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ORIGINAL ARTICLE

Echocardiographic assessment of single-ventricle diastolic function and its correlation to short-term outcomes after the Fontan operation

Erin K. Davis MD[1] | Salil Ginde MD[1] | Jessica Stelter BS, RDCS[2] | Peter Frommelt MD[1] | Garick D. Hill MS, MD[3]

[1]Department of Pediatrics, Medical College of Wisconsin, Milwaukee, Wisconsin
[2]Children's Hospital of Wisconsin, Milwaukee, Wisconsin
[3]Department of Pediatrics, University of Cincinnati, Cincinnati, Ohio

Correspondence
Erin K. Davis, MD, Medical College of Wisconsin, 9000 W. Wisconsin Avenue, MS 713, Milwaukee, WI 53226.
Email: edavis@chw.org

Abstract

Background/Hypothesis/Objectives: Postoperative complications after the Fontan operation for single ventricle heart disease are common and include persistent pleural drainage and prolonged length of hospital stay (LOS). Diastolic ventricular dysfunction may increase risk for postoperative complications by raising central venous pressures. We sought to determine the relationship between preoperative echocardiographic measurements of diastolic function, including myocardial deformation imaging, on (a) preoperative invasive catheterization measurements and (b) postoperative outcomes after the Fontan procedure.

Design/Methods: All patients that underwent Fontan procedure from 2011 to 2017 were included. Echocardiograms performed within 6 months prior to Fontan operation were evaluated. Measurements of ventricular global and diastolic strain and strain rate were performed offline with TomTec speckle tracking software. Other diastolic function measurements included atrioventricular valve inflow and annular tissue Doppler imaging. Diastolic function measurements were correlated with pre-Fontan catheterization measurements and postoperative Fontan outcomes using Spearman's rho. Multivariable logistic regression for a prolonged LOS (>75%ile for postoperative LOS) was performed to adjust for preoperative risk factors.

Results: A total of 141 patients were included in the study. Majority had single morphologic right ventricle (58.9%). Median age at time of Fontan was 3.4 years (IQR 2.9-4). Median hospital LOS was 9 days (IQR 7-11). Circumferential diastolic strain rate weakly correlated with LOS (rho = −0.21, P = .01). There was no correlation between any other diastolic strain measurements and pre-Fontan end-diastolic pressure or postoperative LOS. In multivariable analysis, E/E′ was the only echo measurement that predicted prolonged hospital LOS (OR 1.4, 95%CI: 1.1-1.8, P = .003).

Conclusion: Preoperative diastolic strain measurements did not have a strong association with postoperative Fontan outcomes. Increased E/E′ ratio, however, did predict greater LOS after Fontan procedure, and may be useful in preoperative risk

Abbreviations: A, late diastolic velocities on atrioventricular inflow; A′, late diastolic inflow velocities on Doppler tissue imaging; AV, atrioventricular; DTI, Doppler tissue imaging; E, early diastolic wave on atrioventricular inflow; E′, early diastolic inflow velocities on Doppler tissue imaging; EDP, end diastolic pressure; LOS, length of stay; LV, left ventricle; RV, right ventricle.

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stratification. Future studies are needed to further assess the utility of diastolic strain imaging in the single-ventricle population.

KEYWORDS
diastolic function, echocardiography, Fontan, single ventricle, strain and strain rate

1 | BACKGROUND

Patients with single-ventricle congenital heart disease (CHD) undergo staged surgical palliation with the final stage being the total cavopulmonary connection or the Fontan operation. The Fontan operation consists of baffling the inferior vena cava and hepatic veins to the pulmonary arteries, resulting in separation of the systemic and pulmonary venous circuits and a passive flow pulmonary circulation. Although survival has improved after the Fontan operation, postoperative complications are common including prolonged pleural effusions and long postoperative length of stay (LOS).[1,2]

Risk factors for postoperative complications after the Fontan operation include pre-Fontan elevated pulmonary pressures, ventricular morphology, and ventricular dysfunction.[3,4] Diastolic ventricular dysfunction, in particular, may increase central venous pressures and the risk for postoperative complications, such as pleural effusions, edema, and ascites, all of which can lead to increased hospital LOS.

