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Review Article

Liver disease and heart failure: Back and forth

Michele Correale[a], Nicola Tarantino[b], Rossella Petrucci[b], Lucia Tricarico[b], Irma Laonigro[a], Matteo Di Biase[b], Natale Daniele Brunetti[b,*]

[a] Ospedali Riuniti University Hospital, Foggia, Italy
[b] Department of Medical & Surgical Sciences, University of Foggia, Italy

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ABSTRACT

In their clinical practice, physicians can face heart diseases (chronic or acute heart failure) affecting the liver and liver diseases affecting the heart. Systemic diseases can also affect both heart and liver. Therefore, it is crucial in clinical practice to identify complex interactions between heart and liver, in order to provide the best treatment for both.

In this review, we sought to summarize principal evidence explaining the mechanisms and supporting the existence of this complicate cross-talk between heart and liver. Hepatic involvement after heart failure, its pathophysiology, clinical presentation (congestive and ischemic hepatopathy), laboratory and echocardiographic prognostic markers are discussed; likewise, hepatic diseases influencing cardiac function (cirrhotic cardiomyopathy). Several clinical conditions (congenital, metabolic and infectious causes) possibly affecting simultaneously liver and heart have been also discussed.

Cardiovascular drug therapy may present important side effects on the liver and hepato-biliary drug therapy on heart and vessels; post-transplantation immunosuppressive drugs may show reciprocal cardio-hepatotoxicity.

A heart-liver axis is drafted by inflammatory reactants from the heart and the liver, and liver acts a source of energy substrates for the heart.

1. Introduction

Several conditions (infections, inflammatory and systemic diseases, chronic alcoholism [1]) may affect both the heart and the liver [2]. Common conditions, such as the non-alcoholic fatty liver disease, may increase the risk of cardiac dysfunction [3]. Conversely, acute and chronic heart failure (HF) may lead to acute ischemic hepatitis or chronic congestive hepatopathy; so, it is crucial for cardiologists, internists, hepatologists, and primary physicians to acknowledge such relevant complications intertwining cardiovascular system and the liver.

The evaluation of both cardiac and hepatic function is very important in patients with advanced HF and hepatic injury; laboratory anomalies of hepatic function may predict the outcome of patients with advanced HF [4]. White adipose tissue and liver have been identified as the physiological targets of some cardiac signaling [5]. Recently, basic experiments showed that the paradoxical production of triglycerides in fasting rats with congestive HF is associated with a proinflammatory response in the liver [6]; in an animal model of end-stage HF some authors interpreted abnormal hepatic metabolism as a maladaptive response during the progression of chronic HF. Magida et al. demonstrated that a primary genetic defect in the heart might results in aberrant hepatic lipid metabolism [7], which consequently exacerbates hypertrophic cardiomyopathy: that supports the hypothesis that cross-talk occurs between heart and liver, and that, in particular situations, this may occur as malfunction.

In this review, we therefore sought to highlight principal evidence explaining the mechanisms and supporting the existence of this complicate cross-talk between heart and liver.

2. Methods

An online search on PubMed was performed until January 2017 by using the following main keywords alone or in logic combination: acute heart failure; chronic heart failure; acute liver failure; chronic hepatitis; alcohol; cardiomyopathy; cardiotoxicity; cirrhosis; hepatotoxicity. Only articles in English were selected for the review, which focused on the most consistent and relevant trials, original papers, reviews and case reports, preferentially involving humans (Fig. 1).

* Corresponding author at: Viale Pinto 1, 71122 Foggia, Italy.
E-mail addresses: opsfco@tin.it (M. Correale), nicolatarantinomd@gmail.com (N. Tarantino), rossella.petrucci@icloud.com (R. Petrucci), lucia.tricarico@gmail.com (L. Tricarico), irmalao@gmail.com (I. Laonigro), matteo.dibiase@unifg.it (M. Di Biase), natale.brunetti@unifg.it (N.D. Brunetti).

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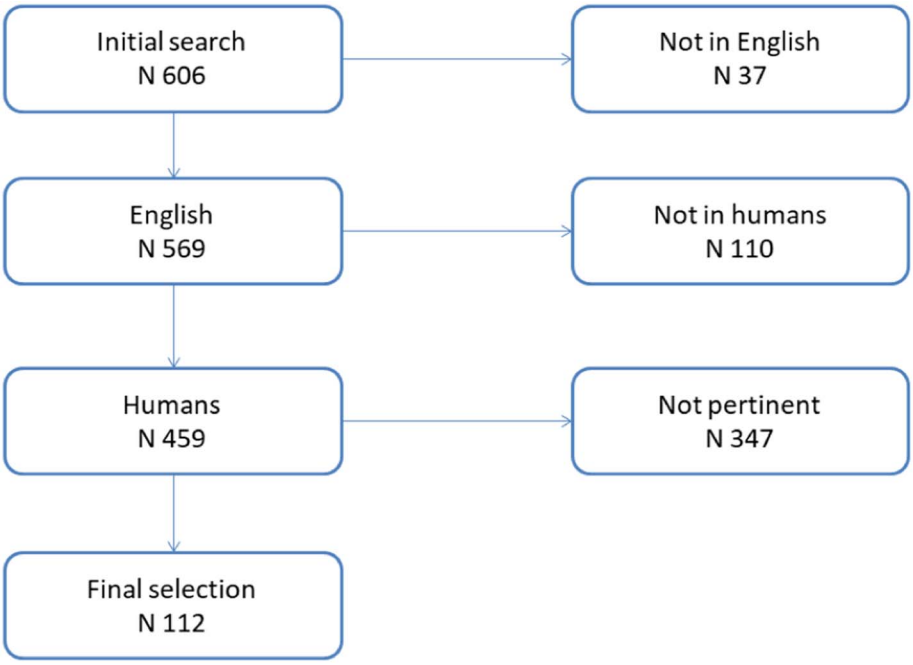

