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Suma P. Goudar
Children's Mercy Hospital

Victor Zak

Andrew M. Atz

Karen Altmann

Steven D. Colan

See next page for additional authors

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Creator(s)
Suma P. Goudar, Victor Zak, Andrew M. Atz, Karen Altmann, Steven D. Colan, Christine B. Falkensammer, Mark K. Friedberg, Michele Frommelt, Kevin D. Hill, Daphne T. Hsu, Jami C. Levine, Renee Margossian, Christopher R. Mart, Joshua Sticka, Peter Shrader, Girish S. Shirali, and Pediatric Heart Network Investigators

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Comparison of echocardiographic measurements to invasive measurements of diastolic function in infants with single ventricle physiology: a report from the Pediatric Heart Network Infant Single Ventricle Trial

Suma P. Goudar[1], **Victor Zak**[2], **Andrew M. Atz**[3], **Karen Altmann**[4], **Steven D. Colan**[5], **Christine B. Falkensammer**[6], **Mark K. Friedberg**[7], **Michele Frommelt**[8], **Kevin D. Hill**[9], **Daphne T. Hsu**[10], **Jami C. Levine**[5], **Renee Margossian**[5], **Christopher R. Mart**[11], **Joshua Sticka**[12], **Peter Shrader**[2], **Girish Shirali**[1], **Pediatric Heart Network Investigators**

[1]Department of Cardiology, Ward Family Heart Center, Children's Mercy Hospital, Kansas City, MO, USA;

[2]New England Research Institute, Watertown, MA, USA;

[3]Division of Pediatric Cardiology, Medical University of South Carolina, Charleston, SC, USA;

[4]Division of Pediatric Cardiology, Columbia University Medical Center, New York, NY, USA;

[5]Boston Children's Hospital, Boston, MA, USA;

[6]Children's Hospital Philadelphia, Philadelphia, PA, USA;

[7]Division of Pediatric Cardiology, The Hospital for Sick Children, Toronto, ON, Canada;

[8]Children's Hospital of Wisconsin, Milwaukee, WI, USA;

[9]Duke University, Durham, NC, USA;

[10]Children's Hospital at Montefiore, Bronx, NY, USA;

[11]Primary Children's Medical Hospital, Salt Lake City, UT, USA

[12]Cincinnati Children's Hospital, Cincinnati, OH, USA

Abstract

Background: While echocardiographic parameters are used to quantify ventricular function in infants with single ventricle physiology, there are few data comparing these to invasive measurements. This study correlates echocardiographic measures of diastolic function with ventricular end-diastolic pressure in infants with single ventricle physiology prior to superior cavopulmonary anastomosis.

Author for correspondence: S. P. Goudar, Ward Family Heart Center, Children's Mercy Hospital, 2401 Gillham Road, Kansas City, MO 64108, USA. Tel: +1 (816)234-3255; Fax: +1 (816)234-3701; potiny@yahoo.com.

Conflicts of Interest. None.

Ethical Standards. The trial involved human subjects. The trial protocal was approved by an independent protocol review committee, a data and safety monitoring board, and by the institutional review board at each clinical center and at the data coordinating center. The trial was registered at http://www.cinical-trials.gov/ct2/show/NCT00113087.

Methods: Data from 173 patients enrolled in the Pediatric Heart Network Infant Single Ventricle enalapril trial were analysed. Those with mixed ventricular types (n = 17) and one outlier (end-diastolic pressure = 32 mmHg) were excluded from the analysis, leaving a total sample size of 155 patients. Echocardiographic measurements were correlated to end-diastolic pressure using Spearman's test.

Results: Median age at echocardiogram was 4.6 (range 2.5–7.4) months. Median ventricular end-diastolic pressure was 7 (range 3–19) mmHg. Median time difference between the echocardiogram and catheterisation was 0 days (range −35 to 59 days). Examining the entire cohort of 155 patients, no echocardiographic diastolic function variable correlated with ventricular end-diastolic pressure. When the analysis was limited to the 86 patients who had similar sedation for both studies, the systolic:diastolic duration ratio had a significant but weak negative correlation with end-diastolic pressure ($r = -0.3$, $p = 0.004$). The remaining echocardiographic variables did not correlate with ventricular end-diastolic pressure.

Conclusion: In this cohort of infants with single ventricle physiology prior to superior cavopulmonary anastomosis, most conventional echocardiographic measures of diastolic function did not correlate with ventricular end-diastolic pressure at cardiac catheterisation. These limitations should be factored into the interpretation of quantitative echo data in this patient population.

Keywords

Diastolic function; infants; single ventricle

In patients with single ventricle physiology, the presence and preservation of normal cardiac function is important for long-term survival. After the Fontan procedure, diastolic dysfunction has been shown to be more prevalent than systolic dysfunction.[1] Although various echocardiographic parameters are used to evaluate diastolic ventricular function, there is a paucity of data comparing these to invasive pressure measurements in infants with single ventricle physiology.

Studies in adults with two-ventricle hearts have demonstrated that several echocardiographic Doppler indices correlate with invasively measured left ventricular end-diastolic pressure.[2–7] Studies comparing echocardiographic measures of diastolic function to invasive measurements in paediatric populations with biventricular circulation have shown mixed results.[8–10] In addition, concerns have been raised regarding the reproducibility of many of these measurements in children.[11] Three studies have been performed in the single ventricle population evaluating the relationship of echocardiographic measures of diastolic function to invasive measures of ventricular function at cardiac catheterisation. While these studies demonstrated that the ratio of early to late diastolic pulsed Doppler atrioventricular valve inflow velocity, ratio of early filling velocity to early Tissue Doppler velocity, and ratio of early filling velocity to global longitudinal early diastolic strain rate correlate well with invasive measures of diastolic function (Tau and/or ventricular end-diastolic pressure), these studies are limited by overall sample size (13, 27, and 32 patients each) and the diverse group of patients who were studied at various stages of palliation and ages.[12–14]

The Pediatric Heart Network Infant Single Ventricle trial was a randomised, double-blind, placebo-controlled trial designed to determine if enalapril improves somatic growth in infants with single ventricle physiology.[15] The patient cohort from this multi-institutional study provides a unique opportunity to compare echocardiographic estimates of diastolic ventricular function to invasive measurements prior to superior cavopulmonary anastomosis. The purpose of the present study was to identify whether echocardiographic measurements of diastolic function correlate with ventricular end-diastolic pressure in infants with single ventricle physiology prior to superior cavopulmonary anastomosis.

