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The Impact of the Left Ventricle on Right Ventricular Function and Clinical Outcomes in Infants with Single–Right Ventricle Anomalies up to 14 Months of Age

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Abstract

Background: Children with single-right ventricle anomalies such as hypoplastic left heart syndrome (HLHS) have left ventricles of variable size and function. The impact of the left ventricle on the performance of the right ventricle and on survival remains unclear. The aim of this study was to identify whether left ventricular (LV) size and function influence right ventricular (RV) function and clinical outcome after staged palliation for single-right ventricle anomalies.

Methods: In the Single Ventricle Reconstruction trial, echocardiography-derived measures of LV size and function were compared with measures of RV systolic and diastolic function, tricuspid regurgitation, and outcomes (death and/or heart transplantation) at baseline (preoperatively), early after Norwood palliation, before stage 2 palliation, and at 14 months of age.

Results: Of the 522 subjects who met the study inclusion criteria, 381 (73%) had measurable left ventricles. The HLHS subtype of aortic atresia/mitral atresia was significantly less likely to have a measurable left ventricle (41%) compared with the other HLHS subtypes: aortic stenosis/mitral stenosis (100%), aortic atresia/mitral stenosis (96%), and those without HLHS (83%). RV end-diastolic and end-systolic volumes were significantly larger, while diastolic indices suggested better diastolic properties in those subjects with no left ventricles compared with those with measurable left ventricles. However, RV ejection fraction was not different on the basis of LV size and function after staged palliation. Moreover, there was no difference in transplantation-free survival to Norwood discharge, through the interstage period, or at 14 months of age between those subjects who had measurable left ventricles compared with those who did not.

Conclusions: LV size varies by anatomic subtype in infants with single-right ventricle anomalies. Although indices of RV size and diastolic function were influenced by the presence of a left ventricle, there was no difference in RV systolic function or transplantation-free survival on the basis of LV measures.

Keywords

Hypoplastic left heart syndrome; Norwood procedure; Echocardiography; Single right ventricle; Aortic atresia; Mitral atresia

In hypoplastic left heart syndrome (HLHS) and variations of single-right ventricle anomalies, the left ventricle is unable to support the systemic circulation. In the current era, HLHS remains a congenital heart lesion with significant morbidity and mortality. In the recent Pediatric Heart Network Single Ventricle Reconstruction (SVR) trial, overall transplantation-free survival to 14 months of age was 69%.¹ In HLHS, LV size may affect the performance of the systemic right ventricle and may alter outcomes for this high-risk population. Left ventricular (LV) size is often closely associated with the size and patency of the left-sided valves. In the setting of aortic atresia with mitral atresia, the left ventricle is expected to be quite diminutive (Figure 1A) and in some cases is too small to even measure. With a small or absent left ventricle, cardiac output is dependent entirely on the right ventricle. In those with patent mitral valves and aortic atresia, the left ventricle is variable in size dependent on the size of the mitral valve and may be compromised by coronary fistulous connections, with the potential for a detrimental effect on right ventricular (RV) function and outcome (Figures 1B and 1C).²⁻⁴ In patients with patency of both the mitral and aortic valves, LV ejection may augment cardiac output and has been shown to be associated with improved short-term survival after single-ventricle palliation in infancy.⁵

In the SVR trial, an echocardiography core laboratory measured LV size, mass, and function as well as aortic and mitral valve patency. We sought to identify whether LV size and function influence RV function and clinical outcomes in children with single-right ventricle anomalies. We hypothesized that a left ventricle that could augment cardiac output might result in better ventricular performance and improved outcome.

METHODS

Study Design

The design⁶ and results¹ of the SVR trial have been previously published. In brief, 549 infants with single-right ventricle anomalies and planned Norwood surgical palliation were randomized at 15 North American centers to a modified Blalock-Taussig shunt or a right ventricle-to-pulmonary artery shunt and followed to 14 months of age with a primary outcome of transplantation-free survival by 12 months of age. As part of the SVR trial, transthoracic echocardiograms were collected in a standardized, prospective fashion and evaluated at a core laboratory at four time points during the study: (1) baseline (before the Norwood procedure); (2) post-Norwood, either at time of discharge or at approximately 30 days of age if still hospitalized, at a median age of 20 days; (3) before the stage 2 procedure (at a median age of 4.6 months); and (4) at 14 months of age (at a median age of 14.2 months). The impact of shunt type on echocardiographic parameters of RV and valve function has also been previously reported, and no significant differences were found.⁷ All subjects who participated in the Pediatric Heart Network SVR trial and had interpretable echocardiograms in the preoperative period and had the specific anatomic features of aortic