Fig. 1. Studies' selection.

2.1. Hepatic involvement after heart failure: pathophysiology, clinical, laboratory and echocardiographic prognostic markers

Liver dysfunction is frequent in HF; almost every condition that affects the function of the right ventricle can affect the liver by "backward" congestion. Every reduction of right ventricular flow may therefore lead to liver congestion because of reduced blood outflow: indeed, the liver can resist low cardiac flow, thanks to its double blood supply [8]. The liver is vascularized from two sources; the first is the hepatic artery which delivers oxygenated blood from the general circulation, the second is the hepatic portal vein delivering deoxygenated blood from the small intestine and containing nutrients.

Constrictive pericarditis, severe pulmonary hypertension, mitral stenosis, tricuspid regurgitation, cor pulmonale, and ischemic cardiomyopathy may lead to hepatic disorders too (Table 1). Tricuspid regurgitation, however, is usually a sign of pulmonary hypertension and not a primary condition. The underlying mechanism is passive congestion due to elevated right ventricular pressure. The increase in venous pressure caused by right ventricular dysfunction may lead to hepatocytes atrophy and cause perisinusoidal edema, which eventually impairs oxygen and nutrients diffusion [4]. Centrolobular liver necrosis can be found in case of acute HF, when both congestion and low blood supply occur [9]. Old studies on liver physiology showed that inferior vena cava blood pressure is related to liver metabolism in terms of arterial ketone body ratio, a parameter reflecting the hepatic mitochondrial redox state and utilized as an index of hepatic energy status. From the simple regression line obtained between inferior vena cava blood pressure and arterial ketone body ratio, it was determined that an upper safety limit of inferior vena cava blood pressure may lie at about 27 cm H_2O (20.5 mm Hg), and that an inferior vena cava blood pressure of 35 cm H_2O (26.6 mm Hg) seems to be the critical level for maintaining liver viability [10].

There are no clear clinical parameters that can predict liver involvement in case of HF. However, some echocardiographic parameters may correlate to abnormal liver tests. Styczynski et al. showed that right ventricular end-diastolic diameter, right atrial area, tricuspid regurgitation, TAPSE, portal vein pulsatility index and left ventricular ejection fraction were significant predictors of total bilirubin elevation [11]. In a multivariate logistic regression analysis, only portal vein pulsatility index remained a statistically significant predictor of total bilirubin level. The same authors found that elevation of transaminases was associated with left ventricular end-diastolic diameter indexed to body surface area and right ventricular end-diastolic diameter. No correlation was found with other echocardiographic markers, with cardiac index and left ventricular ejection fraction.

In addition to the evaluation of right ventricular systolic function, the assessment of right ventricular diastolic dysfunction is even more important for some patients to prove the presence of congestive hepatopathy [12].

Table 1
Heart diseases affecting the liver.

Constrictive pericarditis
Cor pulmonale
Fontan procedure
Ischemic cardiomyopathy
Mitral stenosis
Non-ischemic dilated cardiomyopathy
Pulmonary embolism
Restrictive cardiomyopathy
Severe pulmonary hypertension
Tricuspid regurgitation

2.2. Liver function tests in heart failure

Cardiac hepatopathy has been generally used to describe any liver damage caused by cardiac disorders in the absence of other possible causes of liver damage; it is caused by passive venous congestion of the liver that can be a consequence of chronic HF, constrictive pericarditis, tricuspid regurgitation.

Primary laboratory findings of cardiac hepatopathy are elevated serum cholestasis markers as: bilirubin, alkaline phosphatase, γ-glutamyl-transpeptidase and transaminases levels. According to a study from Vasconcelos et al. based on a population of 337 patients divided into 4 NYHA classes, alanine transaminase (ALT) and aspartate transaminase (AST) values are out of range only in NYHA class IV, γ-glutamyl-transpeptidase value is increased in classes II, III, IV, while alkaline phosphatase values are out of range in all classes [13].

Liver injury in HF is characterized more frequently by a cholestatic damage; elevation of alkaline phosphatase, gamma-