Heart, Lung and Circulation (2019) **28,** 632–636
1443-9506/04/$36.00
https://doi.org/10.1016/j.hlc.2018.02.014

ORIGINAL ARTICLE

Balloon Aortic Valvuloplasty for Congenital Aortic Stenosis: A 14-Year Single Centre Review

Benjamin Auld, MBBS, FRACP [a,b*], Lindsay Carrigan, MBBS [a,b], Cameron Ward, MBBS, FRACP [a,b,c], Robert Justo, MBBS, FRACP [a,b,c], Nelson Alphonso, FRACS [a,b,c], Ben Anderson, MBBS, FRACP [a,b,c]

[a]Queensland Paediatric Cardiac Service, Lady Cilento Children's Hospital, Brisbane, Qld, Australia
[b]School of Medicine, The University of Queensland, Brisbane, Qld, Australia
[c]Mater Medical Research Institute, The University of Queensland, Brisbane, Qld, Australia

Received 15 June 2017; received in revised form 31 January 2018; accepted 18 February 2018; online published-ahead-of-print 1 March 2018

Background The approach to intervention for congenital aortic valve stenosis (AS) differs depending upon centre bias toward a primary catheter or surgical approach. We therefore investigated associations with freedom from re-intervention (FFI) in the cohort of children who underwent primary balloon aortic valvuloplasty (BAV) for congenital AS in our centre.

Methods All patients who underwent BAV as a primary procedure in the period between 2001 and 2015 in a single service were included. Echocardiographic parameters before and after catheterisation and procedural data was collected on all patients.

Results Sixty-four (64) patients underwent BAV as the primary intervention during the study period. Follow-up data was available for 60 of these. Balloon aortic valvuloplasty was performed at a median age of 143 days (range 2 days–18.8 years). Freedom from re-intervention was observed in 75% of patients with a median follow-up of 6.8 years and a mean follow-up of 3 years. Catheter-based peak-to-peak aortic valve gradients decreased from 58 ± 15.9 mmHg to 22.9 ± 13.1 mmHg. There was no short- or long-term mortality. FFI was predicted by aortic valve morphology ($p < 0.01$), post-BAV mean echo gradient ($p = 0.03$) and post-BAV regurgitation ($p < 0.01$). No patient had re-intervention for restenosis with post-BAV mean echo gradient <30 mmHg. Catheter gradients before and after BAV approached significance for predicting FFI ($p = 0.06$ and $p = 0.09$ respectively). Fifteen (15) patients were neonates with significantly lower aortic valve (AoV) Z-scores (mean 0.63 vs 1.76, $p = 0.002$) and no difference in FFI ($p = 0.19$). Annulus size, balloon/annulus ratio (within the range utilised) and pre-BAV echo findings were not predictive for re-intervention.

Conclusions Balloon aortic valvuloplasty is an effective primary approach to congenital valvular AS with the potential of avoiding surgical intervention in the majority of patients at all ages. Freedom from re-intervention in our cohort was associated with valve morphology and the degree of stenosis and regurgitation immediately post BAV.

Keywords Aortic valve disease • Percutaneous intervention • Congenital heart disease • Paediatrics • Balloon angioplasty

*Corresponding author at: Queensland Paediatric Cardiac Service, Lady Cilento Children's Hospital, 501 Stanley Street, South Brisbane, QLD, Australia 4101., Email: auld.mb@gmail.com

Introduction

Balloon aortic valvuloplasty (BAV) is a widely-accepted intervention for congenital aortic valve stenosis (AS). Since its first description in children by Lababidi in 1983 [1,2] BAV has evolved to become the standard of care in many tertiary paediatric centres for primary and secondary treatment of congenital AS in the absence of significant regurgitation. BAV has been previously shown to be an effective and relatively safe alternative to surgical aortic valvotomy (SAV) and, in addition, may extend the time until attempted SAV or ultimate valve replacement in those cases where BAV does not provide a long-term solution [3–5]. As an alternative to surgery, BAV offers a bypass-free intervention with the potential for shorter hospital admission, avoidance of ICU admission, significantly less pain and scarring, lower procedural and admission costs, and a more easily standardised and reproducible intervention. Recent developments in surgical techniques for aortic valvotomy have led to re-analysis of surgical versus percutaneous treatment of AS in young children [6–8]. This has led to a relative equipoise in the contemporary literature between the two techniques [9]. Our centre has utilised a primary catheter based approach to AS with the hypothesis that freedom from re-intervention (FFI) and complication rates compare favourably with previously published data using both BAV and SAV techniques. We have examined our own experience with BAV with the purposes of informing future treatment decisions in our patients and providing a contemporary study of catheter based aortic valve intervention from an Australian centre.

Materials and Methods

Between 2002 and 2015, 64 consecutive patients with congenital aortic valve stenosis underwent attempted BAV as a primary intervention. Follow-up data was not available for four patients who were excluded from the analysis. Eleven (11) additional patients had BAV as a secondary procedure either subsequent to primary BAV (n = 3) or primary surgical intervention (n = 8) and were not included in the analysis. The study was approved by the institutional Ethics Board with waiver of the need for informed consent.

Pre-intervention echocardiographic data was collected including: aortic valve (AoV) annulus and Z-score, AoV leaflet number and morphology, pre-intervention LV function, mean and peak AoV gradient, and degree of regurgitation. The same measurements were made at most recent follow-up or at the latest echocardiographic evaluation prior to further intervention. The degree of aortic regurgitation (AR) was assessed from echocardiographic images using previously published valve dysfunction descriptors [10].

