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## Non-Geometric Echocardiographic Indices of Ventricular Function in Patients with a Fontan Circulation

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### Abstract

**Background**—Complex anatomy and limited windows complicate echocardiographic assessments of ventricular function in Fontan patients. For the Pediatric Heart Network Fontan Cross-Sectional Study, data were acquired from which mean dP/dt during isovolumetric contraction (mean dP/dt<sub>ic</sub>), Tei index and maximal systolic annular velocity (S') could be measured. The purpose of this study was to compare these non-geometric indices of ventricular function to Cardiac Magnetic Resonance (CMR) measurements of ventricular ejection fraction (EF).

**Methods**—Echocardiograms and CMRs were obtained prospectively using standardized protocols; measurements were completed by core laboratories. Data from both modalities were available from 137 patients.

**Results**—A weak, but statistically significant correlation was observed between mean dP/dt<sub>ic</sub> and CMR-derived EF (R=0.20, p=0.022). This correlation was strengthened when preload was taken into account (R=0.30, p=0.001). Statistically significant correlations did not exist between CMR-derived EF and the Tei index or S'.

**Conclusions**—Among Fontan patients, the correlation between CMR-derived EF and non-geometric echocardiographic indices of ventricular function is not strong. Of the indices evaluated, however, mean dP/dt<sub>ic</sub> appears to be the best.

## Introduction

Patients with single ventricle physiology who have undergone the Fontan procedure often have complex abnormalities of ventricular anatomy and segmental wall motion. Consequently, obtaining a quantitative, objective, and reproducible echocardiographic assessment of ventricular function in these patients is challenging. Standard echocardiographic indices, such as the shortening fraction and the ejection fraction (EF), rely upon assumptions regarding ventricular geometry and symmetry that may not be valid for many Fontan patients. Furthermore, many of these patients have limited echocardiographic windows, and adequate visualization of the endocardial border at end-systole and end-diastole is often difficult or impossible. Indeed, perhaps as a result of these limitations, many past clinical studies of Fontan patients have not included echocardiographic assessments of ventricular function or have reported only subjective and semi-quantitative assessments.<sup>1-5</sup>

In contrast, cardiac magnetic resonance imaging (CMR) can provide accurate measurements of ventricular volume and EF, even in the presence of complex anatomy and segmental wall motion abnormalities. However, CMR expertise and facilities are not widely available. The procedure is relatively expensive, and may be contraindicated in patients with pacemakers and implantable cardioverters. Image artifacts from metallic implants also limit quantitative volumetric analyses in some Fontan patients. Furthermore, in young patients acquisition of CMR images often requires sedation. Hence, there still exists a need for a reliable, quantitative echocardiographic index of ventricular function that would be valid for patients with Fontan physiology.

For the National Heart, Lung and Blood Institute-sponsored Pediatric Heart Network Fontan Cross-Sectional Study, systemic blood pressures, pulsed Doppler echocardiographic tracings of systemic ventricular inflow and outflow, and tissue Doppler tracings of annular velocities were recorded according to a standardized protocol (these tracings can usually be obtained even in patients with poor echocardiographic windows).<sup>6</sup> From these data the following geometry-independent indices of ventricular function may be calculated: mean ventricular pressure change during isovolumetric contraction (mean  $dP/dt_{ic}$ ), the Tei index, and the maximum annular velocity during systole ( $S'$ ). Furthermore, CMR studies were obtained in approximately one-third of study subjects. The primary purpose of this analysis was to assess the value of these easily-obtained, geometry-independent echocardiographic indices of ventricular function by comparing them to CMR-based estimates of ventricular EF, and to examine the relationship of these indices to each other. In addition, in light of Margossian et al.'s<sup>7</sup> recent observation from the Fontan Cross-Sectional Study database that the mean difference between echocardiographic and CMR-based estimates of EF is small (although with wide limits of agreement) we also compared the geometry-independent indices of ventricular function with echocardiography-based estimates of EF.

## Methods

### Patient Sample

The Fontan Cross-Sectional Study was undertaken by the Pediatric Heart Network which consists of 7 pediatric cardiac centers in the United States and Canada and performs multicenter clinical studies with funding from the National Heart, Lung and Blood Institute of the National Institutes of Health. The purpose of the Fontan Cross-Sectional Study was to prospectively assess the correlation between measures of functional health status, ventricular function and exercise performance in young Fontan survivors. A total of 546 subjects aged 6 to 18 years were enrolled in the Fontan Cross-Sectional Study, at the time of their routine cardiologic follow-up, in 2003–2004. The Fontan Study design has been described.<sup>6</sup> Two

analytic cohorts from the study sample were used in this report: 1) subjects who had both CMR and echocardiographic data permitting the calculation of the echocardiographic indices of interest (patients who could not lie still without sedation and patients with metallic artifacts that precluded acquisition of a full CMR volumetric dataset were not included in this cohort); and 2) subjects with echocardiographic data irrespective of CMR completion. All institutions obtained Institutional Review Board approval to conduct the study and the parent or guardian of each provided written informed consent.

