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Original Article

Quantitative echocardiographic assessment of the performance of the functionally single right ventricle after the Fontan operation

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Abstract *Background:* Performance of the functionally single right ventricle may deteriorate over time. Quantitative assessment of this chamber, however, is complicated by its asymmetric geometry. Automatic detection of borders, and the Doppler-derived index of myocardial performance, are echocardiographic techniques that allow for quantitative assessment regardless of ventricular shape. We sought to evaluate the mechanics of contraction and relaxation in the functionally single right ventricle using these parameters. *Methods:* We evaluated systemic ventricular function in 35 asymptomatic patients with functionally single right ventricle, having a mean age of 7.8 ± 3.1 years, who had undergone the Fontan procedure. We compared them with 32 age-matched normal controls using both automatic detection of borders and Doppler indexes. *Results:* When compared with the controls, the group with a functionally single right ventricle demonstrated diminished systolic function as evidenced by a lower fractional change in area (42.7 ± 10.1% vs. 54.6 ± 10.5%, $p = 0.001$), and diminished diastolic function, as demonstrated by a greater reliance on atrial contraction to achieve ventricular filling (32.0 ± 4.4% vs. 22.2 ± 4.1%, $p = 0.001$). The mean index of myocardial performance in those with functionally single right ventricles was also greater than in controls (0.41 ± 0.12 vs. 0.30 ± 0.05, $p = 0.001$), and the indexed ejection time was shorter (0.35 ± 0.05 vs. 0.39 ± 0.05, $p = 0.01$), suggesting less efficient ventricular mechanics. *Conclusions:* These data demonstrate that the systolic and diastolic properties of the functionally single right ventricle differ significantly from those of the normal systemic left ventricle. Use of the echocardiographic techniques provide insight into ventricular mechanics in patients with functionally single ventricles, and may be valuable tools for serial quantitative follow-up.

Keywords: Univentricular heart; single ventricle; follow-up studies; congenital cardiac malformations

THE OUTCOME FOR PATIENTS WITH COMPLEX functionally univentricular anatomy undergoing the Fontan procedure continues to improve, resulting in an increasing number of intermediate- and long-term survivors.[1,2] The performance of the functionally single ventricle, however, may deteriorate over time.[3] In addition, experience with atrial switch procedures, such as the Mustard or Senning operations, for patients with discordant ventriculo-arterial connections suggests that the morphologically right ventricle, even in the setting of biventricular circulations, may be poorly suited to support the systemic circulation over the long-term.[4] As such, serial assessment of ventricular function is of importance in the long-term care of these patients. To date, there is no widely accepted echocardiographic technique for quantifying ventricular function in those patients with functionally single ventricles, primarily since quantitative assessment is complicated by asymmetric ventricular geometry.

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In order to overcome this geometric challenge, we investigated the echocardiographic modalities of automatic detection of borders and the Doppler-derived index of myocardial performance in the evaluation of the functionally single right ventricle. Automatic detection of borders allows for real-time tracing of the area of the ventricular cavity throughout the cardiac cycle, and provides valid measurements of cross-sectional area which can be obtained regardless of ventricular shape. Such automated techniques have been applied to both the morphologically right and left ventricles.[5,6] In children, automated detection has been used to assess right ventricular function in patients with normal intracardiac anatomy, those having congenital cardiac malformations in the setting of the biventricular circulation, and in a small number of patients with functionally single ventriclular physiology.[6–8] The index of myocardial performance is a measure of the ratio of combined systolic and diastolic ventricular isovolumic times indexed to ejection time, and is independent of ventricular geometry. This index has been shown to correlate well with catheter-derived measures of ventricular performance.[9] It can be applied to both the right and left ventricles, and has been used to assess the ventricular function in patients with dilated cardiomyopathy, as well as forms of congenital cardiac disease such as Ebstein's malformation.[10,11]

We have now used the techniques of automatic detection of borders and the index of myocardial performance in a population of clinically well, asymptomatic, patients with functionally single right ventricular anatomy after the Fontan procedure. This has enabled us to establish the range of normal values for these echocardiographic variables in this population, and sets the scene for future investigations such as correlation of resting echocardiographic measurements with exercise performance. In addition, we sought to compare the values of the functionally single right ventricle to those obtained for the systemic morphologically left ventricle in the normal biventricular circulation, hoping to gain a better understanding of the mechanics of contraction and relaxation in the functionally single right ventricular heart.