Current strategies for preoperative risk stratification for the Fontan operation typically include echocardiography and cardiac catheterization. However, echocardiographic assessment of single ventricular systolic function is limited due to complex chamber geometry and segmental abnormalities of wall motion. Diastolic assessment is limited by the lack of single measure that defines diastolic function. Traditional two-dimensional echocardiographic assessments rely on qualitative observations of systolic wall shortening, which can have a significant interobserver variability,[5] and do not correlate with postoperative Fontan outcomes.[3] Recent studies have evaluated the utility of echocardiographically derived myocardial deformation imaging in this population as a more sensitive and quantitative measure of myocardial function.[6] Diastolic strain and strain rate correlate with ventricular filling pressures and clinic outcomes in patients with structurally normal heart[7-9] and may better predict postoperative outcomes in patients undergoing the Fontan operation.

The aims of this study are to determine the relationship between preoperative systolic and diastolic myocardial deformation imaging and Doppler derived echocardiographic measurements of diastolic function with (a) preoperative invasive catheterization measurements; and (b) postoperative LOS after the Fontan procedure.

2 | METHODS

After obtaining Institutional Review Board approval, all patients with single-ventricle CHD that underwent the Fontan procedure at Children's Hospital of Wisconsin from 2011 to 2017 were identified. Demographic and baseline characteristics, as well as hemodynamic measurements from pre-Fontan cardiac catheterization, were obtained by retrospective chart review. Digitally stored images from the echocardiogram performed within 6 months prior to Fontan operation were collected and measurements of ventricular function were performed. Clinical variables and echocardiographic measurements were compared with postoperative outcomes prior to hospital discharge. The primary outcome was LOS after the Fontan operation.

2.1 | Echocardiographic measurements

Echocardiographic images were obtained either on Siemens ACUSON Sequoia 512 or SC2000 Ultrasound Machines (Siemens Medical Solutions, Malvern, PA). As part of our institutional protocol during the study period, all clinical echocardiographic studies included a high frame rate image capture utilizing an extended RR format in both the short axis at the level of the papillary muscles, and four-chamber view at the level of the atrioventricular (AV) valves. Images stored using this extended RR format preserve the high frame rate capture when images are stored as Digital Imaging and Communications in Medicine (DICOM) image clips for transfer to TomTec Imaging Systems (GmbH, Unterschleissheim, Germany). Two-dimensional speckle tracking was performed offline using the TomTec Imaging Systems. Speckle tracking uses acoustic reflections in areas of interest and tracks them during the entire cardiac cycle to determine the degree of deformation. Longitudinal strain was obtained from the high frame rate image capture performed in the four-chamber view at the level of the atrioventricular (AV) valve (s), and circumferential strain was obtained from the high frame rate image capture in the parasternal short-axis view at the level of the papillary muscles, as mentioned above. The median frame rate for the stored images used for speckle tracking measurements was 51 frames per second (range = 33-92 fps). Echocardiographic imaging originally captured at less than 30 frames per second were excluded from the study, to maximize the accuracy of the speckle tracking.

The endocardial border was traced from the septal AV hinge point to the apex then to the lateral AV hinge point, and the software automatically divided the tracing into six equidistant segments for each view. Tracings were accepted if the reader inspection and software indicated adequate tracking as seen in Figures 1 and 2. Global strain and strain rate were taken as the average of the maximal value from the six segments during the entire cardiac cycle. Diastolic strain and strain rate measurements were obtained by taking the average