### Echocardiographic Protocol

Two-dimensional and Doppler echocardiograms were obtained according to a standardized protocol. Data were recorded at a paper speed of at least 100 mm/sec and all measurements were completed by a single observer at a core laboratory. The mean  $dP/dt_{ic}$  was calculated from the equation<sup>8</sup>:

$$\text{mean } dP/dt_{ic} = \frac{\text{aortic diastolic pressure} - \text{ventricular end-diastolic pressure}}{\text{isovolumetric contraction time}}$$

The aortic diastolic pressure was obtained from an automated blood pressure monitoring system using an appropriately-sized cuff, during the echocardiogram. An average of at least 3 measurements was used for the calculation. The ventricular end-diastolic pressure was assumed to equal 5 mmHg. The isovolumetric contraction time was calculated by subtracting the time interval between the onset of the QRS complex and the closure of the systemic atrioventricular valve on the systemic ventricular inflow pulse Doppler tracing from the time interval between the onset of the QRS complex and the opening of the aortic valve on the systemic ventricular outflow pulsed Doppler tracing (Figure 1).<sup>9</sup>

The S' was measured from tissue Doppler tracings of the systemic ventricular free wall at the level of the systemic atrioventricular valve. One measurement of an S' velocity of 24 cm/sec was considered unphysiologic and was therefore excluded from analysis. All other S' observations were < 16 cm/sec.

The Tei index was calculated from tissue Doppler imaging time intervals using the equation<sup>10</sup>:

$$\text{Tei index} = \frac{(\text{isovolumetric contraction time}) + (\text{isovolumetric relaxation time})}{\text{ejection time}}$$

Whenever present, the average of measurements from the septum and lateral walls was used; otherwise the single available site was utilized.

The isovolumetric contraction time was measured as the time from the end of the A' wave to the beginning of S'. The isovolumetric relaxation time was measured as the time from the end of S' to the beginning of the E' wave. The ejection time was measured as the duration of S' (Figure 2).

To evaluate the reproducibility of the geometry-independent indices of ventricular function, 20 studies were randomly selected and the relevant measurements were repeated twice by a second observer unaware of the results of the previous measurements.

Tracings the ventricle's endocardial border in the apical (ventricular long axis) and parasternal short axis views at end diastole and end systole were obtained and estimates of ventricular volumes generated using a biplane-modified Simpson's rule. Ventricular

morphology was characterized as left dominant (e.g., tricuspid atresia), right dominant (e.g., hypoplastic left heart syndrome) or mixed (e.g., unbalanced atrioventricular canal defect).<sup>7</sup>

For each patient, a single observer graded each AV valve's regurgitation qualitatively as: absent/trivial, mild, moderate or severe. Subjects were classified as having moderate/severe AV valve regurgitation if the right, left or common AV valve regurgitation was moderate or severe, or if both right and left AV valve regurgitation were graded mild.<sup>11</sup>

**CMR Protocol**—CMR was performed using a standardized imaging protocol developed by the core laboratory.<sup>7</sup> Imaging was performed using locally available 1.5 T whole body scanners (General Electric Signa LX or TwinSpeed; Philips Intera; and Siemens Sonata or Maestro). The standardized imaging protocol included ECG-gated segmented k-space fast (turbo) gradient (14% of studies) or steady state free precession (86% of studies) cine MR acquisitions in the vertical and horizontal long-axis planes, and contiguous short-axis cine imaging from the atrioventricular junction through the cardiac apex. Studies were acquired within 3 months of the echocardiograms. De-identified CMR data were analyzed using commercially available software (MASS, Medis, Leiden, The Netherlands) at the Core CMR laboratory by a single observer.

### Statistical Analysis

Summary statistics are presented as mean  $\pm$  standard deviation (SD) or median and interquartile range. Patient characteristics for the group with a mean  $dP/dt_{ic}$  value and those without this measurement were compared using a Fisher exact test for categorical variables, the t-test for continuous non-skewed variables, and the Wilcoxon rank sum test for other continuous variables. Mean  $dP/dt_{ic}$  was divided by  $EDV/(BSA)^{1.3}$  to account for preload factors. We used generalized additive modeling to assess whether EF was linearly associated with the non-geometric parameters. Log-transformed mean  $dP/dt_{ic}$  had a linear association with EF and was therefore also used in correlation analyses. Linear regression of EF with an interaction term between valve regurgitation grade and predictor was used to identify differential correlations within patient subgroups defined by severity of valve regurgitation. An interaction term between ventricular morphology and  $dP/dt_{ic}$  was also fit to identify differential correlations within patient subgroups defined by ventricular morphology. A p-value of less than 0.05 was considered significant. All analyses were conducted using SAS 9.2 (SAS Institute, Inc., Cary, NC) and S-Plus (Insightful Corp., Seattle, WA).

## Results

### Study subjects

Of the 546 patients enrolled in the Fontan Cross-Sectional Study, 449 had data from which the mean  $dP/dt_{ic}$  could be calculated (Figure 3). Of these, 137 had CMR data from which the CMR-derived EF could be measured. Sample size was similar for the other non-geometric indices of ventricular function. The 137 patients who had both CMR and mean  $dP/dt_{ic}$  data were more likely to have had tricuspid atresia (30% vs. 19%), were older (mean $\pm$ SD 12.1 $\pm$ 3.4 vs. 11.8 $\pm$ 3.4) and had Fontan surgery less recently than the other patients in the cohort.

