Increased common atrioventricular valve tenting is a risk factor for progression to severe regurgitation in patients with a single ventricle with unbalanced atrioventricular septal defect

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Objective: Significant atrioventricular valve regurgitation (AVVR) increases mortality in patients with unbalanced atrioventricular septal defects (uAVSDs) and a single ventricle. We tested the hypothesis that abnormal leaflet tethering is associated with progressive AVVR in patients with a single ventricle with uAVSD.

Methods: We retrospectively reviewed the initial presentation and prebidirectional cavopulmonary anastamosis echocardiograms of 46 consecutive patients with uAVSD with single ventricle palliation. AVVR was graded as moderate to severe if the sum of vena contracta width to dominant valve annulus ratio was $\geq$0.33. We measured tenting height, annular to leaflet angle and annular diameter, indexed to patient size where appropriate. Multivariate analysis of variables to predict progressive AVVR was performed.

Results: At follow-up of 3.3 $\pm$ 2.4 years, 24 patients had mild AVVR (Group A) and 22 had moderate to severe AVVR. Overall mortality was 6%, whereas 10 had valve repair/replacement surgery. Of 22 patients with severe AVVR at follow-up, 9 had severe AVVR at initial presentation (Group B), whereas 13 had mild AVVR at presentation but developed severe AVVR at their prebidirectional cavopulmonary anastamosis echocardiogram (Group C). Group A patients had a smaller tenting height at initial presentation compared with patients in Group B and Group C, and also had early progressive reduction of indexed tenting height ($P < .01$). An absolute tenting height >6 mm (odds ratio, 6.6; 95% confidence interval, 1.1-39.0; $P = .03$) at the initial echocardiogram was identified as an independent predictor of subsequent severe AVVR.

Conclusions: Early leaflet tethering is predictive of subsequent AVVR in patients with a single ventricle with uAVSD. Patients with competent AVV had progressive reduction in the degree of leaflet tethering, whereas patients with AVVR did not. This may represent an important adaptive process to maintain valve competency in uAVSD. (J Thorac Cardiovasc Surg 2014;148:2580-8)

Unbalanced atrioventricular septal defect (uAVSD) is an uncommon congenital heart defect, comprising <1% of all congenital heart disease.[1,2] It is a nonhomogeneous lesion with right ventricular dominance being more frequent[2-4] and it is frequently associated with heterotaxy. Those patients who are not deemed suitable for a biventricular repair are surgically palliated by staged operations to a total cavopulmonary connection. uAVSD with single ventricle circulation has a particularly high morbidity and mortality rate,[5,6] more so than seen in patients with classic hypoplastic left heart syndrome (HLH).[7,8] The presence of associated atrioventricular valve regurgitation (AVVR) is frequent in uAVSD with up to 15% to 30% requiring surgical intervention; it is also an independent predictor of mortality.[9-11]

Leaflet prolapse and tethering of the mitral valve, tricuspid valve (TV), and left atrioventricular valve post-AVSD repair have been previously identified as important mechanisms of valve failure.[12-15] In a more recent study,[16] we noted that prolapse as a mechanism of TV regurgitation in HLH is a later phenomenon, with TV tethering being the predominant feature in neonates with HLH who subsequently developed severe tricuspid regurgitation. With this background, we hypothesized that the presence of leaflet tethering in the common atrioventricular valve (AVV) may be an important precursor to subsequent severe regurgitation in patients with an uAVSD.[17-19]

METHODS

Data Sources and Variables

Following institutional ethics board approval the echocardiogram of all patients with uAVSD between January 2003 and July 2012 was identified from our electronic database. The inclusion criterion was an identifiable echocardiogram at the initial evaluation before any surgical intervention at Stollery Children's hospital. Patients who subsequently underwent

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Abbreviations and Acronyms

AVV = atrioventricular valve
AVVR = atrioventricular valve regurgitation
BCPA = bidirectional cavopulmonary anastamosis
ED = end diastole
ES = end systole
HLH = hypoplastic left heart syndrome
IVS = interventricular septum
TV = tricuspid valve
uAVSD = unbalanced atrioventricular septal defect

biventricular repair at any stage were excluded. Demographic, anatomic, and procedural variables (including date of birth, weight, height, body surface area, presence of isomerism, presence of trisomy 21, dominant ventricular morphology, presence of pulmonary or aortic outflow obstruction, surgical procedures, and date of surgical procedure), and current status (alive or deceased or cardiac transplantation) were recorded.

Two-Dimensional Echocardiographic Measurements

Patients' 2-dimensional echocardiographic images were analyzed at initial presentation, prebidirectional cavopulmonary anastamosis (BCPA), post-BCPA, and at the most recent follow-up.

