Taking care all along the way

Christoph Haller, MD

From the Division of Cardiovascular Surgery, Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada.

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Address for reprints: Christoph Haller, MD, 555 University Ave, Toronto, M5G 1X8 ON, Canada (E-mail: christoph.haller@sickkids.ca).

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Hepatic dysfunction, fibrosis, and even hepatocellular carcinoma are well-documented in patients after the Fontan operation, and it is of ongoing concern that declining liver function limits long-term outcome.¹ Histopathologic studies have previously shown that the fibrotic process seen in patients with Fontan circulations may even start before Fontan completion.² In this issue of the *Journal*, Kutty and colleagues³ report the use of shear wave elastography to analyze the stiffness of hepatic tissue in patients with single-ventricle palliation after bidirectional cavopulmonary connection. Kutty and colleagues³ were able to show that, compared with a matched control group of healthy individuals, patients after bidirectional cavopulmonary connection had higher hepatic stiffness and impaired blood flow indices. This increase was less pronounced than that seen in a historic Fontan group.

The results are interesting and highlight that single-ventricle palliation is a process that should not be seen as separate steps but rather as a continuum. Nevertheless, we have to be cautious in interpreting the results of hepatic stiffness in this patient group. The main limitation certainly is that hepatic stiffness measurements are influenced by multiple factors. Association of central venous pressure with hepatic stiffness has been shown^{3,4} as well as its reversibility.⁵ Estimation of central venous pressure by hepatic stiffness measurements is feasible, although not in the case of patients with intrinsic liver disease.^{6,7} It has also been reported that impaired hepatic venous drainage, as in the setting of elevated central venous pressure, can mimic severe fibrotic changes.⁵ In palliated patients, elastography may reflect the venous congestion but does not necessarily correlate with fibrotic changes in the liver,⁸ and fibrotic changes in turn do not necessarily correlate with global liver function.⁹ We therefore do not know exactly what the measurements are representing. Most likely, it is a combination of both central venous congestion and histologic hepatic changes, with a balance that shifts toward structural pathology the longer the congestive component persists. It remains to be determined when this process starts to become irreversible, how it affects hepatic function, whether we can establish reliable

Christoph Haller, MD

Central Message

Early detection of deteriorating Fontan circulation and liver dysfunction could improve clinical decision making significantly.

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values that represent these changes, and how it should be influenced by therapeutic intervention. Standardized measurements must also take into account that hemodynamic changes can promptly affect hepatic stiffness measurements.⁵

Hypoxia, congestive heart failure, cardiovascular collapse, low-output state, systemic-pulmonary artery shunt, pulmonary arterial banding, and the impact of major surgery all contribute to perioperative liver insult.¹⁰ It therefore is not unexpected to find signs of hepatic impairment in single-ventricle palliation all along the way. It is important to evaluate the resulting clinical implications. If we consider increased hepatic afterload as the source of the pathologic process that leads to fibrosis and dysfunction in single-ventricle palliation, it would be most helpful to assess liver stiffness throughout the palliative steps. It may very well be that the hemodynamic situation after bidirectional cavopulmonary connection is the most favorable with regard to hepatic drainage, because the ventricle benefits from unloading and hepatic drainage is not yet compromised by passive flow of inferior caval blood to the pulmonary artery. But we may also notice that it comes down to a very common question in single ventricle palliation: How can we preserve ventricular function?

The results of the study of Kutty and colleagues³ certainly do not allow us to recommend therapeutic

approaches. Delaying Fontan completion may have both beneficial and detrimental effects with regard to hepatic changes.¹¹ It is reasonable that the optimal time point for Fontan completion depends on more than just a certain age or size but also on oxygenation, arteriovenous malformations, cardiac function, and many other factors. Nevertheless, delaying the procedure indefinitely or even adding a systemic-pulmonary artery shunt or an iatrogenic arteriovenous fistula to improve hepatic stiffness, as suggested by Kutty and colleagues,³ is beyond the limitations of this parameter. This may in turn lead to reduced cardiac function and finally reduced hepatic drainage, thereby counteracting the initial intention.

Hepatic stiffness has the potential to become a valuable additional parameter for noninvasive hemodynamic follow-up of patients with single ventricle palliation, especially if it can be shown that it is sensitive to suboptimal hemodynamic states. Detecting the degree of hepatic dysfunction could guide decisions for Fontan takedown or transplantation. Until then, we need to improve our understanding of pathologic changes in patients with Fontan circulations. It would be ideal to correlate ultrasonographic analysis of hepatic stiffness with techniques such as cardiac catheterization and liver biopsy. Furthermore, periodic examinations would allow us to differentiate between a continuous decline and fluctuating hemodynamic states. If we learn to interpret hepatic stiffness in the context of cardiac function, passive pulmonary blood flow, intrinsic hepatic disease, and its impact on outcomes in patients with single-ventricle palliation, we may be able to preempt continuously declining function

and to improve medical treatment and surgical decision making.

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