Intervention was undertaken based on published catheter guidelines [11] with a mean Doppler gradient used as a surrogate for peak-to-peak catheter gradient in pre-catheter assessment. Catheterisation was performed using standard techniques under general anaesthesia with informed consent. Haemodynamic and angiographic evaluation was undertaken. Stenosis was assessed on haemodynamic grounds and aortic regurgitation and annulus size on angiography. Haemodynamic and angiographic data were collected from cardiac catheter reports. Procedural complications were categorised utilising the IMPACT registry protocols [3]. A low-profile balloon(s) with a diameter similar to the measured AoV annulus (mean ratio of 0.96 ± 0.11) was inflated, aiming for resolution of balloon waist on reinflation. A double balloon strategy was utilised for patients with annulus dimension on angiography higher than 12–13 mm (15 patients) to provide theoretical benefits, including enhanced balloon stability during inflation, potential alignment with the commissures, reduced vascular trauma with reduced sheath size and to aid rapid inflation and deflation to allow resumption of cardiac output. When feasible, balloon stability was also optimised using rapid right ventricular pacing or adenosine.

Reported aortic valve morphology was verified by examination of pre-intervention echocardiographic images where possible. Valve morphologies were grouped into unicuspid, bicuspid and trileaflet types. Differentiating functionally unicuspid/bicuspid valves from 'true' types was not possible retrospectively for all patients. Operative descriptions of valve morphology were used for those patients who progressed to surgical intervention at a later date.

Data analysis was performed using Stata/IC v.10 (StataCorp, College Station, TX, USA), with summary statistics shown as a mean (± SD) for normally distributed data, and as a median (IQR) for non-normally distributed data. Statistics were predominantly non-normally distributed due to the more frequent early age at BAV. Correlation statistics were performed for each independent variable against FFI using Simple Logistical Regression for variables that demonstrated interval characteristics. A Chi-Square Test was used for categorical variables and a Fisher's Exact Test was used in the case of categorical variables with sample sizes less than 5. A p value <0.05 was deemed to show statistical significance. Aortic annulus Z-scores were calculated using published Z-score equations based on body surface area (BSA) from echocardiographic measurements at the time of intervention [12].

Results

The frequency of BAV has increased over the last 7 years (Figure 1) with an average number of BAV cases of 6.1 per year over this period, compared to 2.3 per year for the previous 7 years.

Patient Demographics

The median age at catheterisation was 143 days (range 1 day–18.8 yrs) with 25% of patients falling within the neonatal period. The median patient weight was 5.6 kg (range 2.5–86). Males comprised 72% of the group (43:17).

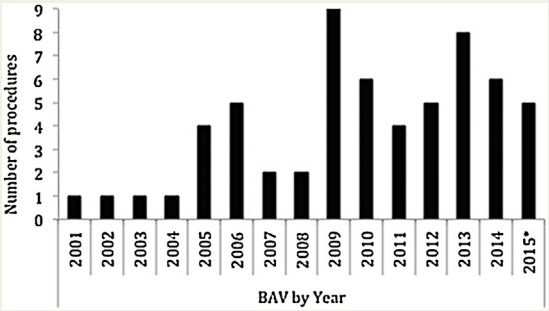

Figure 1 Number of balloon aortic valvuloplasty procedures performed by year.

Associated Congenital Heart Defects

Isolated congenital aortic stenosis with no additional major left-sided congenital heart defects occurred in 90% of patients. Significant LV dysfunction was seen in four patients pre-BAV with one patient demonstrating endocardial fibroelastosis and moderate mitral regurgitation. Two (2) patients had associated coarctation and two others had sub-aortic membranes. One (1) patient had mild Shone's complex with mild mitral valve stenosis, and one patient had associated Ebstein's anomaly.

Aortic Valve Morphology

Aortic valve morphology could be reliably identified in 53 of 60 patients. The predominant aortic leaflet arrangement was functionally bicuspid in 44 (72%) patients. Three (3) patients had a dysplastic trileaflet valve and, of the remaining patients with known valve morphology, six demonstrated a functionally unicuspid valve with either fusion of two valve commissures or a true unicuspid aortic valve leaflet. Of the six unicuspid valves, four went on to ultimately require a Ross procedure and two patients remained free from any further intervention at latest follow-up. Of the 44 bicuspid valves one required a second BAV, one went on to have SAV and four ultimately had a Ross procedure. Of the three trileaflet valves, one went on to have SAV, one had a second balloon dilation and the other remains intervention free.

Haemodynamics

Mean peak-to-peak catheter gradients fell from 58 ± 15.9 mmHg to 23 ± 13.1 mmHg. This correlated well with a mean pre-BAV echo gradient of 57 ± 14.5 mmHg and a mean post-BAV gradient of 26 ± 11.7 mmHg. The peak echo gradient fell from 103 ± 24.7 mmHg to 49 ± 21.9 mmHg. A larger improvement in pre-/post-BAV peak gradients was seen with the number of functional valve leaflets demonstrated pre-procedure (Figure 2). Those patients who showed moderate or severe aortic insufficiency (AI) post BAV demonstrated a relatively higher drop in valve gradient. These patients did not show any significant difference in balloon/annulus ratio ($p = 0.78$), although the range of balloon/annulus ratio used was narrow.

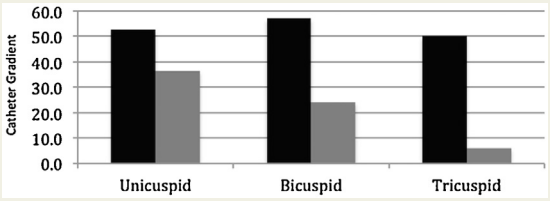

Figure 2 Change in aortic valve gradient in mmHg before (black) and after (grey) balloon aortic valvuloplasty (BAV), based on valve morphology.

Procedural Complications

There was no mortality at either the peