Ventricular Flow Profile in Young Patients With Single Left Ventricle Fontan Using Echocardiographic Contrast Particle Imaging Velocimetry

The modern Fontan palliation directs systemic venous blood from the superior and inferior vena cava to the pulmonary arteries, bypassing the heart. Its success depends on low pulmonary vascular resistance and optimal systolic and diastolic ventricular function.[1,2] Diastolic dysfunction in Fontan circulation is a well-known phenomenon, but its clinical impact remains underappreciated. Assessment of diastolic dysfunction in Fontan patients is challenging but might be enhanced by novel, advanced imaging techniques. Recently, speckle-tracking echocardiographic imaging has been shown to correlate with direct pressure measurements in the Fontan circulation, suggesting the potential value of this technology for assessment of diastolic function in the Fontan population.[3] One application of speckle-tracking echocardiography, echocardiographic particle image velocimetry (echo PIV), allows for quantification of multidirectional, intraventricular flow profiles in contrast-enhanced images. Unlike traditional echocardiographic measurements, echo PIV assesses vortex formation during diastolic filling, a process that is required for efficient redirection of ventricular blood flow during ventricular ejection. Previously we reported that echo PIV can measure flow dissipation in tetralogy of Fallot.[4] The objective of this pilot study was to evaluate intraventricular flow profiles in the palliated single left ventricle (SLV) using high-resolution echo PIV. We hypothesize that echo PIV–derived parameters of SLV flow will differ significantly from those of normal controls.

All examinations were performed using a Sequoia 512 system (Siemens Medical Solutions, Mountain View, CA). Before the administration of ultrasound contrast, all patients underwent complete diagnostic imaging according to institutional standards. Institutional review board approval and informed consent were obtained from the parents of all recruited patients. The primary diagnosis was either tricuspid atresia ($n = 6$) or pulmonary atresia with intact ventricular septum ($n = 4$) in all patients. For echocardiographic PIV, the lipid-encapsulated microbubble Definity (Lantheus Medical Imaging, North Billerica, MA) was infused as a 3% dilution (4-6 mL/min). A mechanical index of 0.4, harmonic frequencies, and 3-beat high-frame rate (>60 Hz) captures were used. The imaging plane was standardized by the 4-chamber view at the apical pulse location. Echocardiographic PIV parameters derived from the vortex field were studied using post-processing software (Hyperflow 6.0-1.3 TomTec). The software evaluated blood velocity across individual speckles and calculated kinetic energy (KE) dissipation, which is a measure of energy loss due to friction and viscous fluid dissipation, and vortex flow parameters, which are measures of the total amount of swirl and circulation in the chamber, across the entire velocity field. Mathematical descriptions of vortex parameters are provided elsewhere in detail.[5] Briefly, vorticity was calculated as the numerical curl of the two-dimensional velocity field, flow rotation intensity was approximated as the integral of vorticity inside the vortex normalized to the integral of vorticity in the entire left ventricle (LV), and dominant force strength was calculated as the integral of vorticity along the LV in cross section. Finally, the LV sphericity index, which is used to assess spherical remodeling, was calculated as the ratio of the long-axis length divided by the short-axis length.[6] Continuous variables are presented as mean ± SD, and categorical variables as counts and percentages. Echocardiographic PIV data were compared between the SLV group and control volunteers with no cardiac disease using Student's *t* test.

Measurable left ventricular (LV) planar maps were obtained in a total of 10 Fontan patients and in 10 controls (mean age, 22 ± 10 and 29 ± 4 years, respectively, $P = .075$). Body surface area was similar between both groups ($P = .278$). Patient demographic and echo PIV parameters are summarized in Table 1. Compared with controls, steady-streaming, heart beat–averaged flow rotation intensities were higher for the SLV group ($P = .0003$). Furthermore, KE dissipation was lower in the SLV group compared with controls ($P < .0001$). The LV sphericity index was significantly elevated ($P = .0165$),