Methods

Population studied

We assessed systemic ventricular performance in subjects with a functionally single right ventricle after the Fontan procedure, using subjects with normal cardiac anatomy as controls, in a prospective cross-sectional study. Patients who presented for routine outpatient echocardiography between June of 1997 and September of 1998 were eligible for enrollment. The cohort with a functionally single right ventricle had undergone the Fontan procedure and were at least 3 years of age. All subjects were evaluated for functional status, which was graded according to the classification of the New York Heart Association as previously applied in children.[12,13] Subjects in classes III or IV were excluded from study in order to obtain data on a cohort of well, asymptomatic subjects with a functionally single right ventricle. In addition, individuals were excluded if they:

- had a permanent pacemaker;
- were receiving anti-arrhythmic medication other than digoxin at the time of the study;
- were not in sinus rhythm;
- had obstruction within the aortic arch;
- or had insufficiency of the atrioventricular or arterial valves that was greater than of a mild degree as assessed by color Doppler echocardiography.

Patients who were receiving either digoxin or an inhibitor of angiotensin-converting enzyme were not excluded from study, since some cardiologists prescribe these medications for all of their patients with functionally single right ventricle, regardless of functional class or qualitative ventricular function. Qualitative assessment of systemic ventricular function was performed in all, and patients with "diminished" systolic function, be it moderate or severe, were not included in the study.

We entered 35 patients with functionally single right ventricle into the study. Their mean age was 7.8 ± 3.1 years. The most common diagnosis was hypoplastic left heart syndrome, which was present in 29 patients (Table 1). Of the overall group, 27 patients (77.1%) had undergone an intermediate staging procedure (hemi-Fontan or bidirectional Glenn) prior to the Fontan operation. Of the

Table 1. Anatomic diagnoses in patients with functionally single right ventricle.

Cardiac lesion	**n**
Hypoplastic left heart syndrome (aortic atresia, mitral atresia)	15
Hypoplastic left heart syndrome (aortic atresia, mitral stenosis)	6
Hypoplastic left heart syndrome (aortic stenosis, mitral stenosis)	8
Mitral stenosis, sub-aortic stenosis, ventricular septal defect	1
Double outlet right ventricle {S, D, D} with aortic stenosis	1
Double outlet right ventricle {S, D, D} with pulmonary stenosis	2
Transposition of the great arteries {S,D,D}, unbalanced complete common atrioventricular canal, sub-pulmonary stenosis	1
Right ventricular aorta {S, D, D}, pulmonary atresia	1

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patients, 24 (68.6%) were receiving an inhibitor of angiotension-converting enzyme, 22 (62.8%) were in class I of the New York Heart Association classification, and 13 (37.1%) were in class II.

The control group, made up of 32 subjects with normal systemic left ventricles, at a mean age of 8.0 ± 4.3 years, was drawn from those referred for echocardiography in the evaluation of a cardiac murmur. Individuals who had received prior chemotherapy, radiation therapy, or those who suffered from chronic illness, were excluded. All the control subjects had normal cardiac anatomy and ventricular function as determined by standard cross-sectional, M-mode, and Doppler techniques.