atresia/mitral atresia (AAMA), aortic atresia/mitral stenosis (AAMS), or aortic stenosis/mitral stenosis (ASMS) identified on the echocardiograms were included. Patients with aortic stenosis/mitral atresia were excluded from this analysis because this anatomic variation is quite rare and typically includes a ventricular septal defect. Patients with non-HLHS (e.g., unbalanced atrioventricular canal defect, double-outlet right ventricle with mitral atresia) were treated as a separate group and included because they have functionally single right ventricles and undergo staged palliation in the same manner as those with HLHS.

Echocardiographic Analysis

Echocardiograms from the preoperative period, immediately after the Norwood procedure, before stage 2 palliation, and at 14 months of age were evaluated. Aortic and mitral valve patency was determined. Echocardiographic parameters of RV size and function, LV presence and size and function, and assessment of tricuspid valve function were also collected (Table 1). RV function and tricuspid valve function were categorized similar to the previous SVR echocardiography study.⁷ Patients were included in the analysis until they met a different endpoint from the usual surgical course (i.e., heart transplantation before 14 months, biventricular repair before 14 months). Core laboratory procedures for image analysis and data management have been previously described.⁷ Analysis was performed using presence or absence of an identifiable left ventricle. An identifiable left ventricle was defined as a left ventricle that had an LV cavity that could be measured. In those who had identifiable left ventricles, parameters of LV size and function were measured, including indexed LV mass, indexed LV end-diastolic volume, LV ejection fraction (when measurable), and LV mass-to-volume ratio.

Outcome Analysis

Outcome variables assessed included transplantation-free survival to Norwood discharge, interstage transplantation-free survival, and overall transplantation-free survival.

Statistical Analysis

Associations between HLHS subcategories and presence of a left ventricle, as well as associations between binary outcomes as death or transplantation or the presence of moderate or severe tricuspid regurgitation with presence of a left ventricle, were assessed using the Fisher exact test. Associations between HLHS subcategories and continuous LV mass-volume outcomes (e.g., LV mass, ejection fraction, and end-diastolic volume) were assessed using regression analysis-of-variance testing. Linear mixed models were used to test whether RV ejection fraction and RV fractional area change were different across HLHS categories at the four time points. Analyses of variance were used to determine the difference in RV ejection fraction or RV fractional area change on the basis of LV mass, LV ejection fraction, and LV end-diastolic volume (all comparisons of upper 50th percentile with lower 50th percentile) at the four time points. Associations between the presence of a left ventricle and each of several echocardiographic outcomes were assessed using *t* tests without adjustment for multiple testing.

Cox proportional-hazards models were used to test whether there was a difference in transplantation-free survival to Norwood discharge, interstage transplantation-free survival, or overall transplantation-free survival between those patients who had measurable left ventricles and those who did not. The odds ratio of being alive and transplantation free on the basis of shunt type at initial operation was assessed using logistic regression.

RESULTS

Demographic Information

Of the 522 subjects who met study inclusion criteria, 208 (40%) had HLHS with AAMA, 136 (26%) had AAMS, 106 (20%) had ASMS, and 72 (14%) had non-HLHS. Of the total cohort, 381 subjects (73%) had measurable left ventricles, while 141 (27%) had no measurable left ventricles. Those with the subtype of AAMA were significantly less likely to have measurable left ventricles (41%) than those with the other subtypes. The majority of subjects with ASMS (100%), AAMS (96%), and non-HLHS (83%) had measurable left ventricles by echocardiography.

Assessment by HLHS Anatomic Subtype

LV indices of size and function were different among the various anatomic subtypes of HLHS. Table 2 shows the differences in the LV indices between the subtypes at the pre-Norwood echocardiographic examination, using the non-HLHS subtype as the baseline against which the other subtypes were compared (zero estimate). LV mass, LV ejection fraction, and LV end-diastolic volume were significantly higher in the ASMS subtype compared with the other subtypes, while the AAMA subtype had the smallest mass and volume, as well as the lowest ejection fraction. With regard to measures of RV function, RV ejection fraction and RV fractional area change were significantly higher in the AAMS subtype compared with the ASMS subtype.