### Mean $dP/dt_{ic}$ and Subgroup Factors

In the cohort of 137 patients with CMR data, mean  $dP/dt_{ic}$  was 1224 $\pm$ 774 mmHg/sec (median 977; range 381–5857). CMR-derived EF was 57 $\pm$ 9%. Twenty percent had moderate atrioventricular valve regurgitation (none had severe). The distribution of ventricular morphology was 53% left (usually tricuspid atresia), 27%, right (usually hypoplastic left heart syndrome), and 20% mixed type (usually unbalanced atrioventricular canal variant). In

the larger cohort of 449 patients with mean  $dP/dt_{ic}$  regardless of availability of CMR, the average value was slightly higher than that of the cohort with CMR data ( $1410 \pm 935$  mmHg/sec  $p < 0.05$ , Table 1). For these patients, the distributions of valve regurgitation and ventricular morphology were similar to those of the smaller CMR cohort.

### **Correlation between CMR-derived measurements of EF and non-geometric indices of ventricular function**

Log (mean  $dP/dt_{ic}$ ) was weakly correlated with CMR-derived EF ( $R=0.20$ ,  $p=0.022$ ; Table 2). It was not significantly correlated with CMR-based measurements of end-diastolic volume, end-systolic volume, mass or stroke volume. Because the mean  $dP/dt_{ic}$  may be influenced by preload, we attempted to correct for ventricular preload by indexing log (mean  $dP/dt_{ic}$ ) using the echocardiographically-derived ventricular end diastolic volume normalized for body surface area  $[EDV/(BSA)]^{1.3}$ .<sup>12</sup> This correction strengthened the correlation with the CMR-derived EF ( $R=0.30$ ,  $p=0.001$ ; Table 2; Figure 4).

The correlation between CMR-derived EF and log (mean  $dP/dt_{ic}$ ) was not affected by the presence vs. absence of moderate atrioventricular valve regurgitation ( $p=0.33$ ). Similarly, the correlation between CMR-derived EF and log (mean  $dP/dt_{ic}$ ) was not influenced by ventricular morphology.

Statistically significant correlations did not exist between the CMR-derived EF and the other non-geometric echocardiographic indices of ventricular function (Tei index and  $S'$ ; Table 2 and Figure 4). Once again, these correlations were not affected by ventricular morphology.

### **Comparison of patients with echocardiographic and CMR studies performed on the same day vs. patients with studies performed on different days**

Of the patients who had CMR studies, 100 had echocardiograms performed on the same day as the CMR (Group 1), and 90 had the studies on different days (within 3 months of each other, without any intervening major therapeutic intervention, Group 2). Patients in Group 1 did not differ from those in Group 2 with regard to age at study ( $11.9 \pm 3.5$  vs.  $12.7 \pm 3.1$  yrs,  $p=0.09$ ) or age at Fontan completion ( $3.5 \pm 2.2$  vs.  $3.4 \pm 1.9$  yrs,  $p=0.72$ ). When the analyses were limited to patients who had studies on the same day, the correlation between log(mean  $dP/dt$ ) divided by  $[EDV/(BSA)]^{1.3}$  with MRI EF remained significant ( $p=0.036$  rather than  $p=0.001$ ) despite the smaller sample size because the correlation coefficient changed very little in the analysis restricted to this smaller subpopulation ( $R=0.27$  rather than  $R=0.30$ ). In this subpopulation, the correlation coefficients between the CMR-based EF and Tei index and  $S'$  were also similar to those encountered in the entire study population and remained statistically insignificant.

### **Correlation between echocardiographically-derived measurements of EF and non-geometric indices of ventricular function**

Of the 546 patients enrolled in the Fontan Cross-Sectional Study, 414 (76%) had echocardiographic images from which the EF could be calculated ( $59 \pm 10\%$ ). Of these, 359 had data from which the mean  $dP/dt_{ic}$  could be calculated. Log (mean  $dP/dt_{ic}$ ) was correlated with the echocardiography-based estimates of EF ( $R=0.18$ ,  $p < 0.001$ ). Once again, this correlation was strengthened modestly when log (mean  $dP/dt_{ic}$ ) was corrected for preload ( $R=0.20$ ,  $p < 0.001$ ). Statistically significant correlations ( $p < 0.001$ ) also existed between  $S'$ , Tei index and echocardiography-based estimates of EF, but these correlations were weaker than the correlation between EF and log (mean  $dP/dt_{ic}$ ) (Table 3).

### Correlation between mean $dP/dt_{ic}$ and other non-geometric indices of ventricular function

Among the 320 patients who had both  $\log(\text{mean } dP/dt_{ic} / [\text{EDV}/(\text{BSA})]^{1.3})$  and the Tei index, a negative correlation was observed ( $R = -0.19$ ;  $p < 0.001$ ). Among the 303 patients with  $\log(\text{mean } dP/dt_{ic} / [\text{EDV}/(\text{BSA})]^{1.3})$  and the  $S'$ , a positive correlation was observed ( $R = 0.19$ ;  $p < 0.001$ ; Table 4).