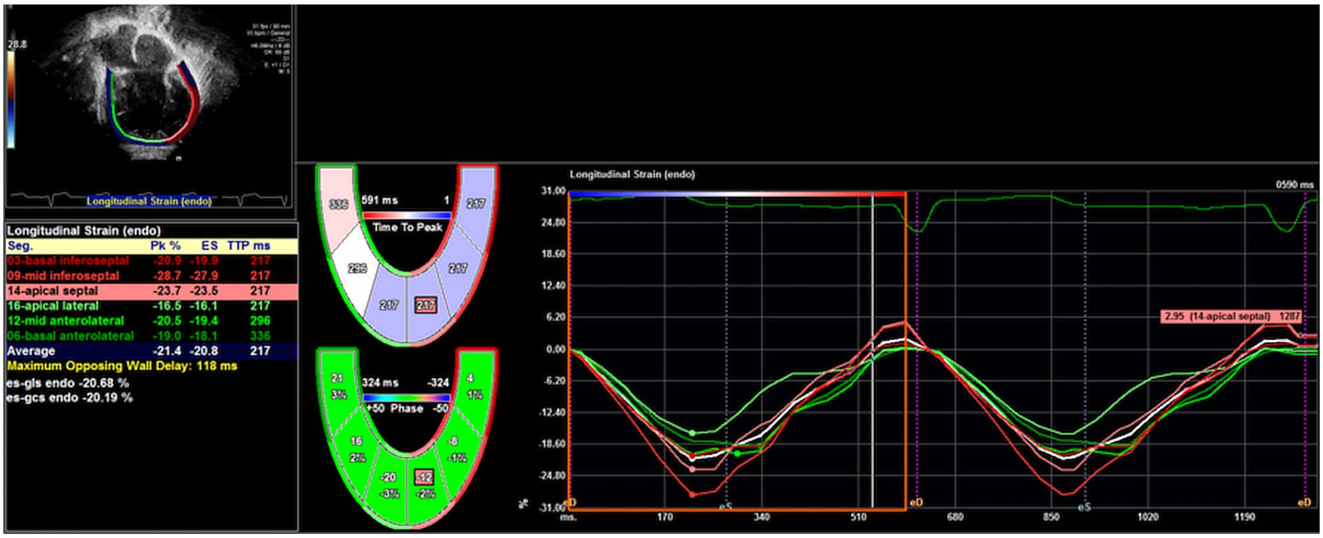

FIGURE 1 Example of a longitudinal deformation echocardiogram tracing. This image of the single ventricle was obtained in the apical view. Strain obtained in each segment (color coded) and also averaged into a global strain, seen in the bottom left. Waveforms of the strain during cardiac cycle is also included in the bottom left

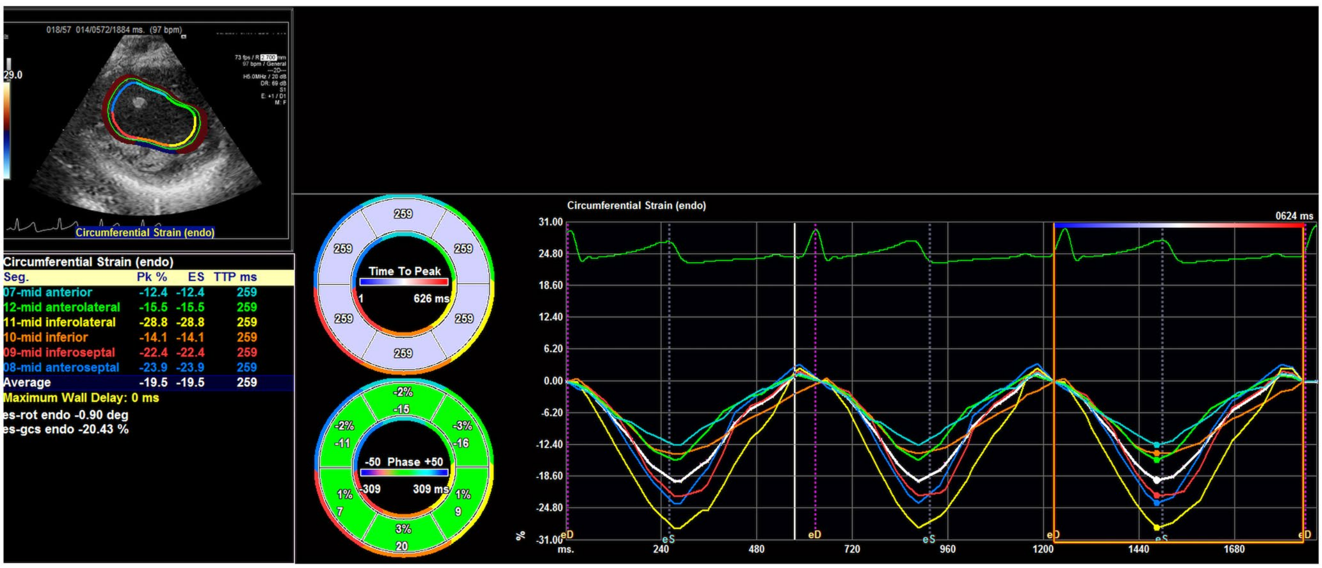

FIGURE 2 Example of a circumferential deformation echocardiogram tracing. Strain obtained in each segment (color coded) and also averaged into a global strain, seen in the bottom left. Waveforms of the strain during cardiac cycle is also included in the bottom left

of the maximal value from the six segments during the diastolic component of the cardiac cycle.