Echocardiographic imaging

All subjects underwent conventional cross-sectional, pulsed-wave, continuous wave, and color-flow Doppler imaging with a variety of transducer frequencies using a Sonos 2500 ultrasonograph (Hewlett-Packard Co., Andover, MA). In order to calculate the index of myocardial performance, Doppler signals of ventricular inflow and outflow were obtained in the systemic ventricle. The inflow velocity curve was obtained from the apical view with the pulsed-wave Doppler sample volume positioned at the tips of the atrioventricular valvar leaflets. The time interval from closure to opening of the systemic atrioventricular valve was measured and the average of 3–5 beats recorded. The ventricular outflow velocity curve was obtained from the apical view with anterior angulation and the pulsed wave Doppler sample volume was positioned just beneath the systemic arterial valve. The time interval from opening to closure of the valve was measured, and the average of 3–5 beats recorded. Outflow signals were obtained immediately after inflow signals with no interval change in heart rate between the two noted. As previously described by Tei et al.,[9] subtracting the ejection time from the time between closure and opening of the valve provided the combined isovolumic contraction and isovolumic relaxation time. Dividing this value by the ejection time yields the index of myocardial performance (Fig. 1). We also examined the two components of the index of myocardial performance for each patient, namely ejection time and combined isovolumic contraction and relaxation times. While the index of myocardial performance varies little within the range of normal heart rate[11], ejection time and combined isovolumic contraction and isovolumic relaxation times are variables dependent upon heart rate.[14–16] Because of this, we indexed these values to heart rate by dividing by the square root of the R-R interval.

Acoustic Quantification (Hewlett-Packard, Andover, MA) was used to obtain automatic detection of borders. An optimal ultrasound image of the systemic ventricle was obtained from the apical long-axis window at the point of greatest ventricular length, and in the parasternal short-axis window at the level of the upper tip of the papillary muscles, thereby providing for orthogonal views of the ventricle. The automatic system was activated and the lateral gain was adjusted until the entire perimeter of the endocardial-blood border was detected and traced. The region of interest was defined around the systemic ventricle. Continuous on-line measurements of ventricular end-diastolic area, end-systolic area, percentage fractional area change [%(end-diastolic area − end-systolic area)/end-diastolic area], and the waveforms showing rate of change of area (dA/dt) were displayed, along with the electrocardiogram and the real-time cross-sectional image for each beat (Fig. 2). In addition, rates of peak filling and emptying were generated from the waveforms. A good quality signal was present when little perturbation was noted due to respiration, and homogeneity of the waveform was noted across the entire spectral screen. The average of 5 beats for each of the above variables as measured automatically was recorded for each subject. Later, off-line review of the tracing showing rate of change of area was performed, with identification of the three phases of ventricular filling: namely early passive filling, diastasis, and atrial contraction (Fig. 3). Using calipers, the change in ventricular area that corresponded to atrial contraction was measured and expressed as a percent of the entire change in area that occurred during ventricular filling in the short-axis view. Analysis of the proportion of atrial contribution and peak filling rate were limited to the short-axis views, as previous studies have suggested that the assessment of these variables in the short axis do not vary significantly with heart rate.[17]

Statistical analysis

The results are expressed as a mean value and standard deviation where appropriate. Comparison between the groups is performed with Student's T-test or Wilcoxon rank sum test, where appropriate. Differences were considered statistically significant when the P value was smaller than 0.05. Statistical analysis was performed with STATA 6.0™ (College Station, TX).

Results

Image data and its acquistion

It was possible to obtain reproducible measurements for all four quantitative parameters in 60 subjects