### Reproducibility of measurements

The intra-rater agreements for mean  $dP/dt_{ic}$  and  $S'$  were excellent, and for Tei index were good, whereas inter-rater agreements were excellent for  $dP/dt$ , moderate for  $S'$ , and poor for Tei index. (Table 5)

### Discussion

The indices chosen for analysis in this study were selected because they are functions solely of velocity, pressure and/or time. Consequently, they are not subject to the geometric assumptions inherent to other echocardiographic indices of ventricular function, nor are they dependent upon adequate visualization of the ventricular endocardial surface. They are therefore theoretically well suited for use in patients with complex ventricular anatomy, wall motion abnormalities and limited echocardiographic windows; conditions commonly encountered among patients who have had Fontan procedures.

We found that there was a weak correlation between the CMR-derived measurement of EF and mean  $dP/dt_{ic}$ . This correlation was strengthened when an adjustment for preload (EDV corrected for body surface area) was incorporated into the model. This observation may be related to the known preload-dependency of peak  $dP/dt$ <sup>13</sup> and/or to the fact that EDV measurements are also used in the calculation of EF. Other non-geometric indices did not correlate with CMR-derived EF. In the larger cohort of patients with echocardiography-derived estimates of EF, mean  $dP/dt_{ic}$  once again emerged as the non-geometric index of ventricular function possessing the strongest correlation with EF.

The trends observed for the entire population persisted when our analyses were limited to patients who had CMR and echocardiographic studies performed on the same day. This observation suggests that the absence of stronger agreement between echo and CMR measures could not be attributed to changes during the time interval between the two studies.

A statistically significant positive correlation was found between mean  $dP/dt_{ic}$  and the  $S'$ . The correlation was in the direction expected as, for each of these indices, higher values are associated with superior ventricular function. A statistically significant negative correlation was found between mean  $dP/dt_{ic}$  and the Tei index. This too is expected, since a higher Tei index is associated with depressed ventricular function. It must be noted, however, that the correlation between the Tei index and mean  $dP/dt_{ic}$  is likely due, at least in part, to the fact that the isovolumetric contraction time is a component of the equations used for the calculation of both indices. In contrast, the mean  $dP/dt_{ic}$  and the  $S'$  are mathematically independent, and the correlation between these two indices cannot be ascribed solely to the presence of common component variables.

Whereas the mean  $dP/dt_{ic}$  is an “isovolumetric” index, and the Tei index is a “mixed” index (i.e., dependent upon events during isovolumetric contraction, ejection and isovolumetric relaxation), EF and  $S'$  are both ejection phase indices. It is therefore surprising that the correlation between the EF and  $S'$  was so weak. We speculate that this observation is due to the fact that  $S'$  measures the systolic motion of only a part (in this case the lateral wall) of the ventricle. In the anatomically complex patient with Fontan physiology, the motion of this

region is may not be representative of other regions of the ventricle. In contrast, the mean  $dP/dt_{ic}$  describes a rate of pressure change that is a consequence of the contraction of the entire ventricle, not just a portion of it. Consequently mean  $dP/dt_{ic}$  correlates more strongly with EF, as they are both indices of global ventricular function.

### Comparison with past studies

In earlier analyses of this study dataset, Paridon et al examined the relationship between exercise performance and mean  $dP/dt_{ic}$ .<sup>14</sup> They found a statistically significant, albeit weak, correlation between mean  $dP/dt_{ic}$  and the oxygen pulse at peak exercise (a surrogate for forward stroke volume at peak exercise). None of the other echocardiographic indices of ventricular function studied (including ventricular volumes, mass, EF, tissue Doppler velocities, Tei index and diastolic function grade) correlated with the oxygen pulse at peak exercise, or other indices of exercise function. Hence, in the current study, the emergence of mean  $dP/dt_{ic}$  as the non-geometric index of ventricular function that correlates best with CMR-derived EF is consistent with the previously observed association between exercise performance and mean  $dP/dt_{ic}$ .

Tissue Doppler velocities, the Tei index and the mean  $dP/dt_{ic}$  have, in past studies, been used to assess the ventricular function of patients with single ventricle physiology. Vitarelli et al<sup>15</sup> studied 24 patients who had undergone Fontan surgery and found a linear correlation between the S' and echocardiographic estimates of EF. Mahle et al<sup>16</sup> found that the Tei index was elevated in a group of 32 patients with functionally single right ventricles who had undergone Fontan procedures. Williams et al.<sup>17</sup> found that the Tei index was higher in patients with single ventricles compared to normal control subjects. Rhodes et al.<sup>8</sup> and Michelfelder<sup>18</sup> et al. found that echocardiographic estimates of  $dP/dt$  correlated well with simultaneous catheterization measurements. However, none of these studies compared these non-geometric echocardiographic indices of ventricular function to CMR-derived estimates of EF.

