Cardiohepatic Interactions

Implications for Management in Advanced Heart Failure

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KEYWORDS

• Chronic heart failure • Advanced heart failure • Hepatic fibrosis • Cirrhosis • Hepatitis C • Liver disease • Heart transplantation • Mechanical circulatory support

KEY POINTS

- Liver disease is common in patients with advanced heart failure and can significantly impact morbidity and mortality.
- It is difficult to diagnose severe liver disease, including hepatic fibrosis and cirrhosis, in advanced heart failure based on history, physical examination, and imaging studies.
- Liver biopsy is the gold standard for diagnosis of hepatic fibrosis and cirrhosis in advanced heart failure.
- Liver disease has important implications for advanced heart failure therapies and should be considered in selecting patients for mechanical circulatory support and heart transplant.
- Hepatitis C is common, and strategies for treatment of hepatitis C in patients with advanced heart failure continue to evolve with the recent development of direct-acting antiviral agents.

Liver disease is a common sequela of advanced heart failure (HF; American College of Cardiology/American Heart Association stage D), ranging from mild reversible liver injury to hepatic fibrosis and, in its most severe form, cardiac cirrhosis.[1] Although it can be challenging to identify in patients with HF, the presence of liver disease has important implications for prognosis, medication management, mechanical circulatory support (MCS), and heart transplantation (HT).

In this review, a framework is provided for approaching liver disease in the advanced HF population. After a brief review of hepatic anatomy and the pathophysiology of liver disease in HF, the authors summarize the current understanding of chronic liver disease in HF and examine the implications of chronic liver disease for MCS and HT. Given the increasing prevalence of hepatitis C virus (HCV) and the recent development and approval of a new class of HCV therapeutics, specific considerations are included for the management of HCV in the advanced HF population.

HEPATIC ANATOMY AND PATHOPHYSIOLOGY

The liver receives 25% to 30% of the total cardiac output from 2 vascular sources, the hepatic artery and the portal vein. The portal vein carries nutrient-rich blood from the mesenteric and splenic veins and provides 70% of the hepatic blood flow. The hepatic artery, a branch of the celiac trunk, supplies oxygenated blood from the heart and lungs

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and accounts for the remainder of hepatic blood flow.[2] On entering the liver, blood from the portal vein and hepatic artery drains into the endothelium-lined hepatic sinusoids. Plasma is filtered through the sinusoidal endothelium to perfuse the hepatocytes, which are rich with metabolic activity. Blood then returns to the inferior vena cava (IVC) through the hepatic veins.[2]

There are 2 models used to describe the functional unit of the liver: the classic lobule (**Fig. 1**A) and the liver acinus (**Fig. 1**B).[2] The classic lobule is a hexagonal structure organized around a central venule, a branch of the hepatic vein. The portal tracts, comprising the hepatic artery, portal vein, bile ducts, lymphatics, and nerves, are located at the corners of the hexagon. In contrast, the liver acinus describes the liver parenchyma in zones. Hepatocytes in zone 1 are closest to the portal triad; thus, they receive the richest supply of oxygen and nutrients but are also more likely to be damaged by drugs and toxins because they are exposed to the highest concentrations. The hepatocytes in zone 3 are near the central vein and have a relatively poor supply of oxygen. These hepatocytes are more susceptible to damage from hypoxia and venous congestion.[2]

Liver chemistries, or liver function tests (LFTs), provide important information for diagnosis and monitoring. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are present in hepatocytes, and elevation of these transaminases signifies hepatocellular injury or necrosis. Elevations in alkaline phosphatase (AP), γ-glutamyl transferase, and bilirubin are reflective of obstructive or cholestatic disease. Low albumin and prolonged prothrombin time (PT) indicate impaired hepatic synthetic function.[2]

The liver's dual blood supply provides substantial physiologic reserve. When portal blood flow is reduced, the liver compensates by vasodilating hepatic arterioles to maintain blood flow, a response that is mediated by adenosine released from injured hepatocytes.[3] The liver is able to increase oxygen extraction to allow up to 95% of oxygen to be extracted in a single pass.[4] Given this reserve, hypotension alone is typically not enough to precipitate ischemic hepatitis.[3]

Ischemic hepatitis is characterized biochemically by a rapid increase in AST and ALT up to 10 to 20 times the upper limit of normal within 24 hours of a hemodynamic insult, and histopathologically by severe hepatocellular injury causing centrilobular (zone 3) necrosis. Although more commonly associated with acute cardiogenic shock, ischemic hepatitis can develop in patients with chronic HF.[4,5] The degree and duration of hemodynamic derangement needed to precipitate acute ischemic hepatitis in HF differ depending on the chronicity of HF and the extent of compensation.[6] For example, in a patient with chronic HF who has been exposed to chronic passive congestion of the liver, a small decrease in blood pressure or cardiac output may be enough to result in ischemic hepatitis. In contrast, in patients with cardiogenic shock due to acute HF or compensated chronic HF without chronic passive congestion, a more profound degree of hypoperfusion is required to cause ischemic hepatitis.[3,6]

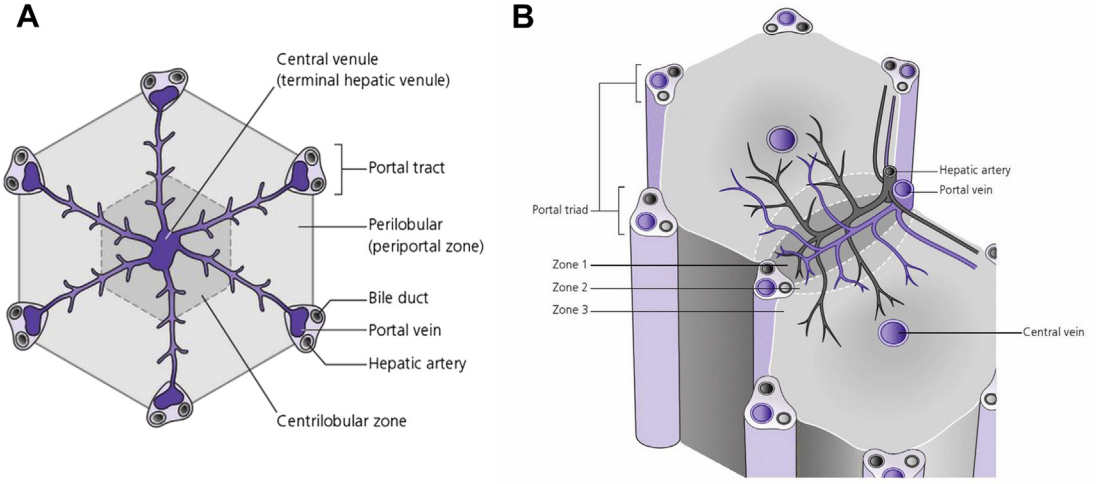

Fig. 1. The functional unit of the liver. (*A*) The classic lobule where the portal tracts form the corners of a hexagon centered around the central vein. (*B*) The liver acinus where hepatocytes in zone 1 are closest to the portal triad and hepatocytes on zone 3 are closest to the central vein. (*From* Nash K. Hepatology: clinical cases uncovered. Hoboken (NJ): Wiley-Blackwell; 2011; with permission.)