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Reply to: "Combined heart-liver transplantation for congestive hepatopathy with bridging fibrosis: Is it warranted?"

A need to identify the good candidates beyond liver fibrosis classification?

To the Editor:

We thank Izzy *et al.*[1] for their interest in our article on the management of congestive hepatopathy,[2] and for identifying diabetes as an independent predictive factor of graft failure and mortality after combined heart-liver transplantation (CHLT).[3] We fully agree that careful selection of the patients with congestive hepatopathy who will benefit from CHLT is mandatory in the era of organ shortage and with regard to the survival observed after such a procedure. However, data are sparse as CHLT represent less than 10% of combined transplantation, 20–30 cases in the USA per year and less than 10 per year in France. Therefore, the identification of good candidates remains a major issue. In most cases, CHLT in the United States has been performed in patients with familial amyloid neuropathy or congenital heart diseases, dealing with a younger population of patients. In these series, indications for CHLT were mainly based on indirect criteria of cirrhosis with explants finding a low proportion of true cirrhosis, which could have contributed to the good outcomes observed in these patients.[4] Data are missing regarding patients with mixed liver lesions such as acute or chronic congestive lesions in combination with chronic advanced liver disease linked to metabolic syndrome, alcohol, or chronic viral hepatitis, a specific population of patients that constitute the majority of our French cohort.[5] They present an increased risk of liver complications following heart transplantation (HT) alone, justifying the consideration of CHLT in case of cirrhosis or even bridging fibrosis (especially for those with liver failure), and hepatocellular carcinoma (HCC).

The term "bridging cirrhosis" warrants further discussion as accurate evaluation for fibrosis stage remains challenging in the setting of end-stage heart failure. The diagnostic performance of non-invasive tests remains low, and individual variability exists when performing a liver biopsy. Moreover, the high risk of complications including bleeding and the absence of specific anatomopathological classification must be considered when deciding whether to perform a liver biopsy. However, specific attention to periportal or perisinusoidal fibrosis appears important to prompt an investigation for the presence of another cause of liver disease, which may favor fibrosis progression through cirrhosis and its related complications.

Even when the accurate classification of liver fibrosis in HT candidates is available, at least 3 questions persist:

- Challenging reports showing regression of fibrosis after HT alone, one for Fontan-associated liver disease and the other for idiopathic dilated cardiomyopathy,[6,7]
- To date, no study is available about the outcome of HT for patients with real cirrhosis, while survival results are similar between CHLT and single HT.
- Further analyses of the influence of preoperative acute liver failure (delta model for end-stage liver disease [MELD]) and postoperative risk factors of fibrosis progression and HCC are needed to identify the patients who will benefit from CHLT or HT alone. Interestingly, MELD score and ascites were independently associated with low postoperative survival in patients who underwent single HT and who did not present with cirrhosis. In this series, dilated and ischemic cardiopathies were the main indication for HT.[5]

Consequently, decision-making in the context of F3 or even F3-F4 fibrosis, while respecting a definition based on histological criteria, can only be done in the context of a multi-collegial and multidisciplinary decision considering the presence of coexisting acute and chronic liver disease and risk factors of fibrosis progression.

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References

[1] Izzy M, Alexopoulos S, Shinina A. Combined heart-liver transplantation for congestive hepatopathy with bridging fibrosis: is it warranted. JHEP Rep 2021;3(4):100292.

[2] Sessa A, Allaire M, Lebray P, Medmoun M, Tiritilli A, Iaria P, et al. From congestive hepatopathy to hepatocellular carcinoma, how can we improve patient management? JHEP Rep 2021;3(2):100249.

[3] Lee S, Matsuoka L, Cao S, Groshen S, Alexopoulos SP. Identifying predictors of outcomes in combined heart and liver transplantation. Transpl Proc 2019;51(6):2002–2008.

[4] Rizvi SSA, Challapalli J, Maynes EJ, Weber MP, Choi JH, O'Malley TJ, et al. Indications and outcomes of combined heart-liver transplant: a systematic review and met-analysis. Transplant Rev 2020;34(2):100517.

[5] Lebray P, Varnous S, Pascale A, Leger P, Luyt CE, Ratziu V, et al. Predictive value of liver damage for severe early complications and survival after heart transplantation: a retrospective analysis. Clin Res Hepatol Gastroenterol 2018;42(5):416–426.

[6] Judith Bouchardy, Meyer Philippe, Patrick Yerly, Coralie Blanche, Roger Hullin, Emiliano Giostra, et al. Regression of advanced liver fibrosis after heart transplantation in a patient with prior fontan surgery for complex congenital heart disease. Circ Heart Fail 2018;11(11):e003754.

[7] Crespo-Leiro MG, Robles O, Paniagua MJ, Marzoa R, Naya C, Flores X, et al. Reversal of cardiac cirrhosis following orthotopic heart transplantation. Am J Transplant 2008;8(6):1336–1339.

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