Past studies have demonstrated that the correlation between echocardiographic and CMR-derived estimates of EF is much stronger than the correlation that we found between mean  $dP/dt_{ic}$  and CMR-derived EF.<sup>7, 19</sup> However, poor echocardiographic windows preclude determination of EF in some Fontan patients and this index of ventricular function is therefore not always available. For example, in this Fontan Cross-Sectional Study only 76% of the patients enrolled had echocardiographic estimates of EF. This statistic probably underestimates the scope of this problem, as the study was limited to patients 6–18 years of age. Older subjects often have more limited echocardiographic windows, and the barriers to the acquisition of echocardiographic estimates of EF would likely have been much greater if an older Fontan population had been studied. In contrast, mean  $dP/dt_{ic}$  can usually be acquired in patients with limited echocardiographic windows. It may therefore constitute the best alternative echocardiographic index of ventricular function in this patient population. Furthermore, even among patients with reliable estimates of EF, data from a second, independent index of ventricular function may be clinically worthwhile. For instance, among patients undergoing mitral valve surgery on account of severe mitral regurgitation, echocardiographic estimates of  $dP/dt$  were the best predictors of post-operative EF, and were superior to pre-operative estimates of EF.<sup>20</sup> In an analogous manner, measurements of mean  $dP/dt_{ic}$  may usefully complement EF-based assessments of ventricular function in patients with Fontan. It is also possible that serial measurements of mean  $dP/dt_{ic}$  will more readily detect changes in ventricular contractility over time. These hypotheses may be worthwhile topics of future research.

Perhaps the central message of this study is, however, that the correlations between CMR-derived measurements of ventricular EF and the non-geometric echocardiographic indices

that we evaluated are not strong. In the Fontan population a need still exists for a reliable and convenient non-invasive index of ventricular function. Potential candidates for this role include the myocardial acceleration during isovolumetric contraction (a recently described tissue Doppler index that reflects myocardial contractile function and is relatively insensitive to changes in preload and afterload<sup>21</sup>), as well as measurements derived from three dimensional echocardiographic and feature tracking technology.

### Study Limitations

Although statistically significant, the relationship between mean  $dP/dt_{ic}$  and the CMR-derived EF observed in this study was modest. A number of factors may have contributed to this phenomenon. Accurate determination of the isovolumetric contraction time using pulse Doppler echocardiography requires clear visualization of the moment of mitral valve closure and aortic valve opening, a stable, clear electrocardiographic tracing, and a rapid sweep speed.<sup>8, 9</sup> However, because the Doppler tracings recorded for the Fontan Cross-Sectional Study were not obtained expressly for the purpose of measuring the isovolumetric contraction time, these parameters may not have been optimized. Error may therefore have been introduced into the measurement of this variable and, consequently, into the calculation of mean  $dP/dt_{ic}$ .

We also utilized an assumed ventricular end-diastolic pressure to calculate mean  $dP/dt_{ic}$ . This too could be a source of error. It must also be noted that changes in preload, afterload, heart rate and contractility will not have identical effects upon the EF and the mean  $dP/dt_{ic}$ . It was not possible, in this study, to control for these disparate effects. Finally, we used the echocardiographically-determined ventricular end-diastolic volume to correct mean  $dP/dt_{ic}$  for ventricular preload. Although it was probably the best echocardiographic index of ventricular preload available for this purpose, the theoretical and practical limitations of this measurement should be acknowledged.<sup>7</sup>

Ventricular  $dP/dt$  may also be measured from continuous wave Doppler tracings of systemic AV valve regurgitation jets. While this approach is more familiar than the conceptually similar but methodologically different pulse Doppler technique employed in this study, the continuous wave Doppler method requires the presence of a measurable and properly oriented AV valve regurgitation jet. These conditions are not reliably encountered among patients following Fontan surgery and the requisite continuous wave Doppler tracings were not acquired for this Fontan Cross-Sectional Study. Consequently, we relied upon the less familiar, but more widely applicable, pulse Doppler methodology. Yilmaz et al have demonstrated that, in patients with mitral regurgitation, there is excellent agreement between measurements of  $dP/dt$  based upon these two techniques.<sup>22</sup>

The complexity of our patient population, variability in AV valve morphology and limitations in data availability permitted only qualitative assessments of AV valve regurgitation. It must therefore be recognized that the classification of AV valve regurgitation severity was only approximate.

In summary, among patients with Fontan circulations the correlation between CMR-derived measurements of ventricular EF and non-geometric echocardiographic indices of ventricular function is not strong. Of the indices evaluated in this study, however, the mean  $dP/dt_{ic}$  appears to be the best non-geometric index, especially when adjusted for ventricular preload. The potential clinical value of these measurements merits further study.



