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STRUCTURAL AND FUNCTIONAL STATE OF THE LIVER IN PATIENTS WITH CHRONIC HEART FAILURE

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Abstract
In clinical practice, combined cardiac and liver dysfunction coexist in the context of heart and liver disease due to complex cardiohepatic interactions. In recent years, the need to identify the interaction between the heart and liver in order to provide effective treatment for patients with heart or liver disease to ensure an improvement in overall prognosis and therapy has become increasingly urgent.

Keywords Heart failure; congestive hepatosis; cardiac cirrhosis.

INTRODUCTION

Heart and liver diseases are considered a major burden on the healthcare system and a leading problem. cause a deterioration in the quality of life and a reduction in life expectancy. In this review, we discuss the complex cardiohepatic interactions in major heart and liver diseases. This review aims to highlight how acute and chronic heart failure can lead to cardiogenic disorders. In each section, we briefly discuss the likely mechanisms underlying this association, clinical manifestations, and diagnostic approaches.

Congestive hepopathy.

The interaction between the heart and liver has been known for a long time. However, in recent years, these cardiohepatic interactions have gained greater interest, prompting the study of these interactions and a rethinking of their pathophysiology. The relationship between the liver and the heart is divided into three groups depending on the role of each organ, which is the primary source of damage. [1,2]: - liver diseases resulting from heart disease; - heart disease resulting from liver disease (for example, cirrhotic cardiomyopathy); -systemic diseases affecting both the heart and liver (for example, systemic amyloidosis). The first group has generally been called “cardiac hepatopathy,” although there is still no consensus on terminology [3,4]. The two main forms of cardiac hepatopathy are acute cardiogenic liver injury (also called hypoxic hepatosis) and congestive hepatopathy (CH). Both conditions often coexist and enhance each other's harmful effects on the liver [3–5]. Any cause of right-sided heart failure due to diseases such as constrictive pericarditis, mitral stenosis, severe tricuspid regurgitation, congenital heart disease or end-stage cardiomyopathy can lead to congestive hepatopathy [7,8]. In summary, the incidence of liver cirrhosis caused by noncongenital heart

failure is decreasing, and ischemic cardiomyopathy is now the leading cause of right heart failure, surpassing rheumatic heart disease and post-Fontan heart failure, which creates non-pulsatile high-pressure flow in the inferior vena cava and this condition leads to chronic hepatic venous congestion. [1,2,4,9].

Pathophysiology. The liver is a highly vascular organ that receives up to 25% of total cardiac output. The hepatic artery delivers well-oxygenated blood and contains approximately 25% of the total hepatic blood flow, while the remaining 75% is blood coming from the portal vein. The liver has robust vascular mechanisms that protect the liver from ischemic injury [1]. The hepatic artery buffer response is a local regulatory mechanism leading to an increase in the concentration of the vasodilator adenosine with a decrease in portal blood flow. [12]. In contrast, the portal vein does not have the ability to self-regulate its own blood flow and depends on cardiac output and the pressure gradient in the portal and hepatic veins [5,8]. The high permeability of the liver sinusoids allows oxygen extraction up to 90%, and during hypoxia, oxygen consumption by the liver decreases, despite normal hepatic blood flow [5,13,14]. This unique resistance to ischemic injury contrasts with the paucity of protective mechanisms. The resulting liver congestion leads to liver damage through several pathogenic mechanisms: Stress promotes fibrogenesis and sinusoidal ischemia by activating hepatic stellate cells and reducing the production of nitric oxide by endothelial cells [10,15]; Reduced portal and arterial flow to the liver aggravates liver ischemia. The former is associated with a decrease in the hepatic venous pressure gradient due to increased central venous pressure on the sinusoidal network, although the latter may also be impaired in patients with left-sided HF [8,10]; Reduced diffusion of oxygen and nutrients due to the accumulation of exudate in the space of Disse also promotes fibrogenesis [8]; Sinusoidal congestion in turn promotes sinusoidal thrombosis, which leads to liver fibrosis by causing parenchymal necrosis and activating hepatic stellate cells through protease-activated receptors [16,17]. Wanless et al demonstrated sinusoidal thrombi confined to areas of fibrosis, suggesting that intrahepatic thrombosis is involved in the progression of liver fibrosis [18]. This is now defined as an area with focal loss of adjacent hepatocytes and adjacent microvascular structures. This microvascular injury causes venous obstruction to spread to larger vessels, resulting in persistence of venous obstruction and worsening congestion [19]. Clinical picture and diagnosis. Chronic hepatosis can be asymptomatic for a long time, and in these patients this is the only sign that allows one to suspect its presence if there are changes in the tests[8]. Hepatic symptoms are usually masked by disorders associated with right-sided HF [6]. Stretching of the liver capsule due to liver congestion is the cause of some symptoms, such as heaviness or dull pain in the right upper quadrant, nausea. Other symptoms include anorexia, general weakness, absence of ascites or edema of the lower extremities [1]. Classic complications of liver cirrhosis, such as hepatic encephalopathy or hepatocarcinoma, occur in late stages of cardiac cirrhosis and may eventually become as clinically important as cardiac disease and further complicate the course [10]. When addressing a patient with new-onset ascites, it is difficult to differentiate the cardiac etiology of ascites since in both cases the serum-ascitic albumin gradient is ≥1.1 g/dL [25]. However, with cardiac ascites, the protein level is higher than >2.5 g/dl, which is due to the preservation of the synthetic function of the liver and the lack of capillarization of the sinusoidal structure of the liver [1,8,26]. In cirrhosis, decreased endothelial cell permeability due to loss of fenestrae and development of the basement membrane prevents the passage of proteins into the space of Disse and from there into the peritoneal fluid, thus explaining lower protein concentrations [27]. Other less reliable indicators of cardiac ascites are increased LDH levels and red blood cell counts due to red blood cell leakage [26]. Recently, in a study, investigators recommended measurement of serum B-type natriuretic peptide (BNP) or its inactive precursor (N-terminal proBNP) in serum at the initial diagnosis of ascites as an adjuvant method in idiopathic cases. In summary, Shire et al

