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Speckle-Tracking Echocardiographic Measures of Right Ventricular Diastolic Function Correlate with Reference-Standard Measures Before and After Preload Alteration in Children

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Abstract

Background—The accuracy of echocardiographic measures of right ventricular (RV) diastolic function has been sparsely studied. Our objective was to evaluate the correlation between echocardiographic and reference standard measures of RV diastolic function derived from micromanometer pressure analysis before and after preload alteration in children.

Methods—Echocardiograms and micromanometer pressure analyses were prospectively performed before and after fluid bolus in children undergoing right heart catheterization. The isovolumic relaxation time constant (tau) and end-diastolic pressure (EDP) were measured. Conventional and speckle-tracking echocardiographic (STE) parameters of RV systolic and diastolic function were assessed. Normal saline bolus was given to increase RV EDP by 20%.

Results—28 studies were performed in 22 patients with congenital heart disease or post heart transplantation. Mean age was 8.7 ± 6.1 yrs. RV longitudinal early diastolic strain rate (EDSR) correlated with tau before ($r = 0.57$, $p = 0.001$) and after fluid bolus ($r = 0.48$, $p = 0.008$). No conventional echocardiographic measures correlated with tau both before and after fluid bolus. Multiple regression analysis revealed RV EDSR and LV circumferential EDSR as independent predictors of RV tau. There were no independent predictors of EDP.

Conclusion—RV EDSR appears to correlate with the reference-standard measure of early active ventricular relaxation in children at baseline and after changes in preload. Conventional echocardiographic measures of diastolic function were not predictive of diastolic function after preload alteration. Future studies should assess the prognostic significance of STE measures of diastolic function in this population.

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Disclosures

None

Keywords

echocardiography; diastole; pediatrics; heart defects - congenital

Introduction

Pediatric right ventricles (RV) are often afflicted with abnormal morphologies and loading conditions resulting from congenital heart disease (CHD). RV diastolic function is an important component of cardiovascular performance and may be an important determinant of outcomes in these children.[1, 2] However, the non-invasive assessment of RV diastolic function is limited in children with CHD.

The interest in the contribution of diastolic dysfunction to adult heart failure has resulted in the development of guidelines for the echocardiographic assessment of diastolic function in the adult left ventricle (LV).[3] However, these guidelines are not applicable to the pediatric population.[4] There are no guidelines for the assessment of RV diastolic function in the pediatric population due to a number of important barriers inhibiting their routine clinical use. [4, 5] First, conventional indices of diastolic function have not been well validated against reference standard measures in this population. Second, newer promising measures of diastolic function, such as those obtained from speckle-tracking echocardiography (STE), have been inadequately investigated. Finally, the effects of acute loading changes on the accuracy of echocardiographic measures of RV diastolic function are poorly understood. Obtaining this information would allow practitioners to determine which echocardiographic measures are most accurate, and potentially useful, in assessing RV diastolic function in this population.

The aims of this study were to: 1) assess the relationship between conventional echocardiographic/STE measures of RV diastolic function and invasive measures of diastolic function derived from micromanometer pressure analysis, 2) assess the effects of an acute increase in preload on invasive and echocardiographic measures of RV diastolic function, and 3) assess for changes in the correlation between invasive and echocardiographic measures after preload alteration. We hypothesized that some echocardiographic measures of RV diastolic function would correlate well with invasive reference standard methods both before and after preload alteration.

Methods

Patient population

All children aged 0–18 years undergoing clinically indicated diagnostic right heart catheterization at the Medical University of South Carolina were recruited prospectively so that correlations between invasive and echocardiographic measures of diastolic function could be assessed in a representative sample of children who undergo cardiac catheterization. Exclusion criteria included: 1) medical status for which participation in the study presented more than minimal risk as determined by the attending physician such as heart failure with an end-diastolic pressure (EDP) > 15 mmHg, history of arrhythmia with

hemodynamic instability, or the development of suboptimal hemodynamic or respiratory status during the routine diagnostic portion of the catheterization, 2) non-sinus rhythm, 3) patients with primary left sided cardiac pathology such as dilated or hypertrophic cardiomyopathy, left-sided obstructive lesions, or left-sided volume loading lesions (e.g. VSD, PDA). The protocol was approved by our institutional review board. Informed consent was obtained from the parent or legal guardian of minors or from the participants of age 18.