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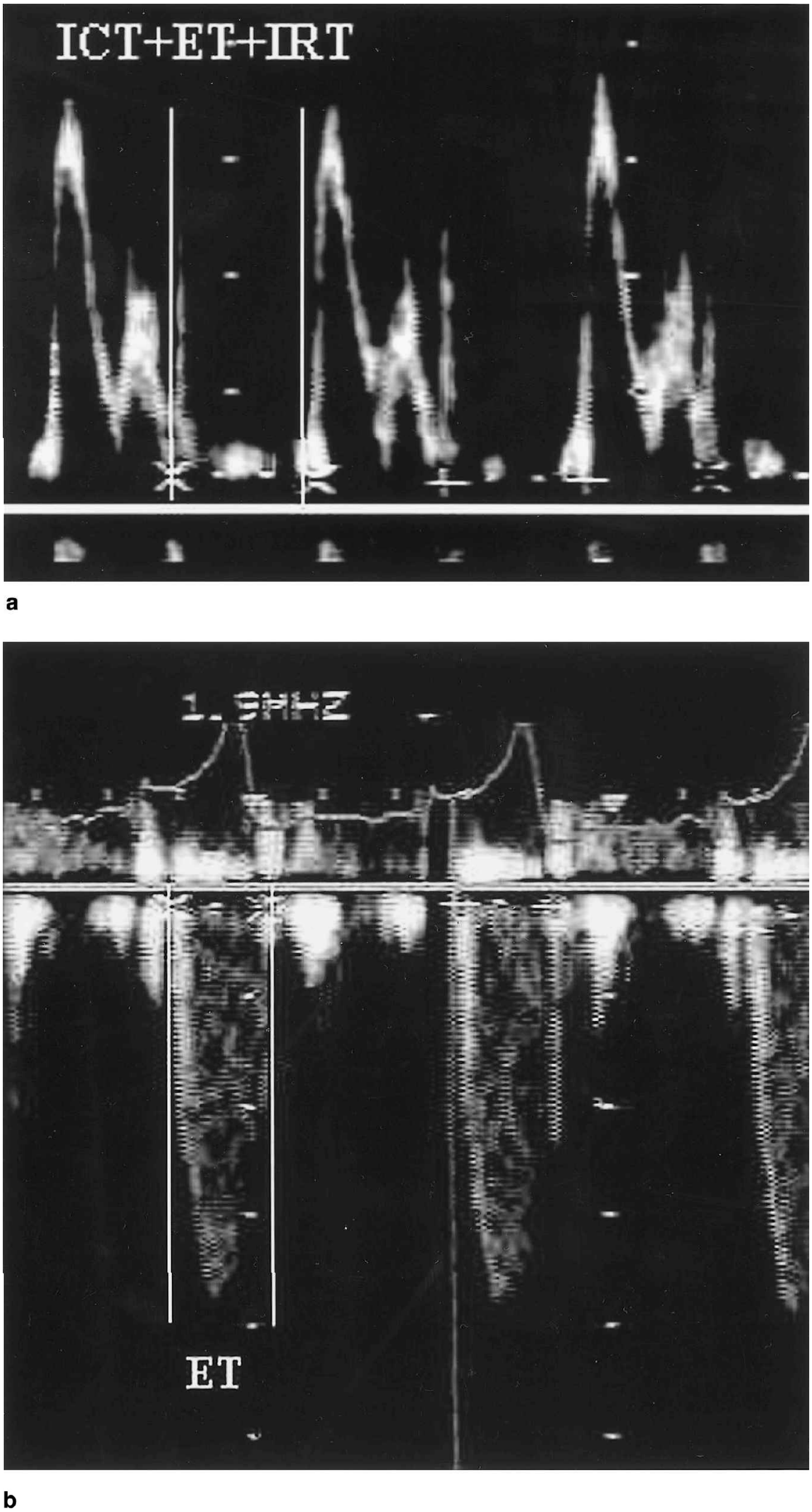

Figure 1.
Doppler velocity curve signals from the (a) atrioventricular valve and (b) arterial valve. ICT = isovolumic contraction time, IRT = isovolumic relaxation time, ET = ejection time.

(90%). In the remaining seven subjects, poor acoustic windows, erratic respiratory patterns, or non-cooperation on the part of the subject prevented accurate assessment of one or more quantitative value. In six subjects, three controls and three patients with a functionally single right ventricle, significant variation in the area versus time tracing prevented a reliable measurement of the atrial

