Congestive Hepatopathy

Subjects: Others

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Liver disease resulting from heart failure (HF) has generally been referred as “cardiac hepatopathy”. One of its main forms is congestive hepatopathy (CH), which results from passive venous congestion in the setting of chronic right-sided HF. The current spectrum of CH differs from earlier reports with HF, due to ischemic cardiomyopathy and congenital heart disease having surpassed rheumatic valvular disease. The chronic passive congestion leads to sinusoidal hypertension, centrilobular fibrosis, and ultimately, cirrhosis (“cardiac cirrhosis”) and hepatocellular carcinoma after several decades of ongoing injury. Contrary to primary liver diseases, in CH, inflammation seems to play no role in the progression of liver fibrosis, bridging fibrosis occurs between central veins to produce a “reversed lobulation” pattern and the performance of non-invasive diagnostic tests of liver fibrosis is poor. Although the clinical picture and prognosis is usually dominated by the underlying heart condition, the improved long-term survival of cardiac patients due to advances in medical and surgical treatments are responsible for the increased number of liver complications in this setting. Eventually, liver disease could become as clinically relevant as cardiac disease and further complicate its management.

Congestive Hepatopathy,cardiac hepatopathy

1. Introduction

The interactions between the heart and the liver have been known for a long time. In recent years, however, these cardio-hepatic interactions have gained greater interest, which has led to a better understanding of their pathophysiology. They are usually classified into three groups, according to the role of each organ as culprit or victim of the other [1][2]: (1) liver disease resulting from heart disease; (2) heart disease resulting from liver disease (e.g., cirrhotic cardiomyopathy); (3) systemic diseases that affect both the heart and liver (e.g., systemic amyloidosis). The former group has generally been referred as “cardiac hepatopathy”, although there is still no consensus on terminology [3][4]. The two main forms of cardiac hepatopathy are acute cardiogenic liver injury (ACLI) (also referred as hypoxic hepatitis) and congestive hepatopathy (CH). Both conditions often coexist and potentiate the deleterious effects of each other on the liver [3][4][5].

Epidemiology

Any cause of right-sided HF (e.g., constrictive pericarditis, mitral stenosis, severe tricuspid regurgitation, congenital heart disease, or end-stage cardiomyopathies) can lead to CH [6][7]. The widespread use of heart transplantation

(HT) and major advances in medical and surgical treatments have significantly changed the profile of patients harboring CH. Thus, compared to earlier reports, cardiac cirrhosis due to non-congenital HF is declining, ischemic cardiomyopathy is now the leading cause of HF having surpassed rheumatic HF, and CH following Fontan surgery is on the rise [1][2][4][8].

The latter surgery is used to treat several complex congenital heart diseases with a functional single ventricle (e.g., tricuspid or mitral atresia and hypoplastic left or right heart syndrome). It is usually performed in children 2 to 5 years in whom a superior cavopulmonary connection has been previously performed through the Glenn procedure. The Fontan technique then creates a total cavopulmonary connection by implanting a surgical shunt to divert blood from the inferior and superior vena cava to the pulmonary arteries, which passively carry the blood to the single ventricular chamber. This bypass leads to chronic hepatic venous congestion secondary to high-pressure nonpulsatile flow in the inferior vena cava. The lack of a subpulmonary ventricle also leads to diminished cardiac preload for the systemic ventricle, resulting in chronically low cardiac output. These hemodynamic changes together with the characteristic mild low arterial blood oxygen saturation are responsible for the damage that can affect virtually all organs. As far as the liver is concerned, the functional and structural alterations that systematically develop after this surgery are referred as Fontan-associated liver disease. Its natural history is poorly understood, and we are presently unable to predict and correctly identify the patients that will develop clinically significant advanced liver disease [9][10][11].

In non-congenital HF, there are no reliable data on the prevalence of CH, with even fewer solid data concerning the stage of liver disease. This is mainly due to the limited validated techniques available to diagnose and, specially, stage the disease [12]. Studies using liver blood tests have described prevalence figures of CH ranging from 15 to 80%, depending on the severity of HF [13][14][15][16][17][18][19]. However, liver blood tests neither accurately diagnose CH nor reflect the stage of liver disease [12].

