Trajectory of Left Ventricular Remodeling in Children With Valvar Aortic Stenosis Following Balloon Aortic Valvuloplasty

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BACKGROUND: Aortic valve stenosis is the most common type of congenital left ventricular (LV) outflow tract obstruction. Balloon aortic valvuloplasty (BAV) has become the first-line treatment pathway in many centers. Our aim was to assess the trajectory of LV remodeling following BAV in children and its relationship to residual aortic stenosis (AS) and insufficiency (AI).

METHODS: Children <18 years of age who underwent BAV for isolated aortic stenosis from 2004 to 2012 were eligible for inclusion. Those with AI before BAV, other complex congenital heart lesions, or <2 accessible follow-up echocardiograms were excluded. Baseline and serial echocardiographic data pertaining to aortic valve and LV size and function were retrospectively collected through December 2017 or the first reintervention. Longitudinal data was assessed using per-patient time profiles with superimposed trend lines using locally estimated scatterplot smoothing. Associations with reintervention or death were also evaluated.

RESULTS: Among the 98 enrolled children, the median (interquartile range) age at BAV was 2.8 months (0.2–75). The median (interquartile range) follow-up was 6.8 years (1.9–9.0). Children with predominantly residual AI (n=11) demonstrated progressive increases in their LV end-diastolic dimension within the first 3 years after the BAV, followed by a plateau (P<0.001). Their mean LV circumferential and longitudinal strain values remained within the normal range but lower than in the non-AI group (P=0.001 and P=0.001, respectively). Children with predominantly residual aortic stenosis (n=44) had no changes in LV dimensions but had a rapid early increase in mean LV circumferential and longitudinal strain. The cumulative proportion (95% CI) of reintervention at 5 years following BAV was 33.7% (23.6%–42.4%).

CONCLUSIONS: Our study demonstrates that LV remodeling occurs mainly during the first 3 years in children with predominantly residual AI after BAV, with no subsequent significant functional changes over the medium term. These data improve our understanding of expected patient trajectories and thus may inform decisions on the timing of reintervention.

Key Words: aortic valve ■ aortic valve stenosis ■ cardiology ■ child ■ ventricular remodeling

Valvar aortic stenosis (AS) has a reported incidence of ≈4 per 10,000 live births and is the most common type of congenital left ventricular (LV) outflow tract obstruction.1 Published studies have demonstrated comparable results with transcatheter balloon aortic valvuloplasty (BAV) and surgical aortic valvuloplasty in the management of congenital valvar AS.2–5 BAV has become the first-line treatment pathway in many centers, and short-term outcomes, including residual AS, aortic insufficiency (AI), and procedural complications,
Aortic valve stenosis is the most common type of congenital left ventricular outflow tract obstruction. Despite being a significant lifelong disease, it is currently managed based on limited data, especially during childhood. Balloon aortic valvuloplasty has become the first-line treatment pathway in many pediatric centers. We present a novel study demonstrating the trajectory of left ventricular remodeling over time in children with aortic valve stenosis who have undergone balloon aortic valvuloplasty. Our study demonstrates that in patients whose predominant residual disease is aortic insufficiency, left ventricular remodeling occurs mainly during the first 3 years after balloon aortic valvuloplasty, with no subsequent significant functional changes over the medium term. These data improve our understanding of expected patient trajectories and thus may inform clinical decisions on the timing of reintervention.

**CLINICAL PERSPECTIVE**

Echocardiographic data pertaining to aortic valve and LV size and function were collected from the baseline echocardiogram just before BAV and serially collected from 3 follow-up echocardiograms until December 2017 or until the first reintervention. Data from 2 follow-up echocardiograms were collected if 3 studies were not available. All measurements were retaken from the echocardiographic images. Study data were collected and managed using REDCap (Research Electronic Data Capture) tools hosted at The Hospital for Sick Children.19,20 Two-dimensional speckle-tracking analysis of the LV endocardium was performed offline using TOMTEC-Arena software version TTA2.30 (TOMTEC Imaging Systems GmbH, Unterschleissheim, Germany) to calculate peak myocardial strain. Circumferential strain was performed using the parametral short-axis view of the LV at the level of the papillary muscles and the mean was obtained by averaging 6 LV segments. Longitudinal strain was calculated using the apical 4-, 3-, and 2-chamber views. In each view, LV strain was measured in six segments and the mean strain value was derived. Any views with >2 poorly tracking segments were excluded. Global longitudinal strain was not included due to the relatively small number of patients who had adequately tracking segments in all 3 apical views (a common challenge with apical imaging in infants and children).

