Fontan-associated liver disease: Is it all about hemodynamics?

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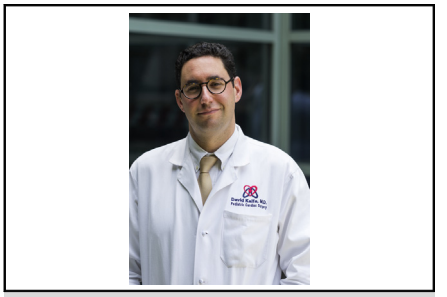

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Central Message

The exact causes and risk factors of Fontan-associated liver disease are multifactorial and remain poorly understood.

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The study by Trusty et al,[1] in this issue of *The Journal of Thoracic and Cardiovascular Surgery*, aims at investigating detailed cardiac magnetic resonance (CMR)-derived flow dynamics and total cavopulmonary connection (TCPC) energetics as potential risk factors for hepatic fibrosis in Fontan patients. Fontan-associated liver disease (FALD) has been a well documented complication for decades[2] and is now recognized as a progressive process affecting all Fontan survivors. The exact causes and risk factors of FALD remain poorly understood.

Trusty et al[1] tackled this controversial topic by combining CMR, computational fluid dynamics, cardiac catheterization, and liver biopsy data to investigate potential relationships between hepatic fibrosis and Fontan hemodynamics. They showed that liver fibrosis was found to be related to global metrics (inferior vena cava [IVC] flow, cardiac output) rather than to local TCPC hemodynamics and efficiency. One of the strengths of this study is that the authors had the opportunity to analyze contemporaneous liver biopsy data in conjunction with detailed blood flow characteristics in each patient.

Interestingly and surprisingly, the study findings do not support the notion that finer aspects of flow hemodynamics through the TCPC mitigate the presence of liver fibrosis. The authors found that Fontan energetics were not associated with hepatic fibrosis, and state that Fontan pathway architecture and TCPC inefficiency is not the key factor contributing to the degree of fibrosis. Nevertheless, it is important to note that this study did not include patients with clinically significant TCPC pathway obstruction. Thus, the pediatric cardiac medical and surgical community should keep in mind that, despite the findings of this valuable CMR/computational fluid dynamics-based study, an optimal Fontan without obstruction remains the very basic goal that we all need to achieve to optimize long-term outcomes for these patients, and that an aggressive diagnostic and therapeutic approach for Fontan obstruction remains warranted during the whole life of these patients.

Stating that the Fontan energetics are not associated with hepatic fibrosis, the authors hypothesize that the positive association seen between the degree of hepatic fibrosis and the IVC flow rate and cardiac output could be related to hepatic arterialization (and subsequent increased hepatic venous return). However, despite the quality of this study from Yoganathan's engineering group and Philadelphia clinical group, we still do not understand if the increased IVC flow is the cause or consequence of the liver fibrosis. Moreover, all computational simulations performed in this study used rigid walls, which obviously is a significant limitation to truly reflect the fluid hemodynamics in these complex patients. Thus, in the absence of data in favor of this "hepatic hyperarterialization" hypothesis (hypervascular nodularity was not assessed on CMR in this study), the underlying mechanisms for the interindividual variability and a higher susceptibility for developing Fontan-related liver fibrosis remain unknown. In the current era of personalized and precision medicine, genetic roots to this FALD susceptibility should be investigated through multi-institutional initiatives such as the Pediatric Cardiac Genomics Consortium.[3] We could envision that genetic variants present in the congenital heart disease patient population might be identified and used to predict the development of FALD in the Fontan population.

References

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