Materials and methods

This is a retrospective study using the database from the Pediatric Heart Network Infant Single Ventricle trial which enrolled 230 patients aged 1 week to 45 days with single ventricle physiology and planned superior cavopulmonary anastomosis palliation. Patients were enrolled from August 2003 through May 2007. Details of the trial design and study population have previously been described.[15,16] Standardised echocardiograms were performed at baseline (study entry, age less than 6 weeks), pre-superior cavopulmonary anastomosis, and 14 months of age and interpreted at a central core laboratory. Only the echocardiograms from the pre-superior cavopulmonary anastomosis time period were included in the analysis. Cardiac catheterisations prior to superior cavopulmonary anastomosis were not required as part of the trial protocol, but were performed in most patients. From the original trial cohort, we excluded patients without a pre-superior cavopulmonary anastomosis catheterisation (n = 57) and patients with mixed ventricular type (neither classifiable as right or left ventricular type, n = 17). Mixed ventricular type was excluded to have a more homogenous single ventricle cohort, since we hypothesised that the type of ventricular morphology may impact echo measurements and therefore the correlation of echocardiographic measurements with end-diastolic pressure. One outlier with a ventricular end-diastolic pressure of 32 was additionally excluded from the analysis as this was suspected to be a spurious value. Therefore, a total of 155 patients were included in the analysis.

Table 1 lists the echocardiographic measures included in the analysis. In order to minimise bias and interobserver error, a single observer at a central core echocardiography laboratory performed all echo measurements. Since 47% of the 173 patients with echo and catheterisation data (n = 81) had a summation wave (fusion of early and atrial atrioventricular valve inflow and/or tissue Doppler wave), echo measurements involving pulse inflow Doppler and tissue Doppler atrial velocities were not included in the analysis. To calculate ventricular volumes, mass, and ejection fraction, apical and parasternal short-axis views were analysed using custom software (EchoTrace, Marcus Laboratories, Boston, Massachusetts, United States of America). Using the apical (ventricular long-axis) and parasternal short-axis views, the endocardial border was traced at end-diastole and end-systole. The epicardial border was traced at end-diastole in both planes. End-diastolic volume, as well as end-systolic volume, and ventricular mass were calculated using a biplane-modified Simpson’s rule. The ejection fraction was derived from these values. Ventricular mass was calculated as myocardial end-diastolic volume (epicardial volume −endocardial volume) × myocardial density (1.05 g/ml). This methodology, as well as interobserver and intra-observer variability of these methods in the single ventricle population, has been described in a previous publication by the Pediatric Heart Network.[17] Two additional echocardiographic variables were derived from the existing tissue Doppler tracing measurements: the Tei index[18] and the systolic:diastolic duration ratio.[19,20] For the systolic:diastolic duration ratio, the isovolumic phases were excluded from the systolic and diastolic duration time measurement since some of the patients had right ventricle to pulmonary artery (Sano) shunts that lack true isovolumic phases. The systolic duration time was measured from the start to the end of the peak systolic annular velocity wave, and the diastolic duration time was measured from the start of the peak early diastolic annular velocity to the end of the peak late diastolic annular velocity. The systolic: diastolic duration ratio was then calculated as the ratio of the systolic and diastolic duration times (systolic duration time/diastolic duration time). If multiple site tissue Doppler tracing measurements were present for an individual subject (e.g. more than one lateral wall and/or septal wall), all available Tei and systolic: diastolic ratio measurements from the septum and lateral walls were averaged to create a single measurement for each subject. The Tei index and systolic:diastolic ratio measurements were also calculated using only lateral values of the dominant ventricle in a separate analysis. Otherwise, the tissue Doppler measurement from the single available site was used.

Statistical analysis

Data are described as frequencies, medians with 25th and 75th percentile values, and means with standard deviations as appropriate. Correlation analysis using Spearman's rank correlation was performed between the echocardiographic variables and ventricular end-diastolic pressure at the pre-superior cavopulmonary anastomosis cardiac catheterisation. Correlation analysis was performed separately in patients with and without summation atrioventricular valve waves for peak early diastolic inflow or tissue velocity and the ratio of atrioventricular valve to tissue Doppler peak early diastolic velocity. In addition, linear regression analysis was performed testing the association of echo variables with end-diastolic pressure; non-linear fit was performed using generalised additive models. In an alternative analysis, the cohort was dichotomised based on ventricular end-diastolic pressure values: end-diastolic pressure ≥10 mmHg (elevated) versus the rest of the cohort (end-diastolic pressure < 10 mmHg; normal). A value of 10 mmHg or greater for an elevated end-diastolic pressure was chosen because this represented the upper quartile of end-diastolic pressure in this cohort. Logistic regression analysis was then performed testing the association of echocardiographic variables with an elevated end-diastolic pressure as the outcome variable of interest. Receiver operating characteristic analysis was done on those variables that showed a significant association with ventricular end-diastolic pressure.

To determine if dominant ventricular morphology impacted correlation of these echo variables with end-diastolic pressure, the patients were divided into two groups: systemic right versus systemic left ventricle and correlation between echocardiographic variables and end-diastolic pressure was compared between these two groups. Regression interaction testing was also performed to verify the impact of ventricular type on association between echocardiographic variables and end-diastolic pressure. Data analyses were performed using Statistical Analysis Software version 9.3 (SAS Institute Inc., Cary, North Carolina, United

States of America). The plots are created using S-PLUS version 8.0 (Insightful Inc., Seattle, Washington, United States of America). A p-value less than 0.05 was considered statistically significant.