Catheterization data, including invasive peak-to-peak aortic valve gradient before BAV and qualitative degree of AI by angiography immediately after BAV, were collected from procedural reports.21 Clinical data on type of reintervention, indication for reintervention, and death during the study period were also collected from electronic medical records. Possible indications for reintervention included residual AS (the presence of AS following BAV), residual AI (the presence of AI following BAV), or mixed AS/AI.

**AS-Dominant and AI-Dominant Classification**

Children were classified based on whether they had predominantly AS (AS-dominant) and whether they had predominantly...
AI (AI-dominant) following BAV. AS-dominant classification (n=44) was defined by having an aortic valve mean gradient ≥30 mm Hg on at least 2 follow-up echocardiograms or hav- ing AS on one echocardiogram that was significant enough to prompt reintervention. AI-dominant classification (n=11) was defined by having at least moderate-to-severe AI on at least 2 follow-up echocardiograms or having progressive AI to moderate-severe on serial echocardiograms.

**Statistical Analysis**

Freedom from death was estimated using the Kaplan-Meier method, and the cumulative proportion of reintervention over time was estimated using a nonparametric competing risk model with death as the competing risk.

The longitudinal parameters from serial follow-up echocardiograms were demonstrated using per-patient time profiles with superimposed trend lines using locally estimated scatterplot smoothing. Only echocardiograms that occurred before reintervention were used. Generalized estimating equations with independent correlation structure and standard errors estimated with the robust sandwich estimator were used to model the effect of time and patient group on echocardiogram parameters of interest. These models assumed linear covariate relationships.

Cox regression models were used to estimate the association of echocardiogram parameters at baseline with reintervention or death. Hazard ratios for reintervention or death were reported with 95% CIs.

Interobserver variability for strain analysis at baseline was assessed using intraclass correlation. Specifically, the intraclass correlation-3 method was applied. Interobserver variability for strain analysis at baseline was assessed using the Bland-Altman agreement plot.

**RESULTS**

The cohort was comprised of 98 children. Eighty-nine (93%) children had bicuspid aortic valve morphology. The echocardiographic parameters on baseline echocardiogram are shown in Tables 1 and 2. Interobserver variability for strain analysis on baseline echocardiogram was good, with intraclass correlation values between 0.89 and 0.93 (Table S1). Bland-Altman agreement analysis also demonstrated that nearly all strain assessments were within the limits of agreement. The exception was LV mean longitudinal strain in the apical 3-chamber view, where the Bland-Altman plot demonstrated that one observer on average obtained higher values than the other, despite high intraclass correlation (0.932 [0.811–0.977]) for this parameter (Figure S1).

The median (interquartile range) duration of follow-up was 6.8 years (1.9–9.0), corresponding to a minimum duration of follow-up of 0.2 years and a maximum of 13.3 years. Seventy-eight (80%) children had 3 follow-up echocardiograms after BAV, whereas the remaining had 2 follow-up echocardiograms. The median (inter- quartile range) age at BAV was 2.8 months (0.2–75; 49 (34–65) mm Hg.