Cardiac catheterization

All patients underwent general anesthesia per the institution's protocol. Patients underwent routine diagnostic testing with fluid-filled catheters. All study data were collected following the patient's hemodynamic data collection and prior to any angiography or interventions. A baseline echocardiogram was performed. Then, a 1.6 F high fidelity micromanometer catheter (Millar Instruments, Inc, Houston, TX) was placed in the right ventricle. RV pressure data was recorded in triplicate over 10 seconds during an expiratory breath hold. Next, a 5 mL/kg normal saline bolus was given with the goal to increase RV EDP by 20%. If after the initial bolus EDP rose less than 20%, a second bolus was administered. A second set of micromanometer pressure measurements were then performed and a second echocardiogram followed. Micromanometer data was recorded at a sampling rate of 1000 Hz. The reference standard measure of early active ventricular relaxation derived from micromanometer pressure analysis included the time constant of RV relaxation (tau). In addition, RV end-diastolic pressure (EDP) was measured. Tau was calculated using the logistic method due to its superior load resistance when compared to the method of Weiss.[6, 7] Pressure data was obtained using standard equipment approved for use in human subjects (INCA® intracardiac analyzer; CD Leycom, Netherlands). Micromanometer pressure analysis was performed offline using specialized software (LabChart Pro v.8; ADInstruments, Colorado Springs, CO).

Echocardiographic measurements

Transthoracic echocardiograms were performed using a Phillips iE33 system (Philips Medical Systems, Andover, MA). Echocardiograms were sent uncompressed and at native frame rates to the encrypted server for analysis. All measurements were made off-line by a single blinded reviewer (SC) and averaged over three beats. Half of the echocardiograms were selected randomly for observer variability analysis. Measurements were repeated 4 weeks later to assess intraobserver variability. Measurements were also repeated by a second blinded reviewer (SG) to assess interobserver variability.

Echocardiograms were performed by a single experienced sonographer following a protocol which included a complete set of standardized views to evaluate ventricular mechanics. Peak early (E), late (A) diastolic Doppler velocities and E deceleration time across the tricuspid valve were analyzed. Pulsed-wave spectral tissue Doppler (TDI) velocities of the tricuspid annulus, septum, and lateral mitral annulus (s′, e′ and a′) were obtained. Derived ratios (E:A, E:e′) were calculated. Isovolumic relaxation time (IVRT′) was derived using TDI at the tricuspid annulus and measured from the end of the s′ wave to the beginning of the e′ wave. Myocardial performance index (MPI) was calculated as [(isovolumic relaxation time + isovolumic contraction time)/ejection time], measured using TDI at the tricuspid annulus.

Left ventricular Doppler and TDI (septal and left lateral) velocities were also assessed. Right atrial (RA) area was assessed by tracing its endocardial border in the apical 4-chamber view at end-systole. RA volume was then estimated by the mono-plane area-length ellipsoid method and indexed to body surface area.[8] The S:D duration ratio was measured using TDI as previously described.[9] Other conventional measures of systolic RV and LV function were also assessed, such as tricuspid annular systolic plane excursion (TAPSE), RV fractional area change (FAC), and LV ejection fraction (EF) by the 5/6 area length method.

Two-dimensional speckle-tracking echocardiography was performed offline by a single, blinded observer using vendor-independent software (2D Cardiac Performance Analysis v. 3.0, TomTec Imaging Systems, Inc, Munich, Germany). Myocardial motion was tracked through the cardiac cycle, calculating myocardial deformation from echogenic speckles in the B-mode image. Images were obtained in the apical 4-chamber window at frame rates between 60 and 120 frames per second. Endocardium and epicardium were manually traced in the RV from the lateral tricuspid annulus to the septal component of the tricuspid annulus (Figure 1). The septum was included because of its importance to global RV function.[10] Speckle-tracking measures of deformation included peak longitudinal strain, strain rate, and early diastolic strain rate (EDSR). The ratio between early tricuspid inflow Doppler velocity and EDSR was then calculated (E:EDSR).[11] Left ventricular measures of deformation were also assessed from the apical 4-chamber (longitudinal) and parasternal short axis (circumferential) views. Global deformation measurements were calculated as an average of 6 segments. Tracking was visually assessed, and deformation curves were not accepted if greater than one segment demonstrated inadequate tracking.