Analysis by Presence or Absence of a Left Ventricle

Tables 3 and 4 show echocardiographic variables assessed for subjects with HLHS with measurable compared with nonmeasurable left ventricles at each of the protocol echocardiographic examinations. With regard to RV echocardiographic measures, most indices were no different whether a left ventricle was present. However, RV end-diastolic and end-systolic volumes were significantly larger in those patients with no left ventricles compared with those with measurable left ventricles before Norwood palliation and during the interstage period; those differences resolved in transplantation-free survivors at 14 months. Although RV ejection fraction was better in those with a left ventricles preoperatively ($P = .008$), there was no difference in RV ejection fraction between the groups after surgical palliation procedures (Figure 2). Moreover, there was no consistent statistically significant difference in RV ejection fraction, RV percentage fractional area change, RV myocardial performance index, tricuspid peak annular systolic velocity, or tricuspid annular isovolumic acceleration on the basis of LV mass, LV ejection fraction, or LV end-diastolic volume (all comparisons of upper 50th percentile with lower 50th percentile) at the four time points.

For those patients with HLHS, diastolic RV indices (E/A ratio, E/E' ratio, and E' velocity) were found to be significantly associated with the presence of an identifiable left ventricle at the preoperative time point. E/A ratio and E' velocity were both lower and E/E' ratio was higher in those with identifiable left ventricles (Table 3). Following the Norwood procedure and at each of the postoperative intervals, both E-wave and A-wave velocity were found to be significantly higher in the subjects with a identifiable left ventricles (Table 4).

Finally, we assessed whether significant tricuspid regurgitation might be more prevalent on the basis of LV size and function. There were no statistically significant differences with regard to the percentage of subjects with moderate to severe tricuspid regurgitation on the basis of LV mass, LV ejection fraction, or LV end-diastolic volume at all four time points.

Assessment of Outcomes

Survival analyses on the basis of Cox regression demonstrated that there was no difference in transplantation-free survival to Norwood discharge, interstage transplantation-free survival, or overall transplantation-free survival to 14 months between those subjects who had identifiable left ventricles and those who did not. There was also no difference in transplantation-free survival on the basis of the presence or absence of a left ventricle at initial operation. Transplantation-free survival was significantly different on the basis of anatomic subtype, with the non-HLHS group having a higher percentage of deaths or heart transplantations than the other three categories (Table 5) when looking at the entire cohort through the end of the study period. Transplantation-free survival was also worse for the non-HLHS group before the post-Norwood study.

DISCUSSION

The diagnosis of single-right ventricle anomalies is associated with a wide range in the size and function of the left ventricle. The goal of this study was to describe the relationship of LV size and function on RV function and outcome in the SVR trial, the largest prospective cohort of single-right ventricle anomalies ever assessed during initial infant single-ventricle palliation. As we anticipated, LV size varied according to anatomic subtype. Those with AAMA typically had no identifiable cavities, while those with patent mitral and aortic valves had the largest LV chambers. We theorized that because LV size was closely associated with anatomic subtype, the subtypes might have very different RV mechanics, RV function, and potentially clinical outcomes. Although a few measures of diastolic RV function varied with LV parameters and therefore with anatomic subtype, the presence of a left ventricle, regardless of cavity size and systolic function, did not significantly influence transplantation-free survival to 14 months.

Since the Norwood procedure became a successful palliation for single-right ventricle anomalies, there has been speculation about the impact of LV size and function on outcomes. Having no measurable left ventricle, as is common in the AAMA subtype, has two important potential consequences for ventricular mechanics: (1) the right ventricle is solely responsible for cardiac output, and (2) there is no ventricular septum for ventriculo-ventricular interaction.⁸ The presence of a left ventricle has the potential to have negative effects. In the cohort of patients with the AAMS subtype, a small, stiff left ventricle with

endocardial fibroelastosis is commonly seen because the left ventricle contracts against an atretic valve. Endocardial fibroelastosis in the left ventricle may alter ventricular septal geometry in a way that reduces RV compliance.⁹ It may also act as a substrate for thrombus formation or eject uselessly into the left atrium.^{9,10} A dilated left ventricle that is noncontractile may also compromise RV filling while adding little to combined ventricular output. For patients with ASMS and those with unbalanced atrioventricular canal defect (non-HLHS type), there is variability in the size and function of the left ventricle. Endocardial fibroelastosis is usually not present in this cohort, and thus the left ventricle is most likely to help augment systemic blood flow. It is reasonable to theorize that this group may have the best RV function and the best clinical outcome.