### Table 1. Baseline Echocardiographic Characteristics by 2-Dimensional and Doppler Imaging

| Baseline patient characteristics |   |
|---------------------------------|--|
| Sex                             |   |
| Male                            | 81 (83%) |
| Female                          | 17 (17%) |

| Baseline measurements |   |
|-----------------------|--|
| Age at baseline echocardiogram, y | 0.20 (0.02 to 6.00) |
| Aortic valve morphology |   |
| Bicuspid              | 89 (93%) |
| Monocuspid            | 7 (7%)  |
| Degree of AI          |   |
| None                  | 55 (57%) |
| Trivial               | 17 (17%) |
| Mild                  | 23 (24%) |
| Mild–moderate         | 2 (2%)  |
| AV annulus in PLAX view, mm | 8.6 (6.2 to 16.0) |
| AV annulus Z score     | –0.4 (–2.2 to 1.0) |
| Sinus of Valsalva in PLAX view, mm | 11.2 (8.5 to 20.1) |
| Sinus of Valsalva Z score | –0.9 (–2.4 to –0.1) |
| Sinotubular junction in PLAX view, mm | 9.9 (7.2 to 15.8) |
| Sinotubular junction Z score | –1.3 (–2.0 to –0.1) |
| Ascending aorta in PLAX view, mm | 13.8 (10.0 to 23.8) |
| Ascending aorta Z score | 2.5 (1.7 to 3.4) |

| M-mode measurements |   |
|---------------------|--|
| LVEDD, cm            | 1.7 (1.1 to 2.4) |
| LVESD, cm            | 2.4 (1.9 to 4.0) |
| LVEDD Z score        | –0.2 (–1.9 to 1.0) |
| LVEF, %              | 72 (67 to 79) |
| LV PW, cm            | 0.5 (0.4 to 0.7) |
| LV PW Z score        | 2.2 (1.0 to 3.0) |
| IVS, cm              | 0.6 (0.4 to 0.7) |
| IVS Z score          | 1.9 (1.0 to 3.4) |

| Ventricular measurements |   |
|--------------------------|--|
| 2D LVEDD in A4C view, cm | 2.33 (1.81 to 3.38) |
| LV area in systole in A4C view, cm² | 5.01 (2.85 to 9.21) |
| LV area in diastole in A4C view, cm² | 7.98 (4.60 to 17.95) |
| LV volume in systole in A4C view, mL | 6.2 (2.5 to 15.3) |
| LV volume in systole in A2C view, mL | 8.5 (4.1 to 19.4) |
| LV volume in diastole in A4C view, mL | 13.5 (5.6 to 45.3) |
| LV volume in diastole in A2C view, mL | 18.4 (10.1 to 55.0) |
| LVEF biplane Simpsons, % | 65.8 (44.3 to 70.5) |
| MV peak A velocity in A4C view, cm/s | 57.0 (53.5 to 70.0) |
| MV peak E velocity in A4C view, cm/s | 107 (94 to 123) |
| MV E/A ratio           | 1.73 (1.42 to 1.97) |

2D indicates 2-dimensional; A2C, apical 2-chamber; A4C, apical 4-chamber; AI, aortic insufficiency; AS, aortic stenosis; E/A, peak E velocity to peak A velocity; IVS, interventricular septum; LV, left ventricle; LVEDD, LV end-diastolic dimension; LVEF, LV ejection fraction; LVESD, LV end-systolic dimension; MV, mitral valve; PLAX, parasternal long axis; and PW, posterior wall.

Table 3. The median (interquartile range) peak-to-peak aortic valve gradient by catheterization before BAV was 49 (34–65) mm Hg.

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Clinical Outcomes

The cumulative proportion (95% CI) of reintervention and death at 5 years following BAV was 33.7% (23.6%–42.4%; Table 4). There was only one death during the study period (Figure 1). Primary indications for initial reintervention were residual AS (57%), AI (14%), or mixed aortic valve disease (30%). The reinterventions included repeat BAV (48%), surgical aortic valve repair (15%), aortic valve replacement (35%), and heart transplant (2%; Table 5). Among those who required reintervention, 29 children had one reintervention, 5 children had 2 reinterventions, 4 children had 3 reinterventions, and 1 child had 6 reinterventions.