Measurements were made by a single observer (C.V.) on Q-Lab (Phillips Medical Systems, Andover, Mass) and they included total common atrioventricular valve annular diameter in end diastole (ED), dominant valve annulus in ED and nondominant valve annulus in ED, with indexing to body surface area where appropriate. Degree of AVVR was defined as being moderate to severe if the sum of vena contracta widths to dominant valve annulus ratio in the 4-chamber view was $\geq$0.33. The parameters of leaflet tethering measured were:

1) Tenting height to common valve, defined as the distance between leaflet coaptation and the common valve annular plane in ED and end-systole (ES);
2) Tenting height to interventricular septum (IVS), defined as the distance from common valve annular plane to crest of the IVS in ED and ES;
3) Annular to leaflet angle, defined as the angle between the annular plane to the nadir of leaflet coaptation of both the nondominant and dominant valve in ES; and
4) Annular to IVS angle, defined as the angle between the annular plane to the crest of the IVS of both the nondominant and dominant valve in ES (Figure 1).

Data Analysis

Patients' baseline characteristics and outcomes were summarized using descriptive statistics. Normally distributed data were presented as the mean $\pm$ standard deviation or, in cases where the distribution was not normal, as median with range. The cumulative prevalence of moderate to severe AVVR, requirement of valve repair, cardiac transplantation, and mortality in all patients were reported.

The patients were divided into 3 groups. Group A included those without or with only mild AVVR at presentation and follow-up, Group B included patients with moderate to severe AVVR at initial presentation and at follow-up, and Group C included patients with mild AVVR at initial presentation but moderate to severe AVVR at the pre-BCPA echocardiogram. χ^2 tests were used to compare discrete data between groups; in those cases where the expected cell count was <5, the Fisher exact test was used. To identify the baseline characteristics associated with outcome, univariate analysis was evaluated and multivariate models were subsequently applied. Initially, candidate variables showing a possible association with prognosis by univariate analysis ($P < .05$) were considered starting with the most significant variable. Significant variables were identified by stepwise regression at the $P < .05$ level. Risk ratios were expressed as odds ratios (ORs) with associated 95% confidence intervals (CIs). Finally, patients who achieved BCPA operation were explored with regard to progression of tenting height and angle change over time. Differences at each echocardiogram time point were compared between the groups with analysis of variance and Dunnett 2-sided post hoc test between Group A and Group C. The statistic analysis was performed with SPSS 13.0 for Windows (IBM-SPSS Inc, Armonk, NY).

RESULTS

Fifty-nine patients were identified, of whom 13 were excluded (9 underwent biventricular repair and in 4 others the initial echocardiogram could not be retrieved). Hence, 46 patients were eligible for the analysis (Figure 2).

Prevalence of Moderate to Severe AVVR, Valve Surgery, and Clinical Outcomes

Table 1 summarizes demographics and outcomes at 3.3 $\pm$ 2.4 years of follow-up. The majority of patients had isomerism (70%) and a dominant right ventricle (76%) and at the time of latest follow-up 50% had total cavopulmonary circulation (Fontan or Kawashima procedure).

Moderate to severe AVVR was present in 22 patients (48%) during the follow-up period with 10 undergoing AVV surgery (9 valve repair and 1 valve replacement). Valve surgical intervention occurred at a mean age of 2.1 $\pm$ 1.5 years. Three patients had their repair in association with BCPA, 2 at Fontan operation, 1 at Kawashima shunt, and 1 at pulmonary artery banding. Of the remaining 3 patients, 2 had valve repair after BCPA and 1 after Fontan operation. Valve repair was successful in 4 patients with less than mild postoperative regurgitation, whereas 6 had ongoing moderate to severe AVVR. One of these patients died from multiorgan failure after repair, another required cardiac transplantation, and a third died 18 months postoperatively from cardiac failure, whereas the other 3 are still alive.

Of 12 patients with moderate to severe AVVR who did not undergo valve surgery, 8 had no change in severity, 1 patient underwent cardiac transplantation due to severe ventricular dysfunction, and 3 had improvement in their AVVR severity after the BCPA.

Analysis of Nonechocardiographic Risk Factors for Development of Moderate to Severe AVVR at Follow-up

Demographics and clinical status during a follow-up period of 3.3 $\pm$ 2.4 years is summarized in Table 2. Using a predictive model, clinical variables (see Table 1) were not different between patients with and without moderate to severe AVVR. Univariate risk analysis did not find any association between clinical variables listed with