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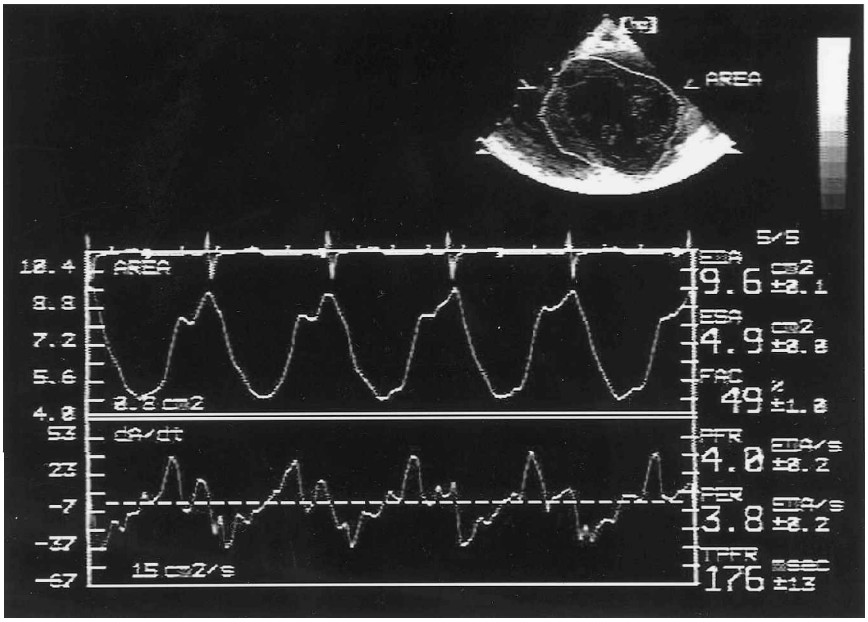

Figure 2.
Short-axis image of systemic morphologically right ventricle in a patient with hypoplastic left heart syndrome. Automatic detection creates tracings of the endocardial borders and produces two waveforms. The upper waveform (AREA) represents the change in ventricular area throughout the cardiac cycle, the lower waveform (dA/dt) represents the corresponding rate of change of ventricular area.

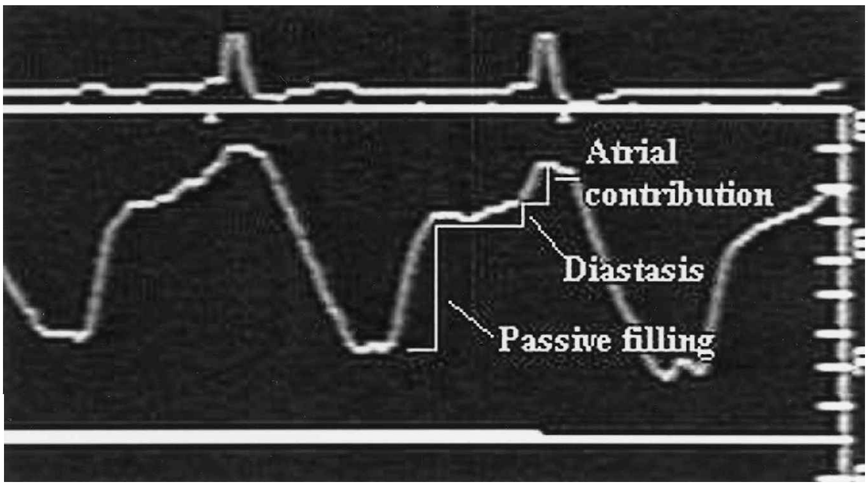

Figure 3.
The waveform produced by automatic detection of borders allows assessment of the relative contribution of the three phases of ventricular filling: rapid passive filling, diastasis and atrial contraction.

proportional contribution. In two patients, both with functionally single right ventricle, poor quality of the cross-sectional images did not allow for satisfactory application of the automatic system to the apical image. The index of myocardial performance was successfully measured in all patients.

Automatic parameters for detection of borders

The data are summarized in Table 2. We found the ventricular diastolic cross-sectional area of the functionally single right ventricle to be smaller than that of the control group in the long-axis plane, but greater than that of the control group in the short axis plane. No difference in proportional fractional change in area was present between the two groups in the long-axis plane. The proportional change in area, however, was significantly lower in those with functionally single right ventricles in the short-axis plane. Rates of both peak emptying and filling were lower in those with functionally single right ventricles in comparison to controls. The proportional atrial contribution was significantly greater in those with functionally single right ventricles in comparison to controls.

Index of myocardial performance

Differences in the Doppler-derived indexes were noted between those with functionally single right ventricles and controls. While there was considerable overlap between the two groups, the mean index of myocardial performance for the control population was 0.30 ± 0.05, as compared to 0.41 ± 0.12 in those with functionally single right ventricles. The higher index of myocardial performance in the setting of a functionally single right ventricle appears to be due primarily to a shortening of ejection time.