Higher LV ejection fraction (LVEF) and mean LV circumferential strain at baseline were each associated with decreased risk of reintervention (1 unit increments: hazard ratio [95% CI], 0.974 [0.959–0.989], <0.001; P = 0.041, respectively). A greater aortic valve annulus Z score at baseline was also associated with decreased risk of reintervention (1 unit increments: hazard ratio [95% CI], 0.806 [0.698–0.93], P = 0.003; Table 6).

LV Remodeling

Children were classified based on whether they had predominantly AS (AS-dominant) and whether they had predominantly AI (AI-dominant) following BAV, as described above. Time profiles of echocardiographic parameters stratified by AS-dominant and AI-dominant status are shown in Figure 2 and Figure 3, as well as Figures S2 through S5.

| Table 2. Baseline Echocardiographic Characteristics by 2-Dimensional Speckle-Tracking, Compared to Normal Institutional Controls Between 0 and 6 Years of Age |
|---|
| Strain measurements | N | Study group | N | Control group | P value |
| LV mean circumferential strain | 60 | 20.1 (14.5–22.8) | 74 | 19.3 (18.8–20.3) | 0.72 |
| LV mean longitudinal strain in A4C view | 81 | 18.1 (12.4–21.6) | 74 | 20.5 (19.7–21.3) | <0.001 |
| LV mean longitudinal strain in A2C view | 51 | 19.2 (13.7–21.1) | 65 | 22.7 (20.6–24.5) | <0.001 |
| LV mean longitudinal strain in A3C view | 44 | 18.2 (12.8–20.1) | 61 | 21.0 (19.3–22.6) | <0.001 |

A2C indicates apical 2-chamber; A3C, apical 3-chamber; A4C, apical 4-chamber; and LV, left ventricle.

Children with predominantly residual AI (n=11) demonstrated progressive increases in their LV end-diastolic dimension (LVEDD) Z score within the first 3 years after BAV, followed by a plateau (P<0.001). Children with predominantly residual AS (n=44) had no changes in LV dimensions but had rapid early increases in their mean LV circumferential and longitudinal strain.

DISCUSSION

Aortic valve stenosis treated with BAV is associated with high rates of reintervention, with ≈34% of children requiring reintervention at 5 years in our study. High reintervention rates have been reported in previous studies as well, with freedom from aortic valve reintervention at 10 years ranging from 29% to 54%. In our series, the most common indication for reintervention was residual AS, which accounted for 57% of the reinterventions. This is related to a conservative approach to dilation, using a balloon-annulus diameter ratio of ≈0.9, in an effort to avoid significant residual AI. The goal of the initial dilation is therefore not to eliminate the aortic valve gradient entirely, but rather to improve it, within the notion that a more aggressive approach to any residual AS may be considered at a later stage if needed. AI or a combination of residual AS and AI was responsible for 43% of the reinterventions. Our study examined the trajectory of echocardiographic LV size and functional parameters after the initial balloon dilation. We distinguished between children with predominantly residual AS and those with predominantly residual AI. LV remodeling differed significantly between the 2 groups. The AS-dominant group did not demonstrate significant changes in LV dimensions when corrected for body growth but demonstrated significant functional changes with early increases in longitudinal and circumferential strain measurements. As can be expected, in the AI-dominant group the LV progressively enlarged during first 3 years after the initial BAV (P<0.001), with relatively lower longitudinal (P=0.001) and circumferential (P<0.001) strain measurements.

Baseline echocardiographic parameters and their relationship to risk of reintervention were evaluated. This analysis demonstrated that better LV function before BAV, measured by LVEF and mean LV circumferential strain, was associated with a decreased risk of reintervention (1 unit increments: hazard ratio [95% CI], 0.974 [0.959–0.989], <0.001; P=0.041, respectively). A greater aortic valve annulus Z score at baseline was associated with decreased risk of reintervention (1 unit increments: hazard ratio [95% CI], 0.806 [0.698–0.93], P=0.003; Table 6).