Results

As noted above, of the 230 enrolled patients in the trial, 156 patients met the inclusion criteria and an additional outlier suspected to have spurious catheter-based data was excluded, leaving a total of 155 patients in the analysis. Analysis of this group demonstrated that there was no significant correlation between end-diastolic pressure and any of the echocardiographic variables. As is common in clinical practice, many patients had different sedation types during the two procedures (catheterisation and echocardiogram) that could potentially alter loading conditions and myocardial function, thus impacting correlations. In order to infer whether loading conditions may differ due to different sedation types and the potential confounding effect of general anesthesia, we compared the ratio of systolic blood pressure recorded during the echo to that recorded during cath. The systolic and diastolic blood pressure ratio between the two measurements was higher in the patients with different sedation types during the two procedures (1.18 ± 0.27 and 1.37 ± 0.42, respectively), compared to those with similar sedation types (1.03 ± 0.23 and 1.17 ± 0.36) during the two procedures. Therefore, a separate analysis was performed on patients with similar sedation type during the two studies (either having general anesthesia for both studies or moderate sedation during both studies).

Eighty-six of the total 155 patients (66%) had the same sedation type for both the catheterisation and echocardiogram. Table 2 summarises baseline characteristics of the study population with similar sedation types. Mean age and weight at the time of echocardiogram were 141.6 ± 32.4 days and 5.7 ± 1.2 kg, respectively. Overall, 84% of the patients had right ventricular dominant morphology. Figure 1 shows the time between the echocardiogram and cardiac catheterisation. For most of these 155 patients (86%), the echocardiogram and catheterisation were performed within a 2-week period with 64% of the patients having the two studies on the same day. Echocardiographic and cardiac catheterisation data used in the analysis are summarised in Table 3. Of note, the early annular velocities mean and standard deviation values in the cohort are as follows: left 9.1 ± 3.1, septal 6.4 ± 2.6, and right 8.0 ± 2.7. Ventricular end-diastolic pressure ranged from 2 to 20 mmHg, with 76% of patients having an end-diastolic pressure less than 10 mmHg.

Table 4 summarises the results of the linear correlation analysis of echo parameters versus end-diastolic pressure for the patients with similar sedation type. Most of the echocardiographic variables did not have a statistically significant correlation with ventricular end-diastolic pressure except for systolic: diastolic duration ratio, which had a weak negative correlation with end-diastolic pressure. Duration of pulmonary vein flow reversal did not correlate with ventricular end-diastolic pressure, even when only those patients with a flow reversal duration greater than zero (n = 26) were included ($r = 0.22$, $p = 0.06$). In addition, the ratio of early atrioventricular valve inflow velocity to early diastolic annular velocity, peak systolic velocity by tissue Doppler, systemic flow propagation velocity, ventricular ejection fraction, mass:volume ratio, and ventricular mass z-score did not correlate significantly with ventricular end-diastolic pressure (Figs 2–4). Tei index did not correlate with end-diastolic pressure (Fig 5). Linear regression analysis did not show a significant association between any of the echo-cardiographic variables and end-diastolic pressure. Interaction regression testing of ventricular type on the association between echocardiographic variables and end-diastolic pressure was not significant for any of the echocardiographic variables.

Table 5 describes results from logistic regression analysis testing the association of echocardiographic parameters with elevated end-diastolic pressure in the cohort with the same sedation type during the two studies. There was no significant association of any of the echo measures with an elevated end-diastolic pressure except for systolic:diastolic duration ratio. Systolic:diastolic duration ratio was found to have a weak but statistically significant negative association with end-diastolic pressure (Fig 6 and Table 5). This relationship held true even when controlling for heart rate using a multivariable regression model ($p = 0.02$). When only the lateral velocity measurements were included, only patients with right dominant ventricular type had statistically significant negative correlation with end-diastolic pressure ($r = -0.32$, $p = 0.01$). Left ventricular dominant patients had no significant correlation between systolic:diastolic duration ratio and end-diastolic pressure.

Discussion

Based on our findings, most conventional 2D, pulsed wave, and tissue Doppler echocardiographic measures of diastolic ventricular function do not correlate with ventricular end-diastolic pressure at cardiac catheterisation in infants with single ventricle physiology prior to superior cavopulmonary anastomosis. Interestingly, systolic:diastolic duration ratio exhibited a weak negative correlation with end-diastolic pressure due to an increased duration of diastole in those patients with elevated end-diastolic pressure. This relationship held true even when we controlled for variability in heart rate. This relationship is the opposite of what has been demonstrated in other paediatric studies, which have shown that the duration of isovolumic relaxation and of ventricular filling would be expected to shorten with increased filling pressures.[20–22] Possible explanations for the discrepancy between our findings and prior work include heterogeneity in ventricular morphology in our cohort, loading conditions and valve function, different methodology (use of tissue Doppler measurements, averaging of values, and exclusion of isovolumic times), and ventricular dyssynchrony. Single ventricles commonly exhibit dyssynchrony,[23] which, in turn, is associated with elevated end-diastolic pressure.[24] Ventricular dyssynchrony may have more of an effect on systolic time than on diastolic time, which may lead to a decrease in the systolic:diastolic duration ratio. As shown in Figure 5, the scatter around the regression line is relatively wide, the correlation is relatively weak, and four outliers with high end-diastolic pressure may have influenced results. These factors make it difficult to know if this finding is informative or spurious, but it warrants further evaluation.