Atrioventricular (AV) valve inflow and annular tissue Doppler imaging (DTI) were obtained offline using Syngo Dynamics (GmbH, Erlangen, Germany). The AV inflow Dopplers were obtained by pulse wave Doppler at the AV valve leaflet tips from the apical four-chamber view to obtain the peak early diastolic wave (E) and the late diastolic velocities (A). DTI measurements were taken at the dominant ventricular free wall at the level of the AV valve in the apical four-chamber view. Early diastolic (E′) and late diastolic inflow velocities (A′) were measured. These values were used to calculate E/A and E/E′ ratios.

2.2 | Statistical analysis

Deformation measurements and diastolic echocardiographic measurements were correlated with pre-Fontan cardiac catheterization measurements and with post-Fontan outcomes using the Spearman's rho. Multivariable logistic regression for a prolonged hospital length of stay (>75th percentile LOS for the entire cohort) was performed to adjust for preoperative risk factors. Statistical analysis was performed using Stata IC 13 (Stata Corp, College Station TX) with $P < .05$ considered significant. Results are presented as number and percent of total or median with interquartile range (IQR) unless otherwise noted.

2.3 | Observer bias

To calculate interreader reliability, a second reader blindly remeasured 20 randomly selected echocardiograms. Correlation coefficients were obtained.

3 | RESULTS

In total, 151 patients were identified that met inclusion criteria with 10 (6.6%) patients excluded for inadequate echocardiographic imaging. Baseline characteristics for the 141 patients remaining in the study cohort are shown in Table 1. The majority of the subjects were male (n = 81, 57%). The majority also had a morphologically single right ventricle (n = 83, 58.9%). Hypoplastic left heart was the most common diagnosis present in 56 (39.7%) patients. Other diagnoses included double-inlet left ventricle in 27 (19.2%) patients, tricuspid atresia in 16 (11.4%), unbalanced AV septal defect in 14 (9.9%), double-outlet right ventricle in 12 (8.5%), and pulmonary atresia in 9 (6.4%). Heterotaxy syndrome was present in 18 patients. The median age at time of Fontan was 3.4 years old (IQR 2.9-4). The majority had an extracardiac Fontan (n = 139, 98.6%), while the remaining had a lateral tunnel. No patients had an atriopulmonary Fontan. Most patients (n = 124, 88%), had a fenestration placed at the time of the Fontan operation. The median postoperative LOS was 9 days (IQR 7-11 days), including a median of 6 days (IQR 4-8 days) in the intensive care unit. There were no mortalities in the postoperative hospitalization.

As found in Table 2, the median E/A was 1.2 (IQR 1-1.5) and median E/E′ was 7.4 (IQR 5.5-9.6). The median global circumferential peak strain was −19.2% (IQR −23.3% to −16.2%). The global longitudinal peak strain was −21% (IQR −24.3% to −18.3%). The diastolic circumferential strain was 23.6% (IQR 19.2%-28.8%), and the diastolic longitudinal strain was 27% (IQR 21.9%-31.9%).

There was no significant correlation between preoperative ventricular end-diastolic pressure and any of the clinical risk factors or echocardiographic measurements of diastolic function, including E/E′ (rho = −0.07, *P* = .53), circumferential diastolic strain (rho = 0.16, *P* = .07), circumferential strain rate (rho = 0.06, *P* = .52), longitudinal diastolic strain (rho = 0.026, *P* = .8), and longitudinal strain rate (rho = 0.079, *P* = .53). Circumferential diastolic strain was weakly correlated with prolonged LOS (rho = −0.21, *P* = .01). No other global or diastolic strain or strain rate measurement correlated with prolonged LOS. Results of multivariable analysis adjusting for risk factors associated with prolonged LOS is found in Table 3. There was no statistical difference in right vs left ventricular morphology (*P* = .2). The ratio between early AV valve inflow velocity and AV valve annular early diastolic velocity (E/E′) was the only echocardiographic measurement that was associated with prolonged LOS (OR 1.4, 95% CI 1.1-1.8, and *P* = .003). The presence of heterotaxy syndrome was also a significant risk factor for increased hospital length of stay (OR 26.5, 95% CI 2.1-328, and *P* = .01).