reported that serum NT-proBNP levels in unexplained ascitenes have high sensitivity and specificity in predicting heart failure [28]. Also in another study, Farias et al also found that serum BNP levels and protein concentrations in ascitic fluid are elevated in cardiac ascites. A serum BNP cutoff value of >364 pg/mL has been shown to have a sensitivity of 98%, a specificity of 99%, and a diagnostic accuracy of 99% in the diagnosis of cardiac ascites. Conversely, a threshold serum BNP level of <182 pg/mL excludes the cause of HF-related ascites [25]. Differentiating cardiac cirrhotic ascites from cardiac ascites without cirrhosis is of particular importance and may require invasive diagnostic methods, such as liver biopsy and hepatic venous pressure gradient (HVPG) testing. The low prevalence of gastroesophageal varices in this population may be explained by the fact that the varices are collateral vessels from the high pressure portal system to the low venous pressure system, and in cardiac hepatosis without cirrhosis there is no pressure gradient because the pressure remains high throughout venous return pathways to the right atrium [9].

Biochemical blood test results may remain within normal limits. Mild hyperbilirubinemia may occur, with a predominantly increased unconjugated fraction. Elevations of other indicators of cholestasis, such as serum alkaline phosphatase and gamma-glutamyltransferase, are often detected [1]. The degree of cholestasis is associated with the severity of increased venous pressure in the right atrium and tricuspid regurgitation [11,29]. These data suggest that increased right atrial pressure may contribute more to elevated liver enzymes than to decreased cardiac output [6]. It is believed that the mechanism of cholestasis in this case is due to compression of the bile ducts by overloaded sinusoids [30]. Other laboratory findings such as elevated serum aminotransferases two to three times the upper limit of normal and mild hypoalbuminemia may also be detected in cardiac hepatosis. These changes can also be secondary, and occur with malnutrition or protein-losing enteropathy [8]. As liver disease progresses, liver function tests will increase. Heart failure can also lead to acute cardiogenic liver injury (ACLI) in a variety of conditions. In this case, there is a significant and rapid increase of 10–20 times in the level of aminotransferases and lactate dehydrogenase (LDH), usually from 1 to 3 days after hemodynamic deterioration. It is important to note that hemodynamic deterioration is not a constant sign, since shock is observed only in half of the cases. This is likely due to the fact that short periods of hypotension (i.e., 15–20 min) are often unrecognized enough to trigger acute liver injury [22]. Thus, the diagnosis of acute liver injury cannot be rejected due to the absence of shock, and in case of uncertainty, cardiac evaluation is warranted [4,5]. It is equally important to note that after normalization of hemodynamics, these laboratory parameters usually normalize within 7–10 days [1,31]. Progressive increase in bilirubin. usually observed but rarely severe [1,5,20]. However, the mean bilirubin value in these studies was below 103 μmol/L [21,32]. Higher values may indicate progression of acute liver disease [4]. Thus, the liver is an important and complex organ, and its high metabolic activity is associated with many molecular and hemodynamic changes in patients. Liver dysfunction is frequently observed in patients with HF and is closely correlated with hemodynamic parameters. The liver has a double blood circulation, which is regulated by the activity of smooth muscle microcirculation. Features of liver damage depend on hepatic congestion and decreased perfusion. The main targets of congestive hepatopathy are hepatocytes and bile duct epithelium. Most patients experience congestion, pericentral necrosis and fibrosis, and dilated sinusoids. Cardiac cirrhosis represents a continuum of liver disease resulting from right-sided HF. Ischemic hepatitis is massive hepatocellular necrosis, which may be accompanied by cardiogenic shock or hemodynamic collapse. Although early detection of clinical signs and symptoms of cardiac and liver damage has led to important benefits in terms of reduced morbidity and mortality.

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