Table 2. Comparison between the functionally single right ventricle and the normal left ventricle.

	Controls	RV	p value
N	32	35	
Age (years)	8.03 ± 4.3	7.7 ± 3.1	0.74
Body surface area (m^2)	0.92 ± 0.29	0.9 ± 0.2	0.75
Doppler			
Index of myocardial performance	0.30 ± 0.05	0.41 ± 0.12	0.001*
Ejection time†	0.39 ± 0.05	0.35 ± 0.05	0.01*
Combined isovolumic relaxation & contraction time†	0.48 ± 0.11	0.47 ± 0.15	0.58
Automatic border detection			
Long-axis end-diastolic area (cm^2/m^2)‡	15.4 ± 3.8	13.4 ± 3.2	0.03*
Short-axis end-diastolic area (cm^2/m^2)‡	7.5 ± 2.3	9.7 ± 2.5	0.001*
Ratio short-axis/long-axis end-diastolic area	0.50 ± 0.17	0.71 ± 0.21	0.001*
Long-axis % fractional area change	26.6 ± 5.7	30.3 ± 9.1	0.29
Short-axis % fractional area change	54.6 ± 10.5	42.7 ± 10.1	0.001*
Short-axis % atrial contribution	22.2 ± 4.1	32.0 ± 4.4	0.001*
Short-axis peak filling rate	5.7 ± 1.9	3.5 ± 1.0	0.004*
Short-axis time to peak filling	98.1 ± 45.1	95.4 ± 41.7	0.74
Short-axis peak emptying rate	4.3 ± 1.1	3.1 ± 0.9	0.003*

The ejection time divided by the root of the RR interval was 0.35 in those with functionally single right ventricles, versus 0.39 in the control group. There was no difference between the two groups with respect to the indexed combined isovolumic contraction and relaxation times. We also sought to determine the potential impact of inhibitors of angiotensin-converting enzyme on ventricular mechanics in those with functionally single right ventricles. The mean measured ejection time divided by the root of the RR interval was higher in those patients managed by inhibition of angiotensin-converting enzyme (0.36 ± 0.04) as opposed to 0.34 ± 0.06 in the controls, though the difference did not reach statistical significance ($p = 0.17$).

Discussion

In order to understand the mechanism and etiology of ventricular dysfunction in patients with a functionally single ventricle, it is necessary to understand ventricular performance in patients who are well after completion of the Fontan operation. Data from this study demonstrates fundamental differences in ventricular geometry between those having a functionally single right ventricle and the systemic morphologically left ventricle in normal controls. The ratio of short-axis end-diastolic area to long-axis end-diastolic area is greater in the functionally solitary morphologically right ventricle subserving a systemic function than in controls. This difference has been demonstrated previously for the morphologically left ventricle, and accounts for the spherical shape of this ventricle when functionally single when compared to the "bullet shape" of the normal left ventricle.[18] Data from this study suggests that the same phenomenon occurs in the setting of the functionally single right ventricle.

Comparison of ventricular shortening between those with functionally single ventricle and control populations is complicated by these fundamental differences in ventricular geometry. Since automatic detection of borders offers data on change of area, it provides a better approximation of the change in ventricular volumes in comparison to single plane linear dimensional changes. In our study, the proportional change in fractional area in the short axis was lower in the population with functionally single ventricles, while there was no significant difference in this change when assessed in the long axis. Together, these data agree with previous findings using magnetic resonance imaging which showed that the ejection fraction of the functionally single right ventricle is less than that in the normal systemic left ventricle.[19]

Measures of diastolic function also differed between those with functionally single right ventricles and controls. The percentage contribution of atrial contraction to ventricular filling provides an indirect measure of diastolic function. When the ventricular relaxation is impaired, early passive filling decreases, and atrial contraction must contribute more to ventricular filling.[20] Data obtained from radionuclide ventriculography, and previous studies with automatic detection of borders, have demonstrated that atrial contraction typically accounts for almost one-quarter of ventricular filling.[21,22] In our study, the atrial contribution was 22% in the control population, but 32% in those with functionally single ventricles. These findings agree with previous

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data obtained by cardiac catheterization, demonstrating an increased contribution of atrial contraction to ventricular filling in patients with the Fontan circulation.[23,24] This has important clinical implications when one considers the high incidence of sinus nodal dysfunction in patients after the Fontan procedure. Since a significant proportion of right ventricular filling is dependent upon atrial contraction, loss of sinus rhythm results in a marked drop in cardiac output.