These findings have important clinical implications. Single ventricle patients who manifest pre-Fontan diastolic dysfunction, as determined by invasive measures such as elevated Tau and end-diastolic pressure, have worse Fontan outcomes.[25,26] Tau and end-diastolic pressure assess different aspects of diastole: Tau measures the speed of isovolumic pressure fall in the ventricle, reflecting the combined impact of impaired myocardial relaxation, elastic recoil, and synchrony of relaxation, while end-diastolic pressure reflects end-diastolic compliance and is influenced by volume status. If diastolic dysfunction predicts a worse outcome in the pre-superior cavopulmonary anastomosis population, then it is important for the clinical care of these patients to have a reproducible, easily calculated, non-invasive method of assessing diastolic dysfunction. Disappointingly, in this cohort, none of the standard echo measures of diastolic function correlated well enough with end-diastolic pressure to fulfill this role. Other studies in children with single ventricle[14,20] as well as other paediatric populations[8,27] have also shown poor correlations between tissue Doppler echo measurements and catheter-derived ventricular end-diastolic pressure, in contrast to what the adult literature demonstrates.[2,3] This may be because children do not commonly demonstrate impaired relaxation.[27] It is possible that ventricular end-diastolic pressure is not a robust measure of diastolic function in pre-superior cavopulmonary anastomosis volume-loaded physiology, as volume-loaded ventricles are less stiff and more compliant than normal or pressure-loaded hearts.[28] Furthermore, the pre-superior cavopulmonary anastomosis population has an altered atrial and venous reservoir because the systemic and pulmonary venous systems drain into the systemic ventricle. The diastolic function indices that were evaluated in this study were originally derived from patients with a relatively small venous reservoir (pulmonary venous drainage only). It is unsurprising that these echo indices may not reflect end-diastolic compliance in single ventricle anatomy where there are significant alterations in the venous reservoir and, therefore, atrioventricular interaction. Other potential explanations for the lack of correlations include the use of fluid-filled catheters, which have limited fidelity when compared to conductance catheters, and the known volume dependence of ventricular enddiastolic pressure. Additional studies involving the comparison of echo measurements of diastolic function with alternative invasive measurements of diastolic function shown to correlate with outcomes, such as Tau or maximal rate of rise of ventricular pressure, would be useful. As these measurements and the use of conductance catheters were not standard of care in paediatrics at the time of this study, and the risks could impact study recruitment to answer the primary question of the trial, these measurements were not performed as a part of this study and could therefore not be a part of our ancillary analysis.

Three smaller studies of single ventricle patients have demonstrated good correlation between some tissue Doppler indices of ventricular function and invasive measurements of filling pressures.[12,13,29] In comparison to these prior studies, strengths of our study include the larger, more homogenous patient population and the fact that the measurements were blinded. Our cohort was studied prior to the superior cavopulmonary anastomosis and these other studies incorporated patients at various stages of palliation (pre-superior cavopulmonary anastomosis, post-superior cavopulmonary anastomosis, and Fontan).

Approximately half of the patients in the study had a summation wave (fusion of the early and late diastolic inflow pulse wave Doppler), likely due to the higher heart rates typical for infants. As a result, Doppler measurement of the atrial contribution to diastole could not be evaluated. This highlights the practical limitations of using these echo variables to evaluate diastolic dysfunction in this age group.

Limitations

The echocardiograms and cardiac catheterisations in which the data were compared were not simultaneous. In 14% of the patients, 14–60 days elapsed between the echocardiograms and cardiac catheterisation. Therefore, the observed lack of association between echo variables and catheter-derived ventricular end-diastolic pressure may be related to having two points of comparison under differing conditions, although there were unlikely to be significant changes in myocardial properties in the relatively short interval between the studies.

While our study incorporates patients with a range of ventricular end-diastolic pressure that was normally distributed, there were few patients with clinically significant elevations of ventricular end-diastolic pressure. This may have decreased the power of our study to detect important correlations.

Our study included a population of single ventricle infants with heterogenous anatomical types, with only 13 left ventricular dominant patients and 62 right ventricular dominant patients. Analysis incorporating only lateral annular velocities was limited by power.

Conclusions

Conventional two-dimensional, pulsed wave and tissue Doppler echocardiographic measures of ventricular function do not correlate with ventricular end-diastolic pressure at cardiac catheterisation in infants with single ventricle physiology prior to superior cavopulmonary anastomosis. These limitations should be factored into the interpretation of quantitative echocardiographic data in this patient population.

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References

1. Milanesi O, Stellin G, Colan SD, et al. Systolic and diastolic performance late after the Fontan procedure for a single ventricle and comparison of those undergoing operation at <12 months of age and at >12 months of age. Am J Cardiol 2002; 89: 276–280. [PubMed: 11809428]
2. Ommen SR, Nishimura RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. Circulation 2000; 102: 1788–1794. [PubMed: 11023933]
3. Arteaga RB, Hreybe H, Patel D, Landolfo C. Derivation and validation of a diagnostic model for the evaluation of left ventricular filling pressures and diastolic function using mitral annulus tissue Doppler imaging. Am Heart J 2008; 155: 924–929. [PubMed: 18440343]
4. David C, Almeida A. Pulmonary transvalvular and venous flows in the estimation of left ventricular diastolic pressures. A comparative Doppler-catheterization study. Rev Port Cardiol 2001; 20: 987–1000. [PubMed: 11770447]
5. Yamamoto K, Nishimura RA, Burnett JC, Redfield MM. Assessment of left ventricular end-diastolic pressure by Doppler echocardiography: contribution of duration of pulmonary venous versus mitral flow velocity curves at atrial contraction. J Am Soc Echocardiogr 1997; 10: 52–59. [PubMed: 9046493]

6. Kimura K, Murata K, Tanaka N, et al. The importance of pulmonary venous flow measurement for evaluating left ventricular end-diastolic pressure in patients with coronary artery disease in the early stage of diastolic dysfunction. J Am Soc Echocardiogr 2001; 14: 987–993. [PubMed: 11593203]

7. Rossvoll O, Hatle LK. Pulmonary venous flow velocities recorded by transthoracic Doppler ultrasound: relation to left ventricular diastolic pressures. J Am Coll Cardiol 1993; 21: 1687–1696. [PubMed: 8496538]

8. Savage A, Hlavacek A, Ringewald J, Shirali GS. Evaluation of the myocardial performance index and tissue Doppler imaging by comparison to near-simultaneous catheter measurements in pediatric cardiac transplant patients. J Heart Lung Transplant 2010; 29: 853–858. [PubMed: 20471861]

9. O'Leary PW, Durongpisitkul K, Cordes TM, et al. Diastolic ventricular function in children: a Doppler echocardiographic study establishing normal values and predictors of increased ventricular end-diastolic pressure. Mayo Clin Proc 1998; 73: 616–628. [PubMed: 9663189]

10. Border WL, Michelfelder EC, Glascock BJ, et al. Color M-mode and Doppler tissue evaluation of diastolic function in children: simultaneous correlation with invasive indices. J Am Soc Echocardiogr 2003; 16: 988–994. [PubMed: 12931112]

11. Colan SD, Shirali GS, Margossian R, et al. The ventricular volume variability study of the Pediatric Heart Network: study design and impact of beat averaging and variable type on the reproducibility of echocardiographic measurements in children with chronic dilated cardiomyopathy. J Am Soc Echocardiogr 2012; 25: 842–854.e6. [PubMed: 22677278]