| Table 3. Initial BAV Intervention Characteristics |
|---|
| Age at BAV, y | 0.23 (0.02–6.21) |
| Weight at BAV, kg | 6.2 (3.5–24.8) |
| Peak-to-peak invasive gradient before BAV, mm Hg | 49 (34–65) |
| Degree of AI by angiography after BAV |
| None | 34 (35%) |
| Mild | 47 (48%) |
| Moderate | 13 (13%) |
| Moderate–severe | 2 (2%) |
| Severe | 2 (2%) |

AI indicates aortic insufficiency; and BAV, balloon aortic valvuloplasty.
A larger aortic valve annulus before BAV was also found to be associated with a decreased risk of reintervention (1 unit increments: hazard ratio [95% CI], 0.806 [0.698–0.93], P=0.003). This finding contrasts with previous studies where a larger annulus was associated with a higher risk for developing AI.27 This probably reflects a more conservative contemporary approach during the intervention, using smaller-sized balloons in children with larger annuli. Whether this supports a surgical approach in patients with hypoplastic aortic valves as a more durable strategy than BAV remains controversial and requires further investigation.28

Our data depicting the longitudinal changes in LV size and function over time in children following BAV provides novel and interesting information about how the LV responds to residual AS or AI after the procedure. The findings in children with predominantly residual AI are especially revealing and important for clinical care. We observed progressive LV dilation occurring mainly during the first 3 years after BAV, followed by a plateau. The early dilation is consistent with the expected physiological adaptation of the LV to volume loading with eccentric hypertrophy. Our data also demonstrate that the dilation over the first 3 years after intervention does not occur at the expense of LV systolic function, with preservation of LVEF and strain values within normal range. This seems to indicate that the remodeling process is adaptive. The plateau reached after 3 years potentially indicates a period at which a new steady-state occurs through adaptation to the volume loading. Our novel finding may inform clinical decision-making regarding the timing of reintervention, allowing identification of a potentially maladaptive process when the trajectory of LV size or function deviates from the norm. For instance, it would be concerning if the LV dilation process in a given patient resumed again later, after the plateau. Possible causes for such a progression would include worsening AI, which could potentially be addressed surgically, or development of LV dysfunction leading to dilation to maintain cardiac output. Conversely, a stable LVEDD Z score beyond 3 years after BAV with otherwise normal ventricular function would be reassuring in a child with residual AI and may support a decision to defer reintervention and avoid the associated procedural risks.

Earlier studies have suggested that progressive AI is common after BAV.29 This can be related either to valve remodeling after the balloon-associated injury in combination with regression of LV concentric hypertrophy or improved LV compliance, resulting in increasing regurgitant volume through the damaged valve. Our data

Table 4. Cumulative Proportion of Reintervention and Death

|          | 1 y     | 5 y     | 10 y    |
|----------|---------|---------|---------|
| Reintervention | 20.4% (12.0%–28.0%) | 33.7% (23.6%–42.4%) | 43.6% (31.4%–53.6%) |
| Death    | 0.0% (0.0%–0.0%) | 1.0% (0.0%–3.0%) | 1.0% (0.0%–3.0%) |
| Event free | 79.6% (69.8%–86.2%) | 65.3% (54.5%–73.6%) | 55.4% (42.9%–65.2%) |

Table 5. Reintervention Characteristics

| Reintervention characteristic | N   | Statistic |
|-------------------------------|-----|-----------|
| Reintervention following BAV  | 98  |           |
| No                            | 58  | (59%)     |
| Yes                           | 40  | (41%)     |
| Type of first reintervention  | 40  |           |
| BAV                           | 19  | (48%)     |
| AV repair                     | 6   | (15%)     |
| AV replacement                | 14  | (35%)     |
| Heart transplant              | 1   | (2%)      |
| Primary indication for first reintervention | 37 |
| AI                            | 5   | (14%)     |
| AS                            | 21  | (57%)     |
| Mixed AS/AI                   | 11  | (30%)     |
| Peak-to-peak invasive gradient before BAV, mm Hg | 18 | 40 (36 – 52) |

AI indicates aortic insufficiency; AS, aortic stenosis; AV, aortic valve; and BAV, balloon aortic valvuloplasty.
suggest that this residual AI seems to affect the LV most within the first 3 years after the initial intervention.

