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Commentary: Diastolic (dys) function after Fontan completion: Where is the dysfunction?

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Characterizing ventricular mechanics in patients with Fontan physiology has been and remains a rich area for research. Previously published studies conducted using echocardiography-based techniques such as Doppler tissue imaging and speckle tracking¹⁻³ have demonstrated impaired diastolic function in patients with single ventricles as compared with healthy controls. Recent data also suggest that the diastolic impairment is worse in patients with a single right ventricle versus a single left ventricle.⁴

In the last decade, advances in 4-dimensional (4D) flow cardiac magnetic resonance (CMR) techniques have enabled imagers to analyze specific components of ventricular flow patterns, bringing us one step closer to understanding what “impaired diastolic function” really means. Work by Eriksson and colleagues⁵ and Stoll and colleagues⁶ has validated CMR-based methods for separating left ventricular end-diastolic volume (EDV) into functional flow components. When analyzing these components in patients with asymptomatic dilated cardiomyopathy (DCM) and in healthy controls, the patients with DCM had multiple indices of impaired diastolic flow patterns, including increased residual volume percentage and decreased direct flow (blood that enters and leaves the left ventricle in the same cardiac cycle).⁷ In a 2019 study⁸ of adults with DCM or ischemic cardiomyopathy compared with healthy adults, ventricular flow components were used to calculate average kinetic energy throughout the cardiac cycle. Data analysis

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4D flow CMR analysis of ventricular flow components may reveal insights into impairment of diastolic function after Fontan operation.

demonstrated not only the impairments in diastolic flow patterns as seen in earlier work by Eriksson and colleagues but also an independent predictive relationship between average kinetic energy and performance on 6-minute walk test.

In this issue of the *Journal*, Stone and colleagues⁹ have applied these previously validated 4D flow CMR techniques to assess functional flow components within the systemic ventricle of patients after Fontan completion. Their findings demonstrated that EDV was significantly greater in patients with hypoplastic left heart syndrome compared with those with hypoplastic right heart syndrome and controls. Despite the difference in EDV based on ventricular morphology, results using the particle tracking 4D flow techniques revealed that single-ventricle patients as a whole had impaired indices of diastolic function, including increased residual volume percentage and decreased direct flow, when compared with healthy volunteers. Furthermore, both indices were shown to correlate independently with ejection fraction.

These findings provide insight into the mechanisms involved in diastolic dysfunction. One could surmise that increasing direct flow by optimizing atrial contraction or atrioventricular synchrony may improve diastolic function. Yet, we must read the results with caution—while there are significant differences in ventricular flow patterns between the groups, the etiology of those differences and their relationship to clinical status remains unknown.

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Overall, this study is an excellent example of how 4D flow CMR can be used to gain quantitative insights into the pathophysiology of single-ventricle circulation. As 4D flow techniques become incorporated into clinical CMR studies, serial assessment of ventricular flow patterns may provide a noninvasive method of detecting subclinical disease.

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Commentary: Time to climb the ladder of causation

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In a book published in 2018, Turing Awardee Judea Pearl and Dana MacKenzie wrote of the need for science to climb the “ladder of causation,” moving above association, passing through intervention, and finally arriving at counterfactuals, where one can finally address causation.¹ Stone and colleagues² used cardiac magnetic resonance imaging to calculate previously described 4 components of end diastolic blood volume in 10 patients with hypoplastic left heart syndrome, hypoplastic right heart syndrome, and controls.² Compared with controls, patients with hypoplastic left heart syndrome and hypoplastic right heart syndrome had less direct flow volume (DF) and more residual volume (as a percentage of end diastolic volume [EDV]). Based on

Associations lie at the bottom of the Ladder of Causation. Let's climb the ladder! © 2018. Reprinted by permission of Basic Books, an imprint of Hachette Book Group, Inc.

CENTRAL MESSAGE

The association of CMR-derived components of diastolic volume with conventional measures of ventricular function is intriguing, if not mysterious. Science must determine the causal relationships.

these measurements, the authors concluded that these patients have “inefficient flow patterns” and diastolic dysfunction.

The use of these diastolic component volumes as indicators of diastolic function and originated in a 2011 article that hypothesized that diastolic flow patterns could

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