Statistical Analysis

Paired t-tests (or Wilcoxon Signed Rank Test for non-parametric data) were used to assess for changes between variables before and after saline bolus to assess for load sensitivity. Pearson's (or Spearman's for non-parametric data) correlation was used to assess for a linear relationship between echocardiographic variables and invasive variables. Echocardiographic measures that correlated with invasive measurements either before or after preload alteration were included in a multivariable stepwise linear regression analysis to assess for independent association with the dependent variable, adjusted for age and heart rate. Observer variability was assessed using intraclass correlation coefficient for absolute agreement utilizing a two-way random effects model. In addition, the percent error between the 2 measurements as (measure 1–measure 2)/mean of the two measures was calculated. A p-value ≤ 0.01 was considered significant when assessing correlations between echocardiographic and invasive indices to account for multiple comparisons. A p-value of < 0.05 was considered significant for all other tests. Statistics were analyzed using SPSS v. 22 (IBM, New York, NY, USA).

Results

Twenty-eight studies were performed in 24 patients. Demographic and clinical data from these patients are presented in Table 1. Most patient indications for catheterization included either routine surveillance biopsy after orthotopic heart transplantation or hemodynamic

evaluation in patients with CHD (atrial septal defect, pulmonary valve stenosis, RV to pulmonary artery conduit stenosis or insufficiency) +/− intervention (9/14 patients in CHD group) such as atrial septal defect device closure (n = 3) or balloon angioplasty of the pulmonary valve (n = 1) or RV-PA conduit (n = 5). Therefore we classified patients into one of those two groups. A total of 10 transplant patients were enrolled, four of whom underwent two separate catheterizations during the study period – totaling 14 studies. All 14 patients in the CHD group had a single study catheterization. Two studies displayed fused E and A waves and e′ and a′ waves – these measures and their associated ratios were excluded from analysis.

Baseline echocardiographic and invasive data

Baseline data from the entire cohort and a comparison between the transplant and CHD cohorts is summarized in Table 2. There were no statistically significant differences in tau or EDP between groups. Doppler E and A velocity, TDI tricuspid e′, MPI, and E/EDSR ratio were different between groups. No other statistically significant differences were found.

Baseline correlations with invasive parameters

There was no correlation between tau and EDP. Baseline correlations between invasive and echocardiographic parameters of RV diastolic function are reported in Table 3. In the entire cohort, TV TDI e′, a′, and RV EDSR (Figure 2) correlated with tau. Tricuspid E:e′ ratio and E:EDSR ratio correlated with EDP at baseline. The only LV diastolic parameter to correlate with RV tau was LV circumferential EDSR ($r = -0.55$, $p = 0.003$). No LV diastolic parameter correlated with EDP. No RV or LV systolic parameters correlated with tau or EDP.

Correlations were then performed separately in the transplant and CHD groups. In the transplant group, the only measures to correlate with RV tau prebolus were LV circumferential strain rate ($r = 0.70$, $p = 0.005$) and LV early diastolic strain rate ($r = -0.80$, $p = 0.001$). No measure correlated with EDP in the transplant group. In the CHD group, only RV EDSR correlated with tau ($r = -0.69$, $p = 0.006$). No measure correlated with RV EDP in the CHD group.

Effect of volume loading on invasive and echocardiographic parameters

All patients had an adequate response to fluid bolus, with an increase in RV EDP > 20% (14 patients required 10 mL/kg). Heart rate decreased from 84 ± 16 bpm to 81 ± 15 bpm, $p < 0.01$. Changes in both invasive and echocardiographic measures of diastolic function are reported in Table 4. RV tau increased by 5.4%. Spectral Doppler tricuspid E and A significantly changed with fluid bolus conditions while TDI e′ and a′ did not. Tricuspid E:e′ increased by 9.8%. No other conventional measures of RV diastolic function changed with fluid bolus. Speckle-tracking derived RV early diastolic strain rate increased with an acute loading change by 13.2%.