Table 1 PIV parameters in the SLV

	Control LV (n = 10)	SLV (n = 10)	P Value
Patient characteristics:			
Age, years	29 ± 4	22 ± 10	.075
Gender, male:female (%)	3:4 (43)	5:2 (60)	.577
Body surface area, m^2	1.9 ± 0.08	1.8 ± 0.14	.278
General echocardiographic characteristics: LV sphericity index	0.47 ± 0.05	0.64 ± 0.19	**.0165**
PIV parameters:			
Flow rotation intensity	0.27 ± 0.09	0.50 ± 0.09	**.0003**
Vortex depth*	0.42 ± 0.05	0.38 ± 0.04	.5594
Vortex length*	0.47 ± 0.04	0.58 ± 0.05	.1120
KE dissipation, mJ	1.57 ± 0.51	0.32 ± 0.16	**<.0001**
KE fluctuation, mJ	1.62 ± 0.55	1.78 ± 0.20	.4965
Shear stress fluctuation, dynes/cm^2	0.04 ± 0.21	0.14 ± 0.28	.4905
Dominant force strength	0.02 ± 0.01	0.03 ± 0.02	.1780

Bold indicates statistical significance.
*Parameters normalized to ventricular dimensions.

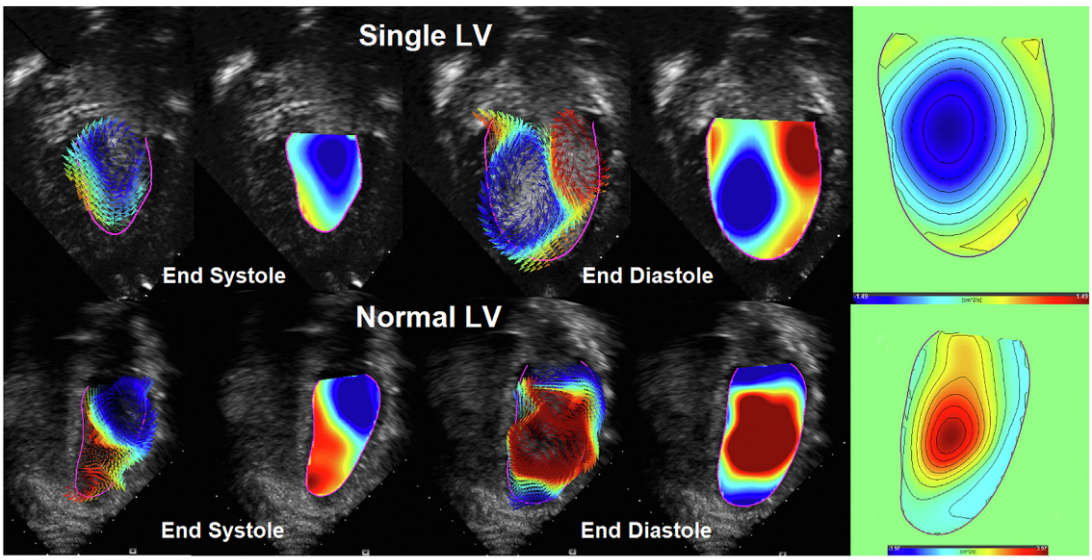

Figure 1 Representative echocardiographic PIV derived velocity fields and vorticity in the SLV *(top)* and normal LV *(bottom)* at end systole and end diastole. For each representative case, images are paired, with the PIV-derived velocity field image on the *left* and vorticity map on the *right* in end systole and end diastole, as indicated. Shown on the *far right* is the average vorticity throughout the entire cardiac cycle. For all vorticity maps, *blue* indicates a counterclockwise rotational velocity, while *red* indicates a clockwise rotational velocity. For all *arrows*, the *arrow tail* emanates from the corresponding pixel. As such, *arrows* that appear just outside the boundary result from velocities of pixels inside the boundary.

suggesting spherical, geometric remodeling in the SLV. In addition, a moderate and significant correlation was observed between the LV sphericity index and KE dissipation (Pearson $R = -0.6$, $P = .015$). No significant differences were observed in any other echocardiographic PIV parameters, including KE fluctuation, shear stress fluctuation, and dominant force strength. Qualitatively, we observed significant alterations in the vortex location and direction in the single ventricle. Representative differences in the ventricular vortex formation during diastolic filling for the SLV patients and controls are shown in Figure 1.