Surprisingly, we found that the presence or absence of a left ventricle, as well as LV size and function (when present), had little impact on echocardiographic measures of RV size and function, including RV fractional area change and RV ejection fraction up to 14 months of age. In a subanalysis, we found that those with AAMS subtype had higher RV systolic indices than those with ASMS. This was not expected, as the left ventricle in the AAMS subtype typically functions poorly and was presumed to negatively affect RV function. This difference may not reflect a true improvement in RV performance, because the regional hyperdynamic systolic septal motion frequently seen in the AAMS subtype as the hypertensive left ventricle displaces the septum into the right ventricle may exaggerate area and volume change in the right ventricle. Deformation and segmental wall motion were not quantified in this study and may better characterize RV functional status and these findings.

Others have reported that LV size does not have an important impact on RV function in HLHS. Schlangen *et al.*¹¹ measured RV function after Fontan operation using pressure conductance catheters in the cardiac catheterization laboratory and found no difference in end-systolic elastance on the basis of LV size. Other single-center studies suggest that LV size may be associated with RV dysfunction in HLHS. Wisler *et al.*¹² showed a weak negative correlation between larger LV size and poor RV systolic function, as measured by fractional area change and Tei index, in a cohort of 48 patients with HLHS before the Fontan procedure. The association was no longer apparent after the Fontan operation. With regard to clinical outcome in patients with HLHS, Walsh *et al.*¹³ reported that increased interventricular septal thickness negatively affected RV function. They also found that a larger LV diastolic area was associated with higher mortality. These findings, particularly interventricular septal thickness, may be a surrogate for other factors, such as RV afterload or coronary anomalies. In our study, we did not find these differences. We surmise that in a larger multicenter cohort, some of the differences in RV function and outcomes detected in a single-center study may be outweighed by center-related factors that affect morbidity and mortality.

As for indices of diastolic function, there were some interesting observations. We found that E/E' in the right ventricle was higher in the group of patients with left ventricles compared with those with no left ventricles. E/E' is considered a surrogate of LV filling pressures in adults.¹⁴ Our findings suggest that a noncompliant left ventricle (as in those patients with AAMA) may negatively affect RV ventricular filling in this cohort of patients. Alternatively, having no left ventricle may allow more efficient filling in a single right ventricle. Frommelt

*et al.*¹⁵ reported that RV E/E' was not significantly different in survivors versus nonsurvivors of staged palliation of single-right ventricle anomalies. However, E/E' did improve (became lower) from 14 months of age to the pre-Fontan evaluation. It will be interesting to see if this finding of better RV E/E' in those with no left ventricles affects RV performance and clinical outcomes in the long term. Low filling pressures are essential to good Fontan physiology in the single-ventricle population.

We did not find an association between severity of tricuspid regurgitation and LV size or anatomic subtype. Stamm *et al.*¹⁶ reported that tricuspid valve dysplasia in HLHS was related to anatomic subtype. Septal position affects tricuspid regurgitation in other disease states. In patients with corrected transposition of the great arteries who have a systemic right ventricle, the position of the ventricular septum affects tricuspid valve competence.^{17,18} The single-right ventricle anomaly population may have other variables affecting tricuspid valve function, such as leaflet or subapparatus abnormalities,¹⁹ and the short-term nature of this study has not demonstrated the chronic effects of the left ventricle on tricuspid valve function.

Several previous studies assessing HLHS subtypes have focused on aortic and mitral valve patency. In early studies, the AAMA cohort had a higher mortality rate, likely related to the diminutive size of the ascending aorta and its effect on coronary perfusion.^{20,21} More recent studies have suggested that the AAMS group has a higher mortality; it has been surmised that this finding is related to the presence of coronary cameral fistulous connections in patients with this anatomic subtype of HLHS.^{22–24} However, the SVR trial and other studies did not find anatomic subtype as a risk factor for mortality.^{1,25} Our study also found that there was no significant association between anatomic subtype or LV size and clinical outcome. We surmise that LV size is not the determining factor in early outcome after staged palliation for single-right ventricle anomalies, likely because there are so many other issues associated with survival in this very vulnerable population, such as distal arch obstruction,²⁶ shunt obstruction,²⁷ and noncardiac issues.²⁸

Limitations

The SVR trial cohort may not be reflective of the larger number of patients with single-right ventricle anomalies. However, this is the largest cohort of patients undergoing the Norwood procedure that has been reported in the literature. It is possible that our measures of LV size and function were not accurately reflective of the impact of the left ventricle on RV function and on clinical outcome. However, this group of patients underwent a comprehensive and protocol-driven echocardiographic assessment of measures that were made at a single core laboratory.