Mitral inflow Doppler E velocity increased from 52.5 ± 17.9 cm/s to 57.5 ± 20.1 cm/s, $p < 0.01$. Other spectral Doppler, TDI, or STE measures of LV diastolic function did not significantly change after saline bolus. No measure of RV or LV systolic function,

conventional or STE, changed with fluid bolus. The percent change in both invasive and non-invasive measures after saline bolus were not significantly different between the transplant and CHD groups.

Influence of volume loading on correlations with invasive parameters

After fluid bolus, only RV EDSR ($r = -0.49$, $p = 0.008$) and TV TDI a′ ($r = -0.60$, $p = 0.001$) retained correlation with tau in the entire cohort. No echocardiographic measures of RV diastolic function retained correlation with EDP, though E:EDSR trended toward statistical significance ($r = 0.47$, $p = 0.016$). No LV measure of diastolic function retained correlation with tau or EDP after fluid bolus. No RV or LV measure of systolic function retained correlation with tau or EDP after fluid bolus. There was no significant association between percent change in invasive measures vs. percent change in non-invasive measures after fluid bolus.

Independent Predictors of Reference Standard Measures of RV Diastolic Function

The results of multivariable analysis are summarized in Table 5. In the group as a whole, RV longitudinal EDSR and LV circumferential EDSR were both independent predictors of tau. There were no independent predictors of RV EDP. Independent predictors of invasive measures of RV diastolic function were not similar between the transplant and CHD groups.

Observer Variability Analysis

Results from observer variability analysis are reported in Table 6.

Discussion

The most robust echocardiographic predictors of RV tau in this study were derived from STE. Specifically, we found that: 1) RV EDSR showed a stronger correlation with tau than conventional echocardiographic measures of RV diastolic function at baseline, 2) Tau and RV EDSR demonstrated changes with an acute increase in preload, 3) RV EDSR retained correlation with tau after fluid bolus and was an independent predictor of tau upon multivariable regression.

Validation of echocardiographic measures of RV early active relaxation

Active relaxation is the energy-consuming process of calcium-cycling in the myocyte that results in extension of the sarcomere to its resting length. This process results in early diastolic ventricular pressure decline during isovolumic relaxation and early ventricular chamber filling. This process is typically represented by tau.

It is clear that RV diastolic dysfunction influences outcomes in patients with right heart disease.[1, 2, 12] However, repetitive invasive assessments of RV hemodynamics and filling pressures are impractical in children. Echocardiographic tools to assess RV diastolic function have the potential to be useful in this population. As such, determining the ability of echocardiography to accurately assess ventricular function by comparing it to reference standard methods is a priority for echocardiography.[13] This issue has been evaluated by many groups in both the left ventricle[14–17] and even the single ventricle[18–20], but it

appears to be less well studied in the pediatric right ventricle. We found that early diastolic STE measures correlated modestlt with invasive measures of early active relaxation at baseline and independently predicted tau in the multivariable model. Okumura et al recently assessed the correlation between echocardiographic and reference standard measures of diastolic function in children with pulmonary artery hypertension.[9] Similar to our study, their group found a modest independent association between tau and RV EDSR. The congruence in echocardiographic and invasive associations between this previous study and the current study suggests that RV EDSR may indeed be a correlate of RV active relaxation. Future studies should assess the clinical utility of this measure by directly assessing its relationship to patient outcomes.

Changes in measures and correlations after preload alteration

Ideally, echocardiographic measures of diastolic function could be relied upon to correlate with reference standard methods under changing physiologic conditions. We found RV tau to be weakly preload sensitive, similar to previous studies investigating the LV.[6, 7, 21] Studies assessing the preload sensitivity of STE strain rates have been mixed, though few studies have been performed in the pediatric RV.[18, 22] The preload sensitivity of RV EDSR appears to be supported by the current study.