12. Menon SC, Gray R, Tani LY. Evaluation of ventricular filling pressures and ventricular function by Doppler echocardiography in patients with functional single ventricle: correlation with simultaneous cardiac catheterization. J Am Soc Echocardiogr 2011; 24: 1220–1225. [PubMed: 21962450]

13. Chowdhury SM, Butts RJ, Buckley J, et al. Comparison of pressure-volume loop and echocardiographic measures of diastolic function in patients with a single-ventricle physiology. Pediatr Cardiol 2014; 35: 998–1006. [PubMed: 24584211]

14. Husain N, Gokhale J, Nicholson L, Cheatham JP, Holzer RJ, Cua CL. Noninvasive estimation of ventricular filling pressures in patients with single right ventricles. J Am Soc Echocardiogr 2013; 26: 1330–1336. [PubMed: 24035700]

15. Hsu DT, Mital S, Ravishankar C, et al. Rationale and design of a trial of angiotensin-converting enzyme inhibition in infants with single ventricle. Am Heart J 2009; 157: 37–45. [PubMed: 19081394]

16. Hsu DT, Zak V, Mahony L, et al. Enalapril in infants with single ventricle: results of a multicenter randomized trial. Circulation 2010; 122: 333–340. [PubMed: 20625111]

17. Margossian R, Schwartz ML, Prakash A, et al. Comparison of echocardiographic and cardiac magnetic resonance imaging measurements of functional single ventricular volumes, mass, and ejection fraction (from the Pediatric Heart Network Multicenter Fontan Cross-Sectional Study). Am J Cardiol 2009; 104: 419–428. [PubMed: 19616678]

18. Tei C, Dujardin KS, Hodge DO, Kyle RA, Tajik J, Seward JB. New noninvasive index for combined systolic and diastolic ventricular function. J Cardiol 1995; 26: 135–136. [PubMed: 7674144]

19. Cui W, Roberson DA, Chen Z, Madronero LF, Cuneo BF. Systolic and diastolic time intervals measured from Doppler tissue imaging: normal values and Z-score tables, and effects of age, heart rate, and body surface area. J Am Soc Echocardiogr 2008; 21: 361–370. [PubMed: 17628402]

20. Friedberg MK, Silverman NH. The systolic to diastolic duration ratio in children with hypoplastic left heart syndrome: a novel Doppler index of right ventricular function. J Am Soc Echocardiogr 2007; 20: 749–755. [PubMed: 17543747]

21. Okumura K, Slorach C, Mroczek D, et al. Right ventricular diastolic performance in children with pulmonary arterial hypertension associated with congenital heart disease: correlation of echocardiographic parameters with invasive reference standards by high-fidelity micromanometer catheter. Circ Cardiovasc Imaging 2014; 7: 491–501. [PubMed: 24577356]

22. Friedberg MK, Silverman NH. The systolic to diastolic duration ratio in children with heart failure secondary to restrictive cardiomyopathy. J Am Soc Echocardiogr 2006; 19: 1326–1331. [PubMed: 17098134]

23. Moiduddin N, Texter KM, Zaidi AN, et al. Two-dimensional speckle strain and dyssynchrony in single left ventricles vs. normal left ventricles. Congenit Heart Dis 2010; 5: 579–586. [PubMed: 21106018]

24. Stiver C, Gokhale J, Husain N, et al. Catheterization diastolic pressures correlate with diastolic dyssynchrony in patients with single right ventricles. Echocardiography 2014; 31: 370–374. [PubMed: 24298988]

25. Williams IA, Sleeper LA, Colan SD, et al. Functional state following the Fontan procedure. Cardiol Young 2009; 19: 320–330. [PubMed: 19523266]

26. Border W, Syed AU, Michelfelder EC, et al. Impaired systemic ventricular relaxation affects postoperative short-term outcome in Fontan patients. J Thorac Cardiovasc Surg 2003; 126: 1760–1764. [PubMed: 14688684]

27. Dragulescu A, Mertens L, Friedberg MK. Interpretation of left ventricular diastolic dysfunction in children with cardiomyopathy by echocardiography: problems and limitations. Circ Cardiovasc Imaging 2013; 6: 254–261. [PubMed: 23343514]

28. Janicki JS, Brower GL. The role of myocardial fibrillar collagen in ventricular remodeling and function. J Card Fail 2002; 8: S319–S325. [PubMed: 12555139]

29. Learn CP, Yates AR, Nicholson L, Milton K, Lloyd E, Cua CL. Tissue Doppler measurements correlate with central venous pressure in pediatric patients after cardiac surgery. ASAIO J 2010; 56: 377–382. [PubMed: 20559128]