CONCLUSION

LV size and function do not appear to have a significant impact on RV size and systolic performance for patients with single-right ventricle anomalies undergoing staged palliation. Moreover, LV size and function were not associated with mortality or need for transplantation in this population. Ventricular filling appears to be improved in infants with no identifiable left ventricles. It remains to be seen whether the left ventricle will affect

clinical outcomes for these patients in the long term. This cohort should continue to be followed longitudinally to answer this question.

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Abbreviations

AAMA	Aortic atresia/mitral atresia
AAMS	Aortic atresia/mitral stenosis
ASMS	Aortic stenosis/mitral stenosis
HLHS	Hypoplastic left heart syndrome
LV	Left ventricular
RV	Right ventricular
SVR	Single Ventricle Reconstruction

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HIGHLIGHTS

- In HLHS, the left ventricle can be of variable size.
- RV size is larger in patients with no measurable left ventricles.
- Diastolic indices are slightly better in patients with no measurable left ventricles.
- RV function and mortality are not affected by LV size.

Figure 1. HLHS (**A**) with absent left ventricular cavity; (**B**) with a markedly hypoplastic left ventricle (LV) with endocardial brightness suggestive of endocardial fibroelastosis; and (**C**) with a large, noncontractile LV. *LA*, Left atrium; *RA*, right atrium; *RV*, right ventricle.

	Pre Norwood	Post Norwood	Pre-Stage 2	14 Months
Age (Months) :	0.1	0.7	4.8	14.3
Mean RVEF (%) with LV :	46.9	46.8	44.1	42.9
Mean RVEF (%) without LV:	44.4	46.1	43.3	42.7

*P-value for comparison at Pre-Norwood is 0.008 (t-test) and is NS at other times points.

Figure 2.

RV ejection fraction (RVEF) in those with measurable left ventricles compared with those with absent left ventricles across the study time periods.

Table 1**Echocardiographic measurements performed**

RV size and function
RV end-diastolic volume (mL)
RV end-systolic volume (mL)
RV ejection fraction (%)
RV percentage fractional area change (%)
Tissue Doppler tricuspid peak annular systolic velocity (cm/sec)
Tissue Doppler tricuspid annular isovolumic acceleration
Myocardial performance index calculated by pulsed-wave Doppler and tissue Doppler
RV diastolic size and function
Peak tricuspid inflow E and A velocity (m/sec)
Tricuspid inflow E/A ratio
Tricuspid annular tissue Doppler e' and a' velocities (cm/sec)
Tricuspid E/e' ratio
Pulmonary vein presence/duration of a-wave reversal at atrial systole
LV size and function
LV presence
LV ejection fraction (%)
LV mass (g)
LV end-diastolic volume (mL)
LV mass-to-volume ratio (g/mL)
Tricuspid valve function
Severity of tricuspid regurgitation measured by jet vena contracta
Aortic size and patency
Ascending aorta diameter (mm)
Peak descending aorta velocity (cm/sec)

Table 2

Regression modeling results for pre-Norwood echocardiographic LV mass-volume characteristics by HLHS subcategories

Parameter	Estimate	SE	P^*	$P^\dagger$
LV mass				<.001
ASMS	7.75	2.38	.001	
AAMS	-1.60	2.30	.487	
AAMA	-17.53	2.17	<.001	<.001
Non-HLHS	Reference			
LV ejection fraction				<.001
ASMS	3.53	3.30	.286	
AAMS	-10.49	3.16	.001	
AAMA	-21.46	2.99	<.001	
Non-HLHS	Reference			
LV end-diastolic volume				<.001
ASMS	3.07	0.92	.001	
AAMS	-3.44	0.88	<.001	
AAMA	-7.92	0.84	<.001	<.001
Non-HLHS	Reference			
LV mass/volume ratio				<.001
ASMS	0.56	0.81	.489	
AAMS	2.59	0.78	.001	
AAMA	-1.02	0.74	.173	
Non-HLHS	Reference			

SE, Standard error.