This study also assessed correlations between echocardiographic and invasive measures before and after preload alteration. Few measures retained correlation with tau after saline bolus. RV EDSR retained its modest correlation with tau before and after fluid bolus and was the only independent predictor of tau in the entire cohort. However, the percent change in tau was not associated with the percent change in RV EDSR. RV EDSR may be a measure of early active ventricular relaxation, but it does not appear to be a true surrogate of tau. We found a modest correlation between RV EDP and both RV E:e′ and E:EDSR at baseline. However, after we raised RV EDP by saline bolus, the correlations between these measures were no longer significant. Data regarding the utility of RV E:e′ as a surrogate for RV EDP has been mixed.[9, 23, 24] This may be secondary to multiple factors. First, E:e′ does not correlate with EDP well in patients with normal early active relaxation or normal EDP.[25] In addition, impairment in early active relaxation (as measured by E:e′) may occur prior to an elevation in EDP, making EDP an insensitive marker of early developing diastolic dysfunction.[26]

Comparisons between the CHD and transplant groups

We found no differences in invasive measures of diastolic function between the transplant and CHD groups. Patients with abnormal loading conditions, such as the CHD cohort in this study, are known to be at risk for diastolic dysfunction. It has been shown that pediatric heart transplant recipients also demonstrate RV diastolic dysfunction after transplantation.[27] This may explain the similarities between groups.

In the transplant group, the only measure that correlated independently with RV tau was LV circumferential EDSR. The importance of LV-RV interactions and ventricular interdependence in biventricular cardiac function is known; however, it especially pronounced in pediatric heart transplant recipients.[28] As RV diastolic dysfunction is

associated with mortality in transplant patients, there appears to be merit in the careful evaluation of biventricular diastolic function in this group.[29]

Speckle-tracking echocardiographic assessment of diastolic function

The independent predictors of tau in this study were derived using STE. Strain rate derived from STE may be advantageous over traditional Doppler and TDI methods for assessment of RV diastolic function due to its angle independence, relative geometry independence, and independence from the effects of tethering. In addition, STE measures assess more segments of myocardium than TDI measures which are conventionally measured at the base. These advantages may contribute to the higher correlation seen between STE and tau when compared to conventional measures. Observer variability in this study was quite good, comparable to other prospective studies.[9] Speckle-tracking measures of deformation, based on our findings, have the potential to be an accurate method to assess diastolic function. Future studies should investigate the clinical application of speckle-tracking assessments of RV diastolic function.

Limitations

The sample was relatively small, from a single center, and heterogeneous in nature. It is likely that correlations between echocardiographic and reference standard measures differ between disease processes (for example, volume vs. pressure loaded hearts) – our small sample size did not allow us to differentiate between smaller subgroups. Correlations may have been disproportionately influenced by patients that had more than one study. The invasive and echocardiographic recordings were not simultaneous, however, they were recorded within seconds to minutes of each other under constant anesthetic conditions, likely making the confounding effect small. All studies were performed under general anesthesia – these findings were not confirmed in a non-sedated group. However, assessing these correlations in a non-sedated group is not feasible in children as no child undergoes catheterization unsedated. We did not assess the reference-standard measure of RV stiffness derived from pressure-volume analysis as conductance catheters were not used in this study. Therefore we could not determine which echocardiographic parameters best correlated with the reference standard measures of ventricular stiffness. Strain rates from 2D STE are undersampled compared to color TDI due to their reliance on lower frame rates. Further validation is needed when technological advancements allow high frame rate 2D imaging.

Conclusion

STE measures of RV diastolic function show a modest correlation to reference standard measures. RV EDSR may adequately represent early active RV relaxation in children at baseline and after changes in preload, but does not appear to be a true surrogate of tau. Conventional echocardiographic measures of diastolic function are less reliable after preload alteration. STE is a promising tool in the non-invasive assessment of RV diastolic function. Future studies should assess the prognostic significance of RV STE in children.

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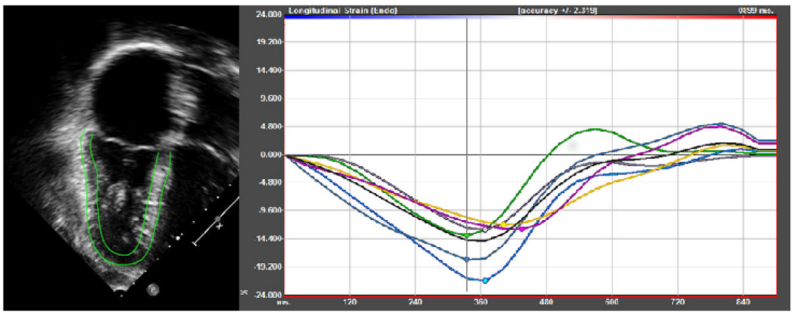

Figure 1.