2. Prognosis and Treatment

The underlying cardiac disease generally determines prognosis in CH. Liver enzymes (i.e., bilirubin, alkaline phosphatase, gamma-glutamyl transferase, and albumin) and scores such as the MELD and MELD-XI have been associated with prognosis in HF patients [15][18][20][21][22][23]. Based on these findings, both the American College of Cardiology and European Society of Cardiology Heart Failure Guidelines recommend the inclusion of liver function tests in the diagnostic workup of all patients presenting with HF [24][25]. However, it must be pointed out that they predict cardiac or overall mortality, not liver-related mortality. Therefore, they seem to act as indirect markers of the severity of cardiac disease rather than reflecting the effect of liver disease on outcomes. Indeed, the effect of cardiac cirrhosis on overall prognosis has not been clearly established [4]. As far as the prognosis of ACLI is concerned, it is usually poor with an overall hospital mortality of 51% [26] and 1-year survival rate of approximately 25% [5]. The cause of death is usually the underlying condition, as it is an uncommon cause of acute liver failure (only 4.4% of the cases in a study from the Acute Liver Failure Study Group) [27].

Management of the underlying cardiac disease is the mainstay of treatment. There is no specific therapy of CH [7]. Concerns about modification of drug dosage have been raised, although there are no solid rules in this regard. This is partially explained by the lack of correlation of available diagnostic tools with the hepatic function [3]. Theoretically more relevant are the detrimental effects that some of the medical therapies used to treat HF may have on the physiopathology of cirrhosis. For instance, vasodilators such as angiotensin-converting-enzyme inhibitors are contraindicated in decompensated cirrhosis and doses of diuretics in HF are often higher than in cirrhosis and may precipitate hepatorenal syndrome [1]. Again, no solid recommendations are available and treatment modifications should be patient specific.

Finally, in patients with ACLI the management of the underlying diseases remains the only established treatment for ACLI. Although data are limited, some experts recommend using N-acetylcysteine, avoiding excessive vascular filling to minimize passive congestion of the liver, and favoring the use of dobutamine in patients with low cardiac index given its inotropic and vasodilating effects [1][5][8][28].

References

1. Ford, R.M.; Book, W.; Spivey, J.R. Liver disease related to the heart. Transpl. Rev. 2015, 29, 33–37.
2. Fouad, Y.M.; Yehia, R. Hepato-cardiac disorders. World J. Hepatol. 2014, 6, 41–54.
3. Cagli, K.; Basar, F.N.; Tok, D.; Turak, O.; Basar, O. How to interpret liver function tests in heart failure patients? Turk. J. Gastroenterol. Off. J. Turk. Soc. Gastroenterol. 2015, 26, 197–203.
4. Moller, S.; Bernardi, M. Interactions of the heart and the liver. Eur. Heart J. 2013, 34, 2804–2811.
5. Henrion, J. Hypoxic hepatitis. Liver Int. 2012, 32, 1039–1052.
6. Kavoliuniene, A.; Vaitiekiene, A.; Cesnaite, G. Congestive hepatopathy and hypoxic hepatitis in heart failure: A cardiologist’s point of view. Int. J. Cardiol. 2013, 166, 554–558.
7. Hilscher, M.; Sanchez, W. Congestive hepatopathy. Clin. Liver Dis. 2016, 8, 68–71.
8. Myers, R.P.; Cerini, R.; Sayegh, R.; Moreau, R.; Degott, C.; Lebrec, D.; Lee, S.S. Cardiac hepatopathy: Clinical, hemodynamic, and histologic characteristics and correlations. Hepatology 2003, 37, 393–400.
9. Téllez, L.; de Santiago, E.R.; Albillos, A. Fontan-associated Liver Disease. Rev. Esp. Cardiol. 2018, 71, 192–202.
10. Emamaullee, J.; Zaidi, A.N.; Schiano, T.; Kahn, J.; Valentino, P.L.; Hofer, R.E.; Taner, T.; Wald, J.W.; Olthoff, K.M.; Bucuvalas, J.; et al. Fontan-Associated Liver Disease: Screening, Management, and Transplant Considerations. Circulation 2020, 142, 591–604.