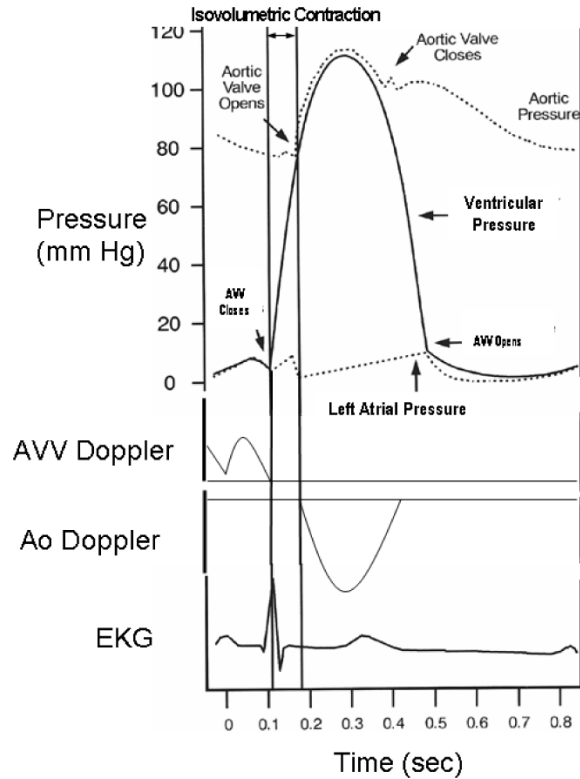
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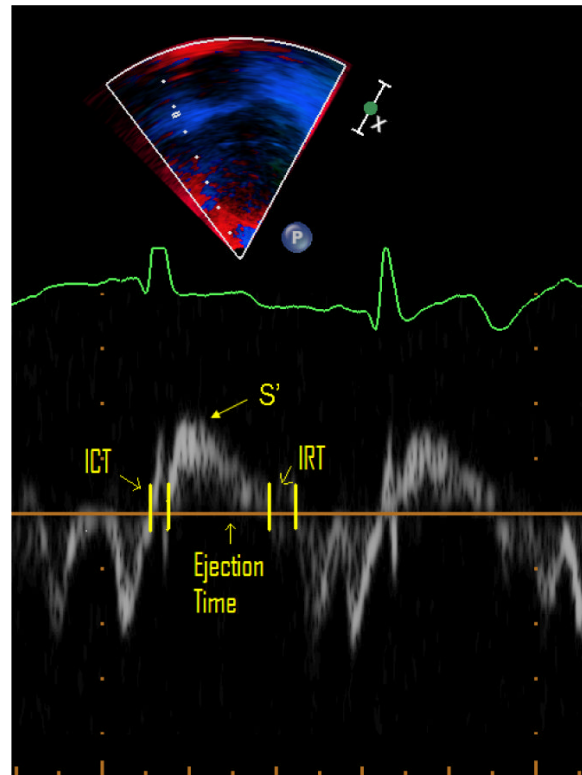


**Figure 1.**

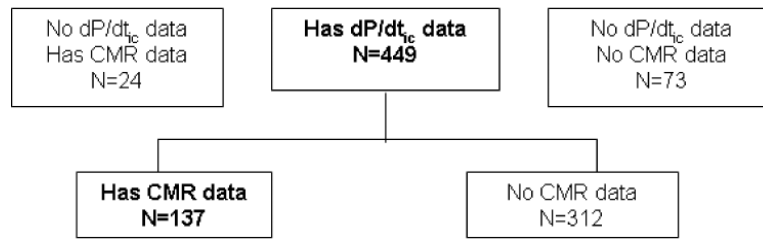
Top panel depicts a hypothetical ventricular, aortic and left atrial pressure tracing; next panels depict AV valve and aortic valve pulse-Doppler tracings, and bottom panel depicts EKG tracing. The peak pressure change during ventricular contraction (peak  $dP/dt$ ) almost always occurs during isovolumetric contraction (IC). However, the ventricular pressure rise during IC is almost linear. Hence, Peak  $dP/dt \approx \text{Mean } dP/dt_{IC} =$

$$(\text{Aortic diastolic pressure} - \text{ventricular end-diastolic pressure}) / (\text{IC time}).$$