This figure demonstrates the endocardial and epicardial tracing when performing speckle-tracking echocardiography and the resultant strain waveforms after analysis.

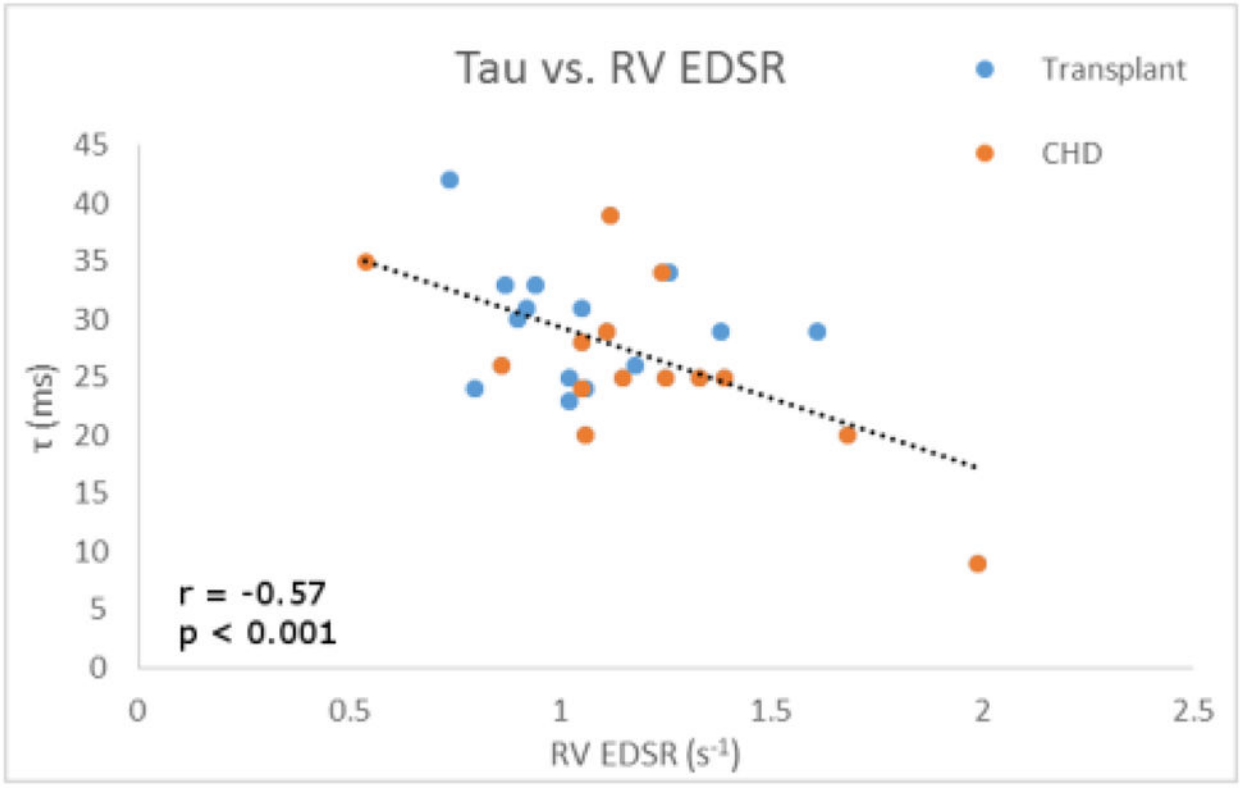

Figure 2.