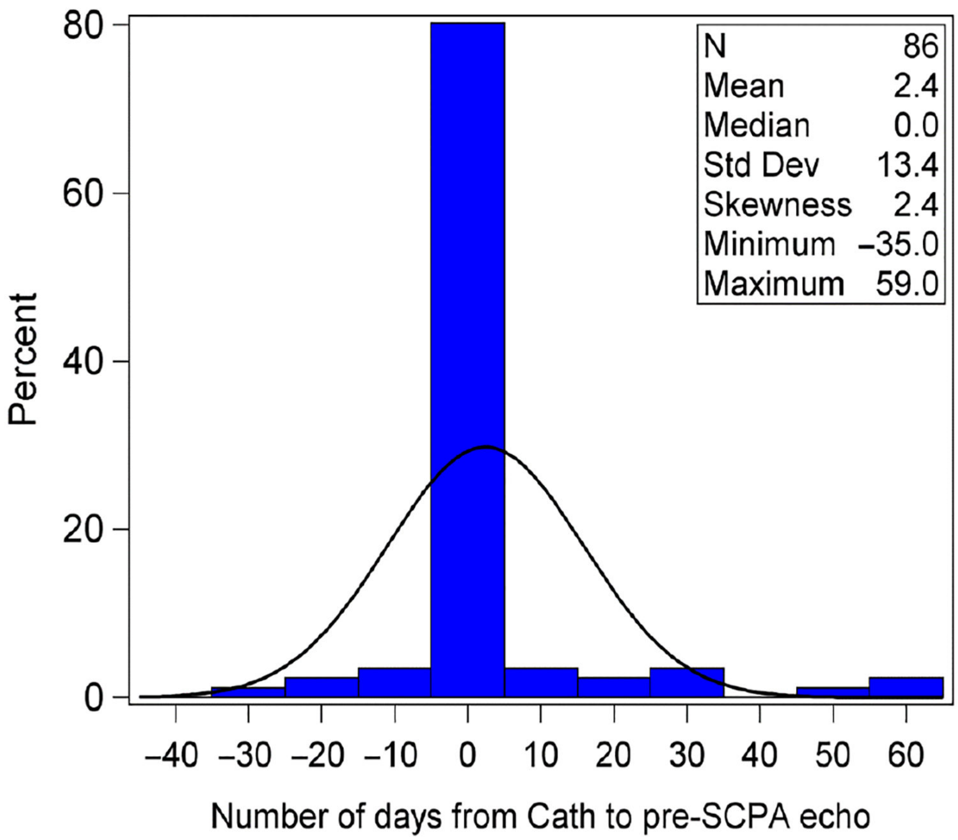

Figure 1.

Days between echocardiogram and cardiac catheterization. This graph illustrates the distribution of the number of days between the echocardiogram and cardiac catheterization among subjects with similar sedation type. A negative value on the x-axis indicates that the catheterization occurred after the echo and a positive value indicates that the catheterization occurred before the echocardiogram. Most of the echocardiograms occurred on the same day (64%) with 86% of subjects having the two studies within a two week time period. Abbreviations: SCPA = superior cavopulmonary anastomosis.

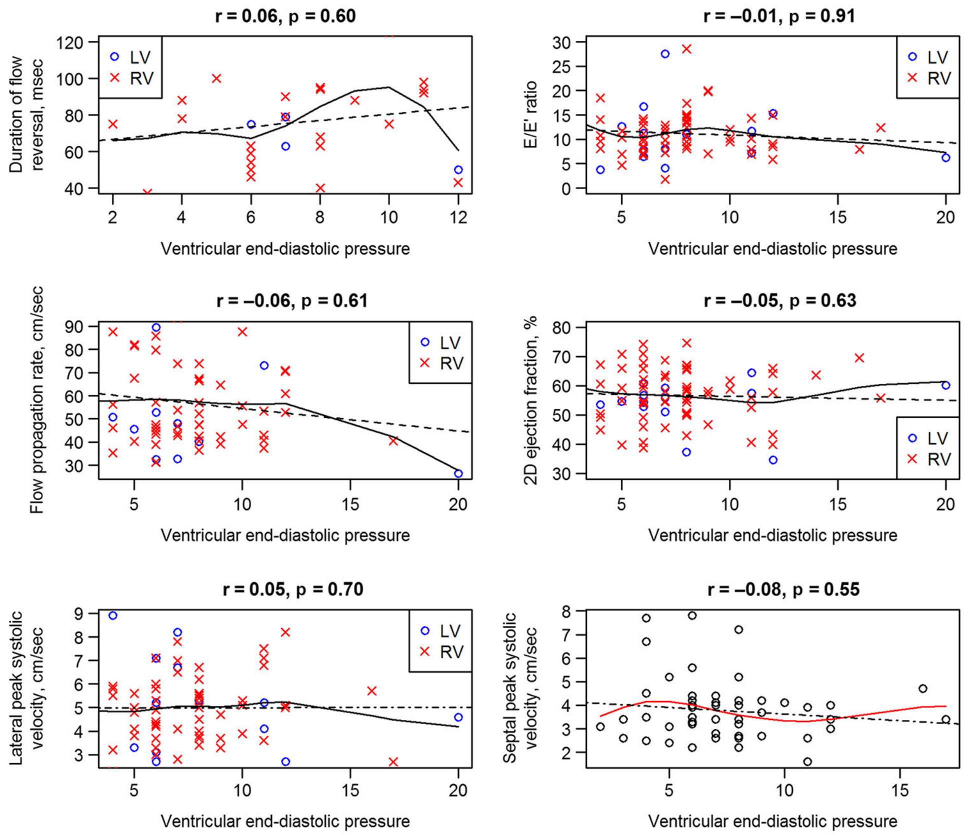

Figure 2.

These figures illustrate the relationship between each echocardiographic measure (labeled in each graph on the y-axis) and the catheter-derived ventricular end-diastolic pressure (on the x-axis). The blue open circles represent those subjects with left ventricular type morphology (LV), and the subjects denoted by a red “X” represent those with a right ventricular type morphology (RV). The solid line represents the linear fit, and dashed line represents the non-parametric fit using the generalized additive model. None of these echocardiographic variables have significant correlation with ventricular end-diastolic pressure.

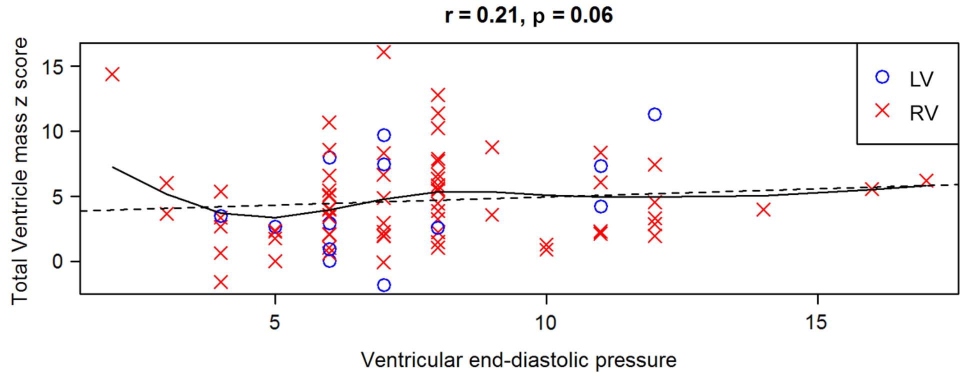

Figure 3.