* T -statistic P value.

† F -statistic P value.

Table 3

Echocardiographic outcomes assessed in subjects with measurable left ventricles compared with those with nonmeasurable left ventricles: pre- and post-Norwood assessment

	Pre-Norwood LV assessment			
	<i>n</i>	Left ventricle present	Left ventricle absent	<i>p</i>
Pre-Norwood outcomes				
RVEF (%)	308	47.2	44.5	.016
RV FAC (%)	431	36.1	33.5	.005
RVEDV/BSA ^{1.3} (mL/m ²)	309	83.1	95.0	<.001
RVESV/BSA ^{1.3} (mL/m ²)	308	44.0	52.6	<.001
E-wave velocity (m/sec)	330	0.9	0.9	.48
A-wave velocity (m/sec)	105	0.9	0.8	.19
E/A ratio	105	0.7	0.8	.012
E´ velocity (cm/sec)	209	12.2	13.8	.024
A´ velocity (cm/sec)	105	0.9	0.8	.19
E/E´ ratio	201	8.6	7.1	.002
Post-Norwood outcomes				
RVEF (%)	318	47.0	45.7	.20
RV FAC (%)	398	37.0	35.8	.17
RVEDV/BSA ^{1.3} (mL/m ²)	318	89.6	100.0	.001
RVESV/BSA ^{1.3} (mL/m ²)	318	48.2	54.9	.003
E-wave velocity (m/sec)	382	0.8	0.7	.001
A-wave velocity (m/sec)	176	0.7	0.6	<.001
E/A ratio	176	1.0	1.0	.16
E´ velocity (cm/sec)	361	7.3	8.3	.002
A´ velocity (cm/sec)	186	6.8	6.6	.61
E/E´ ratio	349	12.8	10.0	<.001

BSA, Body surface area; FAC, fractional area change; RVEDV, RV end-diastolic volume; RVEF, RV ejection fraction; RVESV, RV end-systolic volume.

Table 4

Echocardiographic outcomes assessed in subjects with measurable left ventricles compared with those with nonmeasurable left ventricles: pre-stage II and 14-month assessment

	Pre-stage II LV assessment			
	<i>n</i>	Left ventricle present	Left ventricle absent	<i>p</i> [*]
Pre-stage II outcomes				
RVEF (%)	246	44.8	43.3	.17
RV FAC (%)	323	34.5	32.6	.038
RVEDV/BSA ^{1.3} (mL/m ²)	246	111.0	121.0	.038
RVESV/BSA ^{1.3} (mL/m ²)	246	62.1	69.5	.032
E-wave velocity (m/sec)	311	0.9	0.8	.007
A-wave velocity (m/sec)	173	0.8	0.7	.028
E/A ratio	173	1.0	1.0	.70
E' velocity (cm/sec)	296	8.6	8.8	.66
A' velocity (cm/sec)	182	7.5	7.8	.38
E/E' ratio	286	11.3	10.3	.09
14-month outcomes				
RVEF (%)	202	43.5	42.6	.47
RV FAC (%)	263	32.8	32.5	.77
RVEDV/BSA ^{1.3} (mL/m ²)	202	90.7	93.9	.49
RVESV/BSA ^{1.3} (mL/m ²)	202	52.3	54.1	.63
E-wave velocity (m/sec)	276	0.9	0.8	.009
A-wave velocity (m/sec)	154	0.8	0.6	<.001
E/A ratio	154	0.8	0.6	<.001
E' velocity (cm/sec)	272	8.7	8.6	.84
A' velocity (cm/sec)	152	7.1	6.1	.024
E/E' ratio	266	11.8	10.6	.07

BSA, Body surface area; FAC, fractional area change; RVEDV, RV end-diastolic volume; RVEF, RV ejection fraction; RVESV, RV end-systolic volume.

*
t test.

Table 5

Cumulative death/heart transplantation status at the end of the study period by HLHS anatomic subcategory

	Non-HLHS*	AAMA	AAMS	ASMS	P
Death or heart transplantation					.029
No	38 (53%)	135 (65%)	87 (64%)	79 (75%)	
Yes	34 (47%)	73 (35%)	49 (36%)	27 (25%)	

* Fisher exact test.