Relationship between invasive reference-standard measurements obtained by high-fidelity micromanometer catheter and noninvasive parameters by echocardiography prior to preload alteration

Table 1

Patient Demographics

	All studies (n = 28)	Transplant (n = 14)	CHD (n = 14)	p-value*
Age (years)	8.7 ± 6.1	10.2 ± 5.6	7.2 ± 6.3	0.29
Women, n (%)	15 (54%)	10 (71%)	5 (36%)	0.17
Height (cm)	119 ± 33	124 ± 29	115 ± 38	0.50
Weight (kg)	23.7 (33.8)	29.0 (31.7)	19.5 (38.6)	0.61
BSA (m^2)	0.90 (0.86)	1.00 (0.84)	0.8 (0.96)	0.67
Systolic blood pressure (mm Hg)	99 ± 19	95 ± 18	103 ± 19	0.26
Diastolic blood pressure (mm Hg)	52 ± 16	48 ± 17	56 ± 15	0.35
Baseline heart rate (bpm)	86 ± 18	85 ± 11	88 ± 23	0.57

* p-values represent comparisons between CHD and transplant groups. Results reported as mean ± standard deviation for parametric data and median (interquartile range) for non-parametric data.

BSA = body surface area. CHD = congenital heart disease. EDP = end-diastolic pressure.

Table 2

Baseline Invasive and Echocardiographic Measures of RV Diastolic Function

	All studies (n = 28)	Transplant (n = 14)	CHD (n = 14)	p-value
Invasive measures				
EDP (mm Hg)	7.2 (5.4)	6.9 (2.9)	8.5 (6.1)	0.07
Tau (ms)	27.8 ± 6.5	29.6 ± 5.1	26.0 ± 7.3	0.15
Echocardiographic measures				
TV Doppler E velocity (cm/s)	52.5 ± 17.9	43.2 ± 12.6	63.3 ± 19.0	< 0.01
TV Doppler A velocity (cm/s)	38.7 (25.0)	38.1 (20.4)	58.4 (40.7)	0.02
TV Doppler E:A	1.0 (0.5)	1.0 (0.3)	1.0 (0.8)	0.94
TV E deceleration time (s)	0.18 (0.07)	0.17 (0.05)	0.18 (0.07)	0.38
TV TDI e′ velocity (cm/s)	9.1 ± 3.1	7.5 ± 2.1	10.9 ± 3.3	< 0.01
TV TDI a′ velocity (cm/s)	4.9 (2.4)	4.8 (1.3)	6.4 (3.8)	0.38
TV E:E′	6.1 ± 2.2	5.7 ± 1.7	6.4 ± 2.7	0.45
MPI	0.46 ± 0.12	0.52 ± 0.12	0.42 ± 0.07	0.03
S:D duration ratio	1.03 ± 0.23	0.94 ± 0.17	1.02 ± 0.26	0.09
IVRT′ (s)	0.06 ± 0.02	0.07 ± 0.03	0.06 ± 0.02	0.22
RA volume (mL)	261 (333)	255 (371)	258 (209)	0.98
RV STE EDSR (s^{-1})	1.14 ± 0.31	1.05 ± 0.24	1.20 ± 0.34	0.20
RV E:EDSR	48.9 ± 17.4	41.2 ± 8.9	57.9 ± 20.7	0.01

Results reported as mean ± standard deviation for parametric data and median (interquartile range) for non-parametric data. EDP = end-diastolic pressure; EDSR = early diastolic strain rate; IVRT′ = tissue Doppler derived isovolumic relaxation time; RV = right ventricle; STE = speckle-tracking echocardiography; TDI = tissue Doppler imaging; TV = tricuspid valve. Table –Invasive and non-invasive measures of RV diastolic function before and after fluid bolus

Table 3

Baseline Correlations between Invasive and Echocardiographic Parameters

Echo Measure	Tau	EDP
TV Doppler E velocity	r = −0.24	r = 0.44
TV Doppler A velocity	r = −0.34	r = 0.26
TV Doppler E:A	r = 0.10	r = 0.01
TV E deceleration time	r = 0.09	r = 0.34
TV TDI e′ velocity	r = −0.46*	r = −0.09
TV TDI a′ velocity	r = −0.48*	r = 0.17
TV E:e′	r = −0.04	r = 0.45*
S:D duration	r = −0.37	r = 0.01
IVRT′	r = 0.20	r < 0.01
RA volume	r =−0.23	r = 0.32
RV STE EDSR	r = −0.57**	r = −0.12
RV E:EDSR	r = 0.11	r = 0.49*

Pearson's (or Spearman's correlation for non-parametric data) r-values reported.