Currently, decisions to reintervene on children with residual AI are largely based on meeting thresholds at one moment in time. These threshold criteria from the 2008 update to the American College of Cardiology/American Heart Association guidelines include LV dilation with an LVEDD Z score >4, systolic dysfunction with an LVEF <50%, and associated symptoms. However, it is also important to consider the trajectories of these LV parameters, as suggested by the 2020 American College of Cardiology/American Heart Association guidelines for adults with AI. These guidelines, which do not include parameters for the pediatric population, recommend that intervention may be considered when there is a progressive decline in LVEF to the low-normal range (55%–60%) or a progressive increase in LV dilation into the severe range (LVEDD >65 mm). Similarly, in children, an LVEDD Z score >4 likely has quite different implications when it is stable compared to when it is increasing. Also, functional parameters need to be taken into consideration in combination with LVEDD Z score, as stable LVEF and LV strain parameters in the setting of an enlarged ventricle are likely suggestive of LV adaptation.

The longitudinal trajectory in children with predominantly residual AS differed when compared with all others, showing no significant changes in LV dimensions but a rapid early increase in mean LV circumferential and longitudinal strain. Opening the aortic valve by BAV results in an acute reduction of LV afterload with improvement in LV functional parameters. The residual AS results in a functional adaptation with persistently increased LVEF and increased LV circumferential and longitudinal strain.

The hypertrophic response of the LV to chronic pressure loading in children with congenital AS results in reduced systolic wall stress and above-normal LVEF. This effect appears to differ from adults with acquired AS, who have normal or increased wall stress with either normal or reduced ejection performance. In a hemodynamic study of children who underwent surgical aortic valve repair or replacement, Dorn et al demonstrated that, postoperatively, wall stress increased toward normal and LVEF decreased toward normal. The hyperdynamic state in children with congenital AS should be taken into account when assessing AS severity. Although in adults, reduced contractility can result in low-gradient AS, the reverse may occur in children resulting in potential overestimation of AS severity at younger ages. In addition to the effect of pressure recovery, LV contractile state and hyperdynamic function should likely be taken into account rather than deciding on reintervention based on AS gradient alone.

In patients with predominantly residual AS, a decline in LV strain parameters, potentially reflective of ventricular dysfunction, was not observed in our patient cohort before reintervention or before the end of the follow-up period. Reintervention for residual AS was based mainly on increased aortic valve gradients. The remodeling data demonstrate that the gradient increases occurred at decreasing septal thicknesses and preserved ventricular deformation. This suggests that the gradients may have prompted relatively early reinterventions, before the occurrence of adverse effects on LV function.

We focused mainly on systolic function in our analysis, as assessment of diastolic function in children is very difficult. It is particularly challenging when longitudinal data are used, as most diastolic parameters are affected by LV growth and heart rate, making their clinical use difficult as well. Dusenbery et al showed that in children and young adults with AS and normal LVEF, reduced longitudinal and radial strain was associated with findings of
Figure 2. Time profile of echocardiographic (echo) parameters for aortic stenosis (AS)–dominant patients (red) vs all other study patients (black).

AS-dominant classification (red) was defined by having an aortic valve mean gradient ≥30 mm Hg on at least 2 follow-up echo or having AS on one echo that was significant enough to prompt reintervention. A4C indicates apical 4-chamber; AI, aortic insufficiency; IVS, interventricular septum; LV, left ventricle; LVEF, LV ejection fraction; LVEDD, LV end-diastolic dimension; and PW, posterior wall.
Figure 3. Time profile of echocardiographic (echo) parameters for aortic insufficiency (AI)–dominant patients (red) vs all other study patients (black).

