection fraction, severe valvular stenosis or regurgitation), the "inevitable consequence" of the HF syndrome is the progressive end-organ dysfunction. Failure of one or more organ systems (heart itself, lungs, kidneys, liver, intestine, brain, skeletal muscle) has been the main determinant of survival in HF.^{1,2} Integration of new pharmacologic agents (sacubitril/valsartan, sodium-glucose cotransporter-2 (SGLT-2) inhibitors) into guideline-directed medical therapy and advancements in interventional and surgical procedures (complex coronary interventions, transcatheter aortic valve implantation (TAVI), Mitra-clip, left ventricular assist devices) have led to a significant improvement in HF mortality in selected patients.³⁻⁷ However, HF still remains a global health problem associated with reduced survival, frequent hospitalizations, and impaired quality of life.

Among the well-known target organ interactions in HF, much attention has been directed to the kidney, widely described as "cardio-renal syndrome".⁸ Similarly, HF is typically associated with varying degrees of clinical/laboratory signs of liver dysfunction.⁹ The presence of hepatic impairment has been shown to reduce survival in HF patients, both in the acute and chronic settings.^{10,11} The possible mechanisms of cardiogenic liver dysfunction are as follows: 1. Congestive hepatopathy due to long-standing elevated right-sided pressures, and 2. Acute reduction in hepatic arterial blood supply in low-output HF syndromes.⁹ Patients with advanced HF often exhibit varying degrees of cardio-hepatic syndrome. Signs and symptoms are generally indistinguishable from isolated end-stage liver disease. Patients often present with weakness, abdominal distention, jaundice, bleeding diathesis, tremor, and mental disturbances depending on the level of hepatic impairment. Laboratory findings include altered coagulation tests and significantly elevated transaminases in acute cardiogenic liver injury (or ischemic hepatitis), whereas elevated cholestasis markers (lactate dehydrogenase (LDH), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin) and hypoalbuminemia are more commonly associated with chronic congestive hepatopathy.¹²

Developments in cardiac structural interventions have changed the natural course of HF patients. During the past decade, transcatheter aortic valve implantation (TAVI) has gained significant reputation in improving the survival of patients with severe symptomatic aortic stenosis.¹³ Mortality benefits have also been proven in aortic stenosis patients with a low ejection fraction.¹⁴ Current European guidelines recommend using scoring systems such as European System for Cardiac Operative Risk Evaluation II (EUROSCORE II) and Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) models to evaluate the patient's preoperative risk and determine the choice of treatment for aortic stenosis.¹³ The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy-Transcatheter Aortic Valve Replacement (STS/ACC TVT-TAVR) score specifically focuses on mortality predictions in patients after TAVI.¹⁵ Unfortunately, none of these risk prediction models include clinical or laboratory markers of liver dysfunction. In a previous study by Wendt et al,¹⁶ patients with advanced liver disease did not show increased mortality following TAVI. A recent meta-analysis assessing a total of 22 studies revealed that preoperative abnormal liver function is associated with adverse outcomes in terms of short-term and long-term mortality after TAVI.¹⁷

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We read the newly published paper in the latest issue of the Archives of Turkish Society of Cardiology with great interest.¹⁸ The authors retrospectively evaluated the postoperative outcomes of 77 patients with severe symptomatic aortic stenosis and reduced ejection fraction. Liver function was assessed using the albumin-bilirubin (ALBI) score. Patients were divided into two groups based on ALBI scores: high ALBI (>-2.25) and low ALBI (<-2.25). The primary outcome of the study, defined as 30-day and 1-year mortality and HF hospitalization, was found to be significantly higher in patients with a high ALBI score. Although it was a retrospective and single-center study, it brings added value to the literature as it specifically evaluates cardio-hepatic interactions in a specific population. Moreover, the prognostic utility of the ALBI score in TAVI patients with low ejection fraction has been tested for the first time. Another retrospective analysis of 439 patients by Yao et al¹⁹ reported that the Model for End-Stage Liver Disease-11 excluding INR (MELD-XI) score, which combines renal and hepatic dysfunction in the risk model [including serum creatinine and bilirubin but excluding International Normalized Ratio (INR)], predicted 2-year mortality in patients after the TAVI procedure.

Apart from patients with aortic stenosis, liver function also plays an important role in several clinical situations. Patients with long-standing severe mitral regurgitation share the same ultimate outcome in terms of cardio-hepatic interactions. Sawalha et al²⁰ reported a poor outcome following the MitraClip procedure in patients with preoperative advanced liver dysfunction. In Heart Failure with Reduced Ejection Fraction (HFrEF) patients receiving cardiac resynchronization therapy, impaired end-organ functions (assessed by the MELD-XI score) were found to predict worse postoperative outcomes in a previous study.²¹ Similar heart-liver interactions were observed in patients with advanced HF receiving a left ventricular assist device (LVAD). A high preoperative MELD-XI score and low albumin levels were associated with decreased survival in patients after LVAD implantation.²²

In conclusion, the prevention or reversal of target organ impairment represents a main therapeutic focus in HF management. The liver, which is an underrated end-organ in advanced cardiac conditions, requires comprehensive evaluation in clinical practice. The integration of liver function tests into conventional risk models provides additive prognostic information for candidates of cardiovascular interventions.

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