11. Gordon-Walker, T.T.; Bove, K.; Veldtman, G. Fontan-associated liver disease: A review. J. Cardiol. 2019, 74, 223–232.
12. Lemmer, A.; Van Wagner, L.B.; Ganger, D. Assessment of Advanced Liver Fibrosis and the Risk for Hepatic Decompensation in Patients with Congestive Hepatopathy. Hepatology 2018, 68, 1633–1641.
13. Xanthopoulos, A.; Starling, R.C.; Kitai, T.; Triposkiadis, F. Heart Failure and Liver Disease: Cardiohepatic Interactions. JACC Heart Fail. 2019, 7, 87–97.
14. Kubo, S.H.; Walter, B.A.; John, D.H.; Clark, M.; Cody, R.J. Liver function abnormalities in chronic heart failure. Influence of systemic hemodynamics. Arch. Intern. Med. 1987, 147, 1227–1230.
15. Allen, L.A.; Felker, G.M.; Pocock, S.; McMurray, J.J.; Pfeffer, M.A.; Swedberg, K.; Wang, D.; Yusuf, S.; Michelson, E.L.; Granger, C.B. Liver function abnormalities and outcome in patients with chronic heart failure: Data from the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. Eur. J. Heart Fail. 2009, 11, 170–177.
16. Gelow, J.M.; Desai, A.S.; Hochberg, C.P.; Glickman, J.N.; Givertz, M.M.; Fang, J.C. Clinical Predictors of Hepatic Fibrosis in Chronic Advanced Heart Failure. Circ. Heart Fail. 2010, 3, 59–64.
17. Van Deursen, V.M.; Damman, K.; Hillege, H.L.; van Beek, A.P.; van Veldhuisen, D.J.; Voors, A.A. Abnormal liver function in relation to hemodynamic profile in heart failure patients. J. Card. Fail. 2010, 16, 84–90.
18. Poelzl, G.; Ess, M.; Mussner-Seeber, C.; Pachinger, O.; Frick, M.; Ulmer, H. Liver dysfunction in chronic heart failure: Prevalence, characteristics and prognostic significance. Eur. J. Clin. Investig. 2012, 42, 153–163.
19. Megalla, S.; Holtzman, D.; Aronow, W.S.; Nazari, R.; Korenfeld, S.; Schwarcz, A.; Goldberg, Y.; Spevack, D.M. Predictors of cardiac hepatopathy in patients with right heart failure. Med. Sci. Monit. 2011, 17, Cr537–Cr541.
20. Ruttmann, E.; Brant, L.J.; Concin, H.; Diem, G.; Rapp, K.; Ulmer, H. Gamma-glutamyltransferase as a risk factor for cardiovascular disease mortality: An epidemiological investigation in a cohort of 163, 944 Austrian adults. Circulation 2005, 112, 2130–2137.
21. Assenza, G.E.; Graham, D.A.; Landzberg, M.J.; Valente, A.M.; Singh, M.N.; Bashir, A.; Fernandes, S.; Mortele, K.J.; Ukomadu, C.; Volpe, M.; et al. MELD-XI score and cardiac mortality or transplantation in patients after Fontan surgery. Heart 2013, 99, 491–496.
22. Kim, M.S.; Kato, T.S.; Farr, M.; Wu, C.; Givens, R.C.; Collado, E.; Mancini, D.M.; Schulze, P.C. Hepatic dysfunction in ambulatory patients with heart failure: Application of the MELD scoring system for outcome prediction. J. Am. Coll. Cardiol. 2013, 61, 2253–2261.

23. Deo, S.V.; Al-Kindi, S.G.; Altarabsheh, S.E.; Hang, D.; Kumar, S.; Ginwalla, M.B.; ElAmm, C.A.; Sareyyupoglu, B.; Medalion, B.; Oliveira, G.H.; et al. Model for end-stage liver disease excluding international normalized ratio (MELD-XI) score predicts heart transplant outcomes: Evidence from the registry of the United Network for Organ Sharing. J. Heart Lung Transpl. 2016, 35, 222–227.
24. Ponikowski, P.; Voors, A.A.; Anker, S.D.; Bueno, H.; Cleland, J.G.; Coats, A.J.; Falk, V.; Gonzalez-Juanatey, J.R.; Harjola, V.P.; Jankowska, E.A.; et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur. J. Heart Fail. 2016, 18, 891–975.
25. Yancy, C.W.; Jessup, M.; Bozkurt, B.; Butler, J.; Casey, D.E., Jr.; Drazner, M.H.; Fonarow, G.C.; Geraci, S.A.; Horwich, T.; Januzzi, J.L.; et al. 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation 2013, 128, e240–e327.
26. Tapper, E.B.; Sengupta, N.; Bonder, A. The Incidence and Outcomes of Ischemic Hepatitis: A Systematic Review with Meta-analysis. Am. J. Med. 2015, 128, 1314–1321.
27. Taylor, R.M.; Tujios, S.; Jinjuvadia, K.; Davern, T.; Shaikh, O.S.; Han, S.; Chung, R.T.; Lee, W.M.; Fontana, R.J. Short and long-term outcomes in patients with acute liver failure due to ischemic hepatitis. Dig. Dis. Sci. 2012, 57, 777–785.
28. Waseem, N.; Chen, P.H. Hypoxic Hepatitis: A Review and Clinical Update. J. Clin. Transl. Hepatol. 2016, 4, 263–268.