Interreader correlations for systolic and diastolic strain and strain rate are summarized in Table 4. Overall, there was good correlation between the two readers for the strain values, with coefficients >0.72. Measurements of strain rate were less reliable, particularly for longitudinal and circumferential diastolic strain rate.

TABLE 1 Demographic data for the Fontan cohort

Total	141
Male, n	81 (57%)
Diagnosis, n	
Hypoplastic left heart syndrome	56 (39.7%)
Double-inlet left ventricle	27 (19.2%)
Tricuspid atresia	16 (11.4%)
Unbalanced AV septal defect	14 (9.9%)
Double-outlet right ventricle	12 (8.5%)
Pulmonary atresia	9 (6.4%)
Other	7 (5%)
Single right ventricle morphology, n	83 (58.9%)
Heterotaxy syndrome	18 (12.8%)
Age at Fontan (years), median (IQR)	3.4 (2.9-4)
Extracardiac, n	139 (98.6%)
Fenestration, n	124 (88%)
Chest tube duration (days), median (IQR)	5 (3-6)
Inotrope duration (days), median (IQR)	2 (2-3)
Hospital length of stay (days), median (IQR)	9 (7-11)

TABLE 2 Echocardiography measurement data for the Fontan cohort

Echocardiographic measurement	Median	IQR
E/A	1.2	1-1.5
E/E′	7.4	5.5-9.6
Global circ. peak strain	−19.2%	−23.3% to −16.2%
Global long. peak strain	−21%	−24.3% to −18.3%
Diastolic circ. strain	23.6%	19.2%-28.8%
Diastolic long. strain	27%	21.9%-31.9%

Abbreviations: A, late diastolic velocity; E, early diastolic wave; E′, early diastolic annular tissue velocity.

4 | DISCUSSION

In 141 patients with single-ventricle CHD, we found that an increased E/E′ ratio prior to the Fontan was significantly associated with increased postoperative hospital length of stay. Our study is novel in that it is the first study to evaluate the impact of preoperative diastolic ventricular function using Doppler echocardiography and diastolic strain measurements, on postoperative outcomes after

TABLE 3 Multivariable analysis of risk factors associated with increased hospital length of stay after Fontan operation

Variable	OR	95% CI	*P* value
Circ. global peak strain	1	0.7-1.3	.8
Circ. global strain rate	2.2	0.1-45.5	.6
Long. global peak strain	1.3	1-1.7	.08
Long. global strain rate	0.5	0.03-8.1	.6
Diastolic circ. strain	1	0.9-1.2	.9
Diastolic circ. strain rate	1.2	0.2-6.6	.9
Diastolic long. strain	1	0.8-1.2	.9
Diastolic long. strain rate	0.7	0.2-2.6	.6
E/E′ ratio	1.4	1.1-1.8	.003
Ventricular morphology	3	0.5-17.9	.2
Number of prior bypass operations	6.8	0.9-48.8	.06
Heterotaxy syndrome	26.5	2.1-328	.01
Pre-op PA pressure	1.4	1-2.1	.07
Pre-op EDP	1.1	0.9-1.4	.4

Abbreviations: Circ., Circumferential; E, early diastolic wave; E′, early diastolic annular tissue velocity; EDP, end-diastolic pressure; Long., Longitudinal; PA, pulmonary artery.