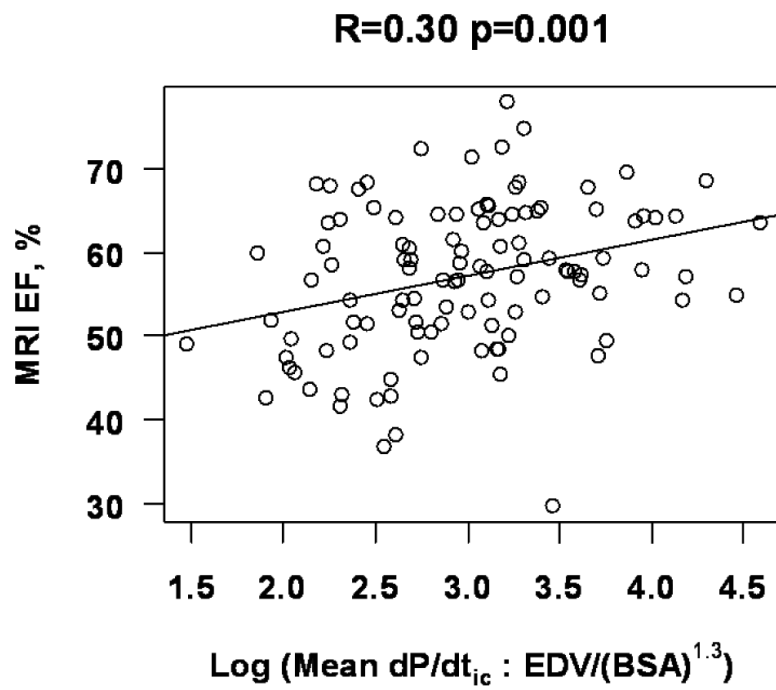
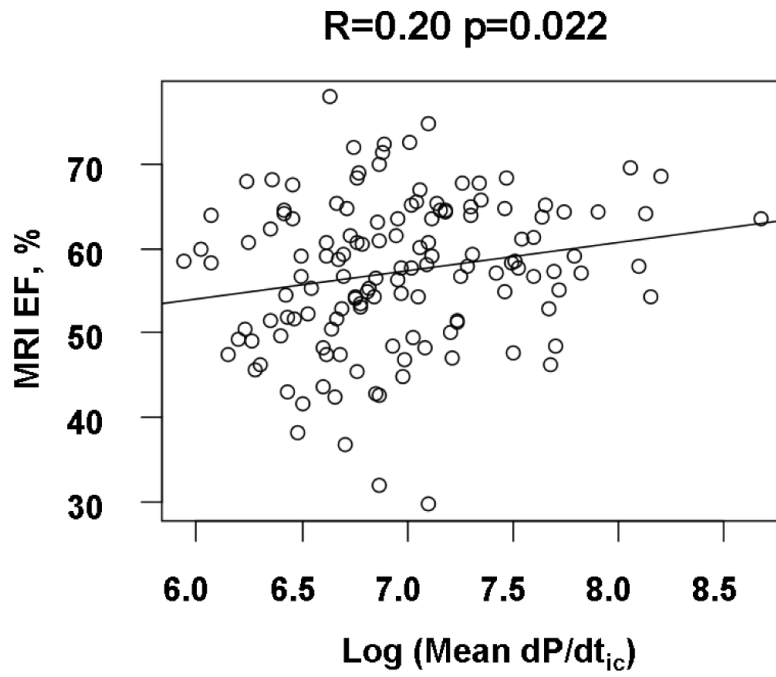
The IC time is calculated by subtracting the time interval between the onset of the QRS complex and the closure of the systemic AV valve (on AV valve inflow pulse Doppler tracing) from the time interval between the onset of the QRS complex and the opening of the aortic valve (on the aortic pulsed Doppler tracing). Aortic diastolic pressure is measured with a blood pressure cuff. Ventricular end-diastolic pressure is assumed to equal 5 mmHg. Because ventricular end-diastolic pressure is usually much less than aortic diastolic pressure, large errors in the estimation of ventricular end-diastolic pressure introduce relatively small errors into the calculation of mean  $dP/dt_{IC}$ .