This figure illustrates the relationship between total ventricular mass z-score on the y-axis and catheter-derived end-diastolic pressure on the x-axis. The blue open circles represent those subjects with left ventricular type morphology (LV), and the subjects denoted by a red "X" represent those with a right ventricular type morphology (RV). The solid line represents the linear fit, and the dashed line represents the non-parametric fit using the generalized additive model. Notice that total ventricular mass z-score does not have a significant correlation with end-diastolic pressure.

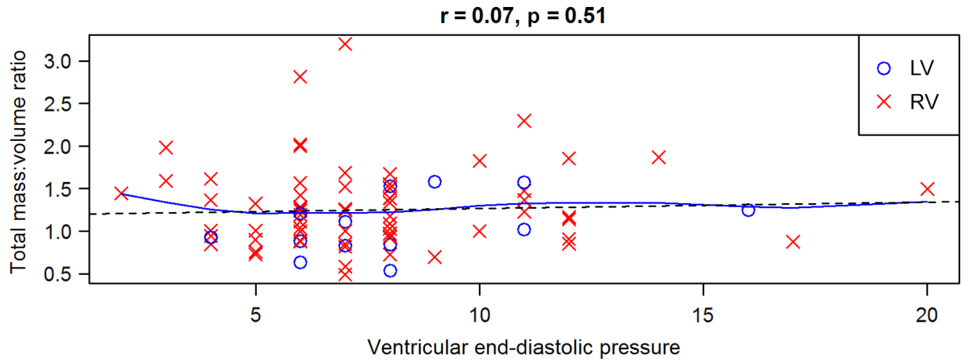

Figure 4.
This figure illustrates the relationship between total mass to volume ratio on the y-axis and catheter-derived end-diastolic pressure on the x-axis. The blue open circles represent those subjects with left ventricular type morphology (LV) and the subjects denoted by a red “X” represent those with a right ventricular type morphology (RV). The solid line represents the linear fit, and the dashed line represents the non-parametric fit using the generalized additive model. Notice that total mass to volume z-score does not have a significant correlation with end-diastolic pressure.

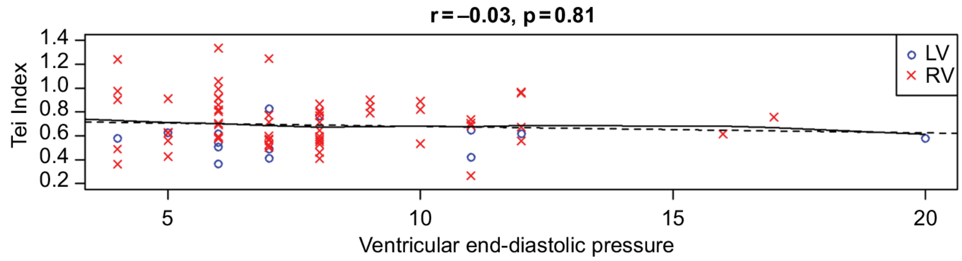

Figure 5.

This figure illustrates the relationship between Tei index* on the y-axis and catheter-derived end-diastolic pressure on the x-axis. The blue open circles represent those subjects with left ventricular type morphology (LV), and the subjects denoted by a red "X" represent those with a right ventricular type morphology (RV). The solid line represents the linear fit, and the dashed line represents the non-parametric fit using the generalized additive model. Notice that Tei index does not have a significant correlation with end-diastolic pressure.

* Tei index = (isovolumic contraction time + isovolumic relaxation time)/ejection time [16].

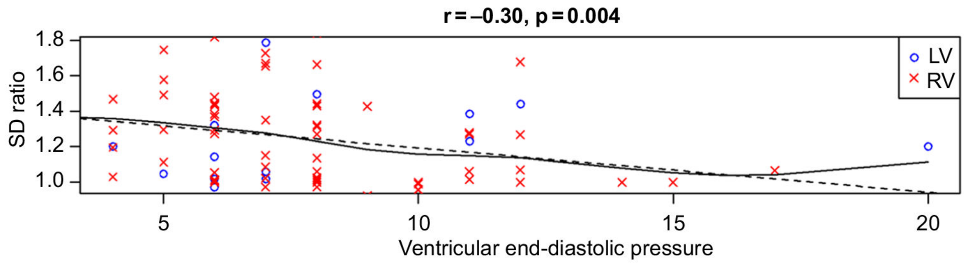

Figure 6.

This figure illustrates the relationship between S:D ratio** on the y-axis and catheter-derived end-diastolic pressure on the x-axis. The blue open circles represent those subjects with left ventricular type morphology (LV), and the subjects denoted by a red "X" represent those with a right ventricular type morphology (RV). The solid line represents the linear fit, and the dashed line represents the non-parametric fit using the generalized additive model. Notice that S:D ratio has a weak correlation with ventricular end-diastolic pressure.

** S:D = systolic duration time to diastolic duration time. *LV = left ventricular type. **RV = right ventricular type.

Table 1.

Echocardiographic variables

Pulmonary vein a-wave duration
Tissue Doppler of left, right, and septal annular velocities
(E′, S′)*
Atrioventricular pulse inflow early velocity (E)
Colour M-mode ventricular flow propagation velocity slope
Systemic ventricular ejection fraction
Total ventricular mass z-score
Mass:volume ratio
Ratio of atrioventricular valve to tissue Doppler peak early diastolic velocity (E/E′)
Tei index**
S:D ratio***

*E′ = early diastolic annular velocity; S′ = peak systolic annular velocity.

**Tei index = (isovolumic contraction time + isovolumic relaxation time)/ejection time.[16]

***S:D = systolic duration time to diastolic duration time.[17,18]

Table 2.

Study population characteristics at pre-superior cavopulmonary anastomosis echo

Variable	Mean ± SD, or n (%)
Age at echo (days)	141.6 ± 32.4
Gender	
Male	63 (73)
Female	23 (27)
Race	
White	70 (82)
Black	13 (15)
Other	2 (2)
Hispanic	8 (10)
Weight (kg)	5.7 ± 1.2
Height (cm)	61.2 ± 7.5
Ventricular dominance	
Left	14 (16)
Right	72 (84)
Type of surgery	
Norwood	69 (81)
Systemic to pulmonary shunt	10 (12)
Pulmonary artery band	3 (4)
Damus-Kaye-Stansel	3 (4)
Degree of atrioventricular valve regurgitation	
None	23 (27)
Mild	38 (44)
Moderate	24 (28)
Severe	1 (1)
Sedation type	
General anesthesia	30 (35)
Moderate sedation	56 (65)

Table 3.