* = $p \leq 0.01$.

** = $p < 0.001$.

EDP = end-diastolic pressure; EDSR = early diastolic strain rate; IVRT′ = tissue Doppler derived isovolumic relaxation time; NS = non-significant p-value; RV = right ventricle; S:D = systolic to diastolic duration ratio; STE = speckle-tracking echocardiography; TDI = tissue Doppler imaging; TV = tricuspid valve.

Table 4

Changes in Measures after Saline Administration

	Prebolus	Postbolus	Percent change	p-value
Invasive measures				
EDP (mm Hg)	7.2 (6.0)	10.5 (5.1)	45.8%	< 0.01
Tau (ms)	27.8 ± 6.5	29.3 ± 5.9	5.4%	0.02
Echocardiographic measures				
TV Doppler E velocity (cm/s)	52.5 ± 17.9	57.5 ± 20.1	9.5%	< 0.01
TV Doppler A velocity (cm/s)	38.7 (25.0)	49.6 (26.8)	28.2%	0.01
TV Doppler E:A	1.0 (0.5)	1.0 (0.5)	0%	0.78
TV E deceleration time (s)	0.18 (0.07)	0.20 (0.07)	11.1%	0.48
TV TDI e′ velocity (cm/s)	9.1 ± 3.1	9.5 ± 3.6	4.3%	0.39
TV TDI a′ velocity (cm/s)	4.9 (2.4)	4.9 (2.4)	0%	0.53
TV E:E′	6.1 ± 2.2	6.7 ± 2.9	9.8%	0.04
MPI	0.46 ± 0.12	0.48 ± 0.12	4.3%	0.39
S:D duration ratio	1.03 ± 0.23	1.03 ± 0.29	0%	0.57
IVRT′ (s)	0.06 ± 0.02	0.06 ± 0.02	0%	0.17
RA volume (mL)	261 (333)	302 (361)	15.7%	0.09
RV STE EDSR (s^{-1})	1.14 ± 0.31	1.29 ± 0.40	13.2%	0.02
RV E:EDSR	48.9 ± 17.4	51.6 ± 16.5	5.5%	0.75

Results reported as mean ± standard deviation for parametric data and median (interquartile range) for non-parametric data. EDP = end-diastolic pressure; EDSR = early diastolic strain rate; IVRT′ = tissue Doppler derived isovolumic relaxation time; RV = right ventricle; STE = speckle-tracking echocardiography; TDI = tissue Doppler imaging; TV = tricuspid valve.

Table 5

Multivariable Regression Analysis of Echocardiographic Predictors of Reference-Standard Measures of Diastolic Function Adjusted for Heart Rate and Age

Group	Measure	Predictor	β	SE	p-value
All patients	τ	RV longitudinal EDSR	−0.436	3.130	0.008
		LV circumferential EDSR	−0.359	2.264	0.037
Transplant	τ	LV circumferential EDSR	−0.460	3.066	0.036
CHD	τ	RV longitudinal EDSR	−0.429	2.735	0.014

EDSR = early diastolic strain rate; E:EDSR = tricuspid early Doppler inflow velocity to EDSR ratio; LV = left ventricle; RV = right ventricle; S:D = systolic to diastolic duration ratio; TV = tricuspid valve.

Table 6

Observer Variability

	Intraobserver ICC	Intraobserver % error	Interobserver ICC	Interobserver % error
TV E velocity	0.99	0.6	0.99	1.4
TV A velocity	0.99	0.9	0.99	1.0
TV E:A	0.97	1.2	0.96	2.5
TDI TV e′velocity	0.99	1.2	0.98	0.9
TV E:e′	0.98	1.7	0.98	2.6
S:D ratio	0.88	5.2	0.76	12.9
RA volume	0.87	6.4	0.86	36.8
RV EDSR	0.97	1.2	0.91	3.1

All p-values < 0.05. EDSR = early diastolic strain rate; ICC = intraclass correlation coefficient; RA = right atrium; RV = right ventricle; S:D = systolic to diastolic time ratio; TDI = tissue Doppler imaging; TV = tricuspid valve.