The automatically derived data suggests that both systolic and diastolic performance is impaired in patients with a functionally single right ventricle when compared to controls. It is not surprising, therefore, that the index of myocardial performance values was significantly higher in those with functionally single ventricles. Examination of the components of the index of myocardial performance suggests that there is a shortening of the ejection time in the setting of a functionally single right ventricle that accounts for the increased index of myocardial performance. One possible explanation for this phenomenon is an increased afterload in this population. In the majority of our patients with functionally single ventricles, the aortic arch has been reconstructed with a pulmonary homograft. This might produce a less compliant aorta, thereby increasing afterload. The relative shortening of ejection time in this population may support the use of afterload-reducing medications. In our patients, the use of inhibitors of angiotensin-converting enzyme was not significantly associated with a higher ejection time when indexed to the root of the RR interval. Further evaluation of this question is warranted in a larger population with and without evidence of ventricular dysfunction.

To our knowledge, values for the index of myocardial performance have not previously been reported in those with functionally single ventricles. The published mean values for index of myocardial performance in the systemic left ventricle is 0.39 ± 0.04 in healthy adults, and 0.35 ± 0.04 in healthy children.[9,11] In our study, the mean value for normal controls was 0.30 ± 0.05. The difference between our control data and that reported previously may be due to the fact that the previously reported normal values were obtained retrospectively. Data in our study were obtained prospectively, and every effort was made to optimize the Doppler signals for measurements.

Limitations

A limitation to this study is its cross-sectional design. While most patients with functionally single ventricle followed at our institution undergo routine echocardiographic studies regardless of clinical status, there is a potential for selection bias in this cohort. The major technical limitation to this study relates to the geometric assumptions made to provide automatic detection of borders. Such automatic assessment of the ventricle is carried out in two orthogonal planes. Whilst this provides a representative measure of ventricular function, it does not evaluate true volumetric changes. There can be significant regional variation in ventricular function. Using magnetic resonance imaging, Fogel et al.[25] demonstrated that twisting and contraction vary considerably in different portions of the ventricle. Studies in adults, however, have shown good correlation between automatic assessment of borders, and angiographic measurements of ejection fraction in the normal left ventricle.[21] Another limitation to the study is the potential influence of pre-load on our non-invasive measures of diastolic function, the atrial contribution to ventricular filling, and the peak filling rate. We elected to eliminate subjects with volume load secondary to either arterial or atrioventricular valvar insufficiency from our study in order minimize differences in pre-load between the subjects. Heart rate can also influence measurements of ventricular function, such as fractional shortening. Previous studies, however, have shown that measurements of the index of myocardial performance and automated detection of borders to measure ventricular filling as obtained in the short-axis do not vary significantly in the normal range of heart rate.[8,16]

Conclusions

We have shown that automatic detection of borders, and Doppler-derived indexes of myocardial performance, are valuable tools in evaluating patients with functionally single ventricles. These modalities can be applied quickly and efficiently at the bedside, or used in an outpatient setting. The techniques demonstrate that there are considerable differences in the mechanics of the functionally single right ventricle when compared to the normal systemic left ventricle. The functionally single ventricle assumes a more spherical shape, and has a diminished fractional change of area. The functionally single right ventricle also has a lower peak rate of filling, and relies more on atrial contraction for ventricular filling, both of which imply diminished ventricular compliance. The shorter ejection times relative to combined isovolumic times in the functionally single right ventricle suggest less efficient ventricular mechanics. Understanding the importance of the role of atrial contraction to ventricular filling, and the potential deleterious effects of increased afterload on the functionally single right ventricle, may

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allow for optimal medical management and a better understanding into the process of ventricular dysfunction in this population.

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