Haemodynamic and echocardiographic variables for patients with similar sedation type

	N	Mean ± standard deviation	Median (interquartile range)	Range
End-diastolic pressure (mmHg)	86	7.9 ± 3.2	7 (6–9)	2–20
Pulmonary vein flow reversal duration (ms)	74	29.8 ± 40.5	0 (0–63)	0–146
Ratio of atrioventricular valve to tissue Doppler peak early diastolic velocity (E/E′)	74	11.2 ± 4.8	10.4 (7.9–13.8)	1.7–28.5
Left colour flow propagation velocity (cm/second)	10	49.2 ± 19.4	46.9 (32.7–52.8)	26.5–89.6
Right colour flow propagation velocity (cm/second)	56	58.3 ± 21.4	53.0 (42.6–70.7)	26.5–89.6
Left ventricular ejection fraction (%)	14	53 ± 8.4	55.2 (52.8–59.2)	34.6–64.5
Right ventricular ejection fraction (%)	67	57.2 ± 9.1	58.1 (50.5–64.1)	38.7–74.6
Total ventricular mass z-score	80	4.7 ± 3.5	3.9 (2.2–6.6)	−1.8–16.1
Mass:volume ratio	81	1.2 ± 0.5	1.2 (0.9–1.5)	0.5–3.2
Left lateral S′* (cm)	13	5.2 ± 2.1	5.2 (3.3–6.7)	1.6–7.8
Septal S′* (cm)	56	3.8 ± 1.3	3.5 (2.9–4.2)	1.6–7.8
Right lateral S′ (cm)	62	5.0 ± 1.4	5.0 (3.8–5.8)	2.3–8.2
Tei index**	79	0.7 ± 0.2	0.64 (0.56–0.82)	0.27–1.34
S:D ratio***	86	1.2 ± 0.3	1.2 (1.0–1.4)	0.8–2.1

* S′ = peak systolic annular velocity.

** Tei index = (isovolumic contraction time + isovolumic relaxation time)/ejection time.[16]

*** S:D = systolic duration time to diastolic duration time.

Table 4.

Correlation between end-diastolic pressure and echo variables in patients with similar sedation type

	All			Left ventricular			Right ventricular		
Echo variable	**N**	**Coefficient**	**p-value**	**N**	**Coefficient**	**p-value**	**N**	**Coefficient**	**p-value**
Pulmonary vein flow reversal duration (ms)	74	0.06	0.6	13	0.2	0.6	61	0.05	0.7
Flow propagation velocity (cm/second)	66	−0.06	0.6	10	−0.3	0.4	56	−0.06	0.7
Ratio of atrioventricular valve to tissue Doppler peak early diastolic velocity (E/E′)	75	−0.01	0.9	14	0.06	0.8	61	−0.04	0.8
Ejection fraction (%)	81	−0.05	0.6	14	0.1	0.7	67	−0.1	0.5
Total ventricular mass z-score	80	0.2	0.06	13	0.4	0.2	67	0.2	0.2
Mass:volume ratio	81	0.1	0.5	14	0.4	0.2	67	0.04	0.8
Lateral peak velocity (S′, cm/second)	75	0.03	0.7	13	−0.2	0.5	62	0.1	0.4
Septal peak systolic velocity (S′, cm/second)	56	−0.1	0.6		na			na	
S:D ratio*	86	−0.3	0.004	14	0.5	0.06	72	−0.4	<0.001
Tei index**	79	−0.03	0.8	14	0.2	0.5	65	−0.06	0.7

*S:D = systolic duration time to diastolic duration time.[17,18]

**Tei index = (isovolumic contraction time + isovolumic relaxation time)/ejection time.[16]

Table 5.

Comparison of echocardiographic variables between patients by end-diastolic pressure severity

	Patients with end-diastolic pressure <10		Patients with end-diastolic pressure ≥10			
Variable	**N**	**Mean ± standard deviation**	**N**	**Mean ± standard deviation**	**Odds ratio (95% confidence interval)**	**p**
Pulmonary vein flow reversal duration (ms)	58	28.1 ± 39.1	16	36.1 ± 46.0	1 (0.99–1.02)	0.5
Left-sided flow propagation velocity (cm/second)	8	49.0 ± 18.1	2	49.8 ± 32.9	1 (0.92–1.09)	1
Right-sided flow propagation velocity (cm/second)	44	59.2 ± 22.9	12	55.1 ± 15.2	1 (0.96–1.02)	0.6
Ratio of atrioventricular valve to tissue Doppler peak early diastolic velocity (E/E′)	58	11.6 ± 5.2	17	10.0 ± 3.0	0.9 (0.8–1.1)	0.2
Right ventricular ejection fraction (%)	53	57.6 ± 9.1	14	55.8 ± 9.3	1 (0.92–1.05)	0.5
Total ventricular mass z-score	63	4.7 ± 3.7	17	4.7 ± 2.8	1 (0.9–1.2)	1
Mass:volume ratio	63	1.2 ± 0.5	18	1.4 ± 0.4	1.7 (0.6–5)	0.3
Left lateral peak systolic velocity (S′, cm/second)	9	5.6 ± 2.3	4	4.2 ± 1.1	0.6 (0.3–1.4)	0.3
Septal peak systolic velocity (S′, cm/second)	46	3.8 ± 1.4	10	3.5 ± 0.9	0.8 (0.4–1.5)	0.4
Right lateral peak systolic velocity (S′, cm/second)	49	4.8 ± 1.3	13	5.5 ± 1.6	1.4 (0.9–2.2)	0.1
S:D ratio *	65	1.3 ± 0.3	21	1.1 ± 0.2	0.1 (0.01–0.8)	0.03
Tei index **	62	0.7 ± 0.2	17	0.7 ± 0.2	0.5 (0.04–7.9)	0.7

*S:D = systolic duration time to diastolic duration time.[17,18]

**Tei index = (isovolumic contraction time + isovolumic relaxation time)/ejection time.[16]