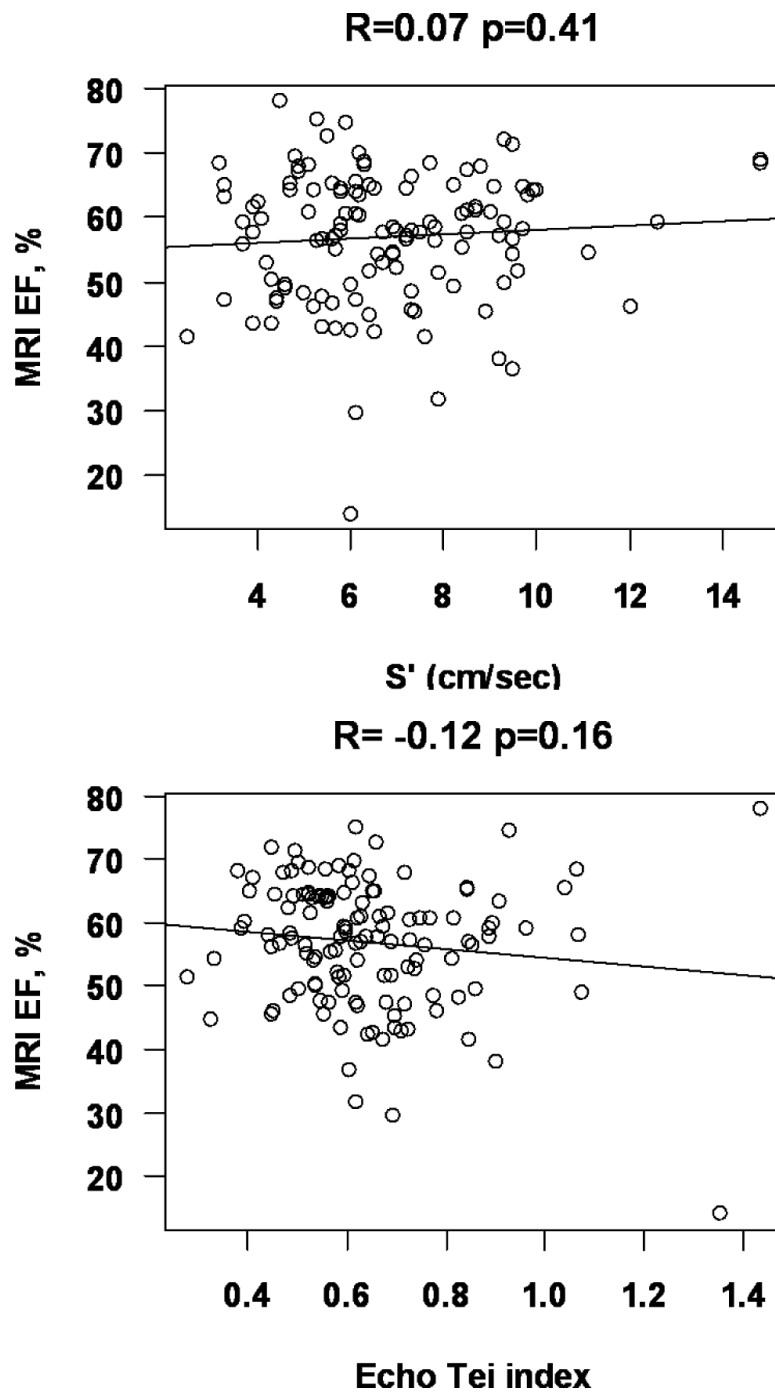


**Figure 2.** Measurement of Tei index from Tissue Doppler tracing. ET: ejection time; ICT: isovolumetric contraction time; IRT: isovolumetric relaxation time; S': peak systolic velocity



**Figure 3.**  
dP/dt<sub>ic</sub>: mean ventricular pressure change during isovolumetric contraction; CMR: cardiac magnetic resonance imaging.





**Figure 4.**

MRI EF: Ejection fraction measured by magnetic resonance imaging;  $dp/dt_{ic}$ : mean ventricular pressure change during isovolumetric contraction; Echo EDV/BSA<sup>1.3</sup>: volume correction based upon echocardiographically-determined ventricular end-diastolic volume.

**Table 1**

Fontan Cross-Section Study Echocardiographic and CMR measures of ventricular function

Variable	N	Mean±SD	Median	IQR	Range
Mean dP/dt <sub>ic</sub> (mmHg/sec)	449	1410±935	1125	802, 1700	239, 5857
Log (Mean dP/dt <sub>ic</sub> )	449	7.1±0.6	7.0	6.7, 7.4	5.5, 8.7
Mean dP/dt <sub>ic</sub> / EDVZ(BSA) <sup>1.3</sup>	359	26.1±19.1	20.8	13.8, 30.8	2.8, 113.1
Log (Mean dP/dt <sub>ic</sub> / EDV/(BSA) <sup>1.3</sup> )	359	3.0±0.7	3.0	2.6, 3.4	1.0, 4.7
Echo ejection fraction (%)	414	58.5±10.4	59.3	52.4, 66.0	25.9, 85.3
S' (cm/sec)	428	6.4±2.0	6.2	5.0, 7.5	2.4, 14.8
Tei index	462	0.64±0.19	0.61	0.52, 0.71	0.27, 1.62
CMR ejection fraction (%)	161	56.9±9.5	57.7	51.4, 64.2	14.2, 78.0

CMR = cardiac magnetic resonance

SD = standard deviation

IQR = interquartile range

EDV = end-diastolic volume

BSA = body surface area



**Table 2**

Pearson correlation (r) between CMR-derived EF and non-geometric indices of ventricular function

<b>Index</b>	<b>N</b>	<b>r</b>	<b>p-value</b>
<b>Log (mean dP/dt<sub>c</sub>)</b>	137	0.20	0.022
<b>Log (mean dP/dt<sub>c</sub> / EDV/(BSA)<sup>1.3</sup>)</b>	110	0.30	0.001
<b>Tei index</b>	130	-0.12	0.16
<b>S', cm/sec</b>	124	0.07	0.41

EDV = end-diastolic volume

BSA = body surface area

**Table 3**

Pearson correlation (r) between echocardiography-derived EF and non-geometric indices of ventricular function

<b>Index</b>	<b>N</b>	<b>r</b>	<b>p-value</b>
<b>Log (mean <math>dP/dt_{ic}</math>)</b>	359	0.18	<0.001
<b>Log (mean <math>dP/dt_{ic}</math> / EDV/(BSA)<sup>1.3</sup>)</b>	359	0.20	<0.001
<b>Tei index</b>	367	-0.13	0.01
<b>S', cm/sec</b>	344	0.15	0.004

EDV = end-diastolic volume

BSA = body surface area

**Table 4**

Pearson correlation (r) of  $\log(\text{mean } dP/dt_{ic})/[EDV/(BSA)]^{1.3}$  vs. non-geometric indices of ventricular function

Index	N	r	p-value
Tei Index	320	-0.19	<0.001
S', cm/sec	303	0.19	<0.001

EDV = end-diastolic volume

BSA = body surface area

**Table 5**

Intra-Class Correlation Coefficient (95% CI) for S', Mean dP/dt<sub>ic</sub>, and Tei index.

<b>Variable</b>	<b>Intra-rater ICC</b>	<b>Inter-rater ICC</b>
S'	0.91 (0.79, 0.96)	0.69 (0.39, 0.86)
Mean dP/dt <sub>ic</sub>	0.93 (0.83, 0.97)	0.91 (0.78, 0.96)
Tei index	0.75 (0.47, 0.89)	0.24 (0.0 0.56)
Log (Mean dP/dt <sub>ic</sub> )	0.96 (0.90, 0.98)	0.94 (0.86, 0.98)

ICC = Intra-class correlation coefficient