In this pilot study, we investigated echocardiographic PIV intraventricular flow characteristics and planar maps for the SLV in Fontan compared to the normal LV and identified key differences in echo PIV parameters. We propose that rotation intensity and energy dissipation indices may be useful in phenotyping ventricular function and subclinical diastolic dysfunction in the SLV. To our knowledge, this is first study to utilize intraventricular flow from PIV in the Fontan population. Our results showed that KE dissipation was lower, while flow rotation intensities were higher in the SLV. Together, these results suggest that the normal KE reservoir produced from vortex formation in the normal LV is absent in the SLV. We further hypothesize that these changes, particularly the changes in KE dissipation, may be a consequence of a poorly compliant dilated LV. Indeed, the spherical geometry of the SLV in Fontan, as demonstrated by the increased LV sphericity index in our cohort, results in increased wall shear stress by the law of Laplace and thus decreased KE dissipation.[7] Future studies are required to confirm this hypothesis by acquiring PIV flow characteristics simultaneously with invasive measures of diastolic function. Interestingly, changes in KE dissipation was observed in tetralogy of Fallot[4] and dilated cardiomyopathy, highlighting the sensitivity of echo PIV parameters for phenotyping ventricular function in congenital populations. Our work has some limitations. The imaging plane is important for the calculation of energy loss, and given the anatomical differences between SLV and controls, it may be difficult to secure similar views and inflow angles in both groups. In conclusion, echocardiographic PIV-derived intraventricular flow characteristics and planar maps for the SLV in Fontan differ from those in the normal LV and may be novel indices of ventricular compliance abnormalities in the SLV. Future studies are required to confirm that these parameters correlate with diastolic dysfunction documented by invasively measured pressure-volume loops, and to evaluate their prognostic value in relation to other clinical parameters, including arrythmia, exercise tolerance, and clinical symptoms.

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Left Ventricular Myocardial Work to Differentiate Cardiac Amyloidosis From Hypertrophic Cardiomyopathy

Cardiac amyloidosis (CA) is a progressive disorder with a reported median survival of 2.5 to 3.5 years after diagnosis.[1] Novel treatment options are emerging that could improve prognosis but seem most efficient when started at an early stage of the disease, underscoring the importance of early diagnosis. Echocardiography is the first-line imaging technique for the assessment of cardiac structure and function and might raise suspicion of CA. Although "relative apical sparing" of speckle-tracking-derived left ventricular (LV) longitudinal strain (LS) measurements was suggested to help diagnose CA,[2] differentiating CA from other causes of LV hypertrophy remains difficult. Assessment of LV myocardial work (MW) is a novel, noninvasive method to characterize LV systolic function, taking into consideration LV afterload. The aim of the current study was to assess the added value of LV MW measurements (and in particular of constructive work [CW]), to distinguish CA from hypertrophic cardiomyopathy (HCM), when evaluating patients presenting with LV hypertrophy.

Eighty-three CA and 83 HCM (excluding apical HCM) patients, diagnosed between 2003 and 2019 and matched for age (59 ± 12 years) and septal thickness (17 ± 3 mm), were included. Disease diagnosis was made according to current guidelines.[3,4] The study was approved by the institutional review boards. Left ventricular LS was measured using automated function imaging (EchoPAC, ver. 202, GE Medical Systems, Horten, Norway). The LV MW calculation has been described elsewhere.[5] Briefly, LV LS measurements and noninvasive brachial blood pressure measures were combined, and the software created a noninvasive LV pressure-strain curve for the entire cardiac cycle. Left ventricular CW was defined as the work that results by shortening during systole and lengthening during isovolumic relaxation. Left ventricular global LS and LV global CW were averaged from 17 LV segments. Relative apical LS was calculated as average apical LS/(average basal LS + average mid LS). A relative apical LS value ≥ 1 ("apical sparing") has previously been proposed for diagnosing CA.[2] *Relative* apical CW was not calculated, because this ratio does not adjust for LV afterload (having the blood pressure in both the numerator and denominator) and is therefore not different from relative apical LS. Receiver operating characteristics curves and binary regression analysis were performed, using CA as the outcome variable, to investigate whether relative apical LS and LV global LS or LV global

Drs. Stassen and Tjahjadi contributed equally to this work.

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