TABLE 4 Interreader reliability for deformation measurements

Deformation measurement	Correlation coefficients
Circ. global peak strain	0.83
Circ. global strain rate	0.82
Long. global peak strain	0.78
Long. global strain rate	0.68
Circ. diastolic strain	0.8
Circ. diastolic strain rate	0.5
Long. diastolic strain	0.72
Long. diastolic strain rate	0.4

Abbreviations: Circ., Circumferential; Long., Longitudinal.

the Fontan operation. Strain echocardiography has several advantages for patients with single-ventricle CHD in that the techniques are not limited by the geometry of the ventricle. However, in this study, these novel diastolic strain imaging measures did not correlate with our primary outcome of hospital LOS following the Fontan operation. Circumferential diastolic strain did correlate with hospital LOS, but was not significant in the multivariable analysis.

Increased E/E′ ratio is a noninvasive marker of diastolic ventricular dysfunction and correlates with elevated ventricular end-diastolic pressure when measured during simultaneous Doppler echocardiographic and catheter measurements in patients with structurally normal hearts[10,11] and single-ventricle CHD.[12] In our study, increased preoperative E/E′ likely indicated those patients at risk for worse ventricular compliance postoperatively, which in turn can lead to higher central venous pressures, increased risk for postoperative complications such as prolonged effusions, and subsequently longer hospital LOS. Although invasive postoperative measurements were not available in this study to confirm that hypothesis, it is clear that E/E′ continues to be a useful marker of diastolic dysfunction in the setting of single-ventricle CHD, and should be utilized as part of preoperative risk assessment for patients prior to the Fontan operation.

Previous studies have tried to evaluate the relationship between echocardiographic measures of diastolic function and either catheter hemodynamic measurements or outcomes in a variety of populations. Park et al reported that preoperative circumferential strain rate correlates with prolonged LOS after total cavopulmonary connection.[13] However, unlike our study, diastolic strain measurements were not included in their analysis. The reasons for why global circumferential strain rate did not correlate with prolonged LOS in our study may be related to differences in image capture, strain measurement technique and software, or study population compared to the study by Park et al.

Studies have shown that following Fontan, diastolic functional indices have been associated with an inability to achieve maximal effort on exercise testing but was not associated with any other clinical measure including functional health status.[14] Similarly, E/E′ measured on echocardiogram negatively correlates with exercise time and peak oxygen uptake (VO2) on cardiopulmonary exercise testing in patients with Fontan circulation, further supporting the importance of this echocardiographic measurement in this population.[15]

This study is limited by a relatively small sample size. There are also several challenges that can limit the accuracy of strain measurements in a single ventricle. Anatomic variations such as ventricular septal defects, differences in ventricular morphology and CHD diagnoses, and acquired abnormalities of wall motion can affect the quality and reproducibility of the tracings used to obtain the measurements. This was demonstrated in our assessments of interobserver reliability, which seemed to be lowest when comparing diastolic strain measurements. Furthermore, strain measurements were obtained from only a single imaging plane for both the circumferential (parasternal short axis) and longitudinal (apical four-chamber) strain analyses. Imaging from multiple short-axis or apical imaging planes, or three-dimensional imaging, would have improved the accuracy of strain measurements, but was not available or feasible in this retrospective study. Finally, echocardiographic imaging and pre-Fontan catheterization data were obtained at different times and under different hemodynamic conditions (awake for the Doppler indices and under general anesthesia for the cardiac cath), thus limited the correlation between these two modalities. A larger study of single ventricle patients with a subgroup assessment of anatomic type is warranted to better assess the utility of diastolic strain measurements in patients with single ventricle CHD.

5 | CONCLUSIONS

An increased E/E′ by pre-Fontan echocardiography significantly predicted a longer hospital LOS after the Fontan operation, and can be used as part of preoperative risk stratification. Global and diastolic deformation measurements did not correlate with Fontan outcomes. Future studies with larger cohorts are needed to further assess the utility of diastolic strain imaging in the single-ventricle population.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Concept/design: Davis, Ginde, Frommelt, Hill
Data collection: Davis, Ginde, Stelter
Data analysis/interpretation: Davis, Ginde, Hill
Drafting article: Davis, Ginde, Hill
Approval of article: Davis, Ginde, Stelter, Frommelt, Hill
Technological support: Stelter
Critical revision of the article: Stelter, Frommelt
Statistics: Hill

ORCID

Erin K. Davis https://orcid.org/0000-0003-1331-3295
Salil Ginde https://orcid.org/0000-0001-9218-1993
Garick D. Hill https://orcid.org/0000-0003-0050-7250

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