AI-dominant classification (red) was defined by having at least moderate-to-severe AI on at least two follow-up echo, or having progressive AI to moderate-to-severe on serial echo. A4C indicates apical 4-chamber; AI, aortic insufficiency; IVS, interventricular septum; LV, left ventricle; LVEF, LV ejection fraction; LVEDD, LV end-diastolic dimension; and PW, posterior wall.
focal fibrosis by late gadolinium enhancement on cardiac magnetic resonance imaging. In those with AS, myocardial extracellular volume fraction, measured by gadolinium contrast T1 mapping cardiac magnetic resonance imaging, was significantly elevated and was associated with echocardiographic features of diastolic dysfunction. This indicates that LV fibrosis and diastolic dysfunction may have to be considered. Longitudinal data on progression of fibrosis and diastolic dysfunction are still limited. Our data provide some evidence that the use of aortic valve threshold gradients as the main indication for reintervention, without studying the effect on LV hypertrophy and function, may require further critical evaluation. The optimal timing for reintervention for residual AS has not been well established, and the criteria are largely consensus-based rather than data-driven. In their review, Jashari et al. described evidence of subclinical myocardial dysfunction in children with AS and coarctation before initial intervention. Long-term follow-up after intervention demonstrated an incomplete improvement in myocardial dysfunction, suggesting a need for longitudinal studies of functional parameters to determine ideal timing of intervention, before irreversible subclinical remodeling of the LV myocardium. Although our study serves as an important step in this pursuit, further studies including a longitudinal description of LV remodeling both before and after reintervention are needed.

For both residual lesions, our data indicate that longitudinal patient trajectories are possibly more important than cross-sectional cutoff points for reintervention. Congenital AS is an important lifelong disease but is currently managed based on limited data, especially during childhood. The decisions made by pediatric cardiologists, pediatric cardiac interventionalists, and pediatric cardiothoracic surgeons to (re)intervene on children with congenital AS after BAV have major lifelong implications. Mechanical aortic valve replacements, with their associated thrombosis and anticoagulation risks, pose significant clinical challenges particularly in active young children with inherent risk of head injury. Compared with mechanical aortic valve replacement, long-term freedom from stroke or major bleeding is superior after the Ross procedure. However, aortic valve replacement by the Ross procedure has only a 79.9% freedom from reoperation at 20 years. Although intervening too late may have dire consequences in this population, intervening too early poses substantial implications including a risk for future reinterventions that otherwise may not have been needed.

More patient-specific clinical and echocardiographic data are required to further define subsets of phenotypes within this population and to predict their individual trajectories and outcomes. To that aim, future steps would involve a multicenter study to access a higher volume and more diverse set of pediatric patient data. A sophisticated analysis, potentially with the use of machine learning technology, may ultimately allow us to build prediction and decision tools for each individual patient based on evidence.

**Study Limitations**

The retrospective nature of this study design was a primary limitation. In addition, patients with <2 follow-up echocardiograms available at our tertiary institution were excluded. This may have introduced bias, as patients with mild residual disease are more likely to be followed at outside institutions, and referred back only if and when reintervention is felt to be indicated.

A quantitative exploration of whether there is an association between time to reintervention and changes over time in LV parameters would involve joint modeling of outcome and longitudinal data. This would require additional data points and could not be done with only two to three follow-up echocardiograms before reintervention.

**Conclusions**

Our data suggest that in infants and children with predominantly residual AI, LV remodeling occurs mainly during the first 3 years after BAV, with no subsequent significant functional changes over time. Patients with predominantly residual AS show rapid early increases in LV strain following BAV, with no significant decline before reintervention. This novel understanding of LV remodeling over time in subgroups of children following BAV may support our clinical decision-making. However, further investigation using a larger cohort is needed.

Superior LV function at baseline, measured by LVEF and mean LV circumferential strain, is associated with a decreased risk of reintervention in neonates and children following BAV. Bigger aortic valve annulus dimension before BAV is also associated with a decreased risk of reintervention, which may be a consideration in choice of intervention and which may inform the way we counsel families on the likely need for reintervention in specific cases.

Future studies are needed for an exploratory analysis of the relationship between LV remodeling and timing of reintervention. More serial data from a larger patient sample is needed to develop risk prediction and decision tools based on individual patient phenotypes.

**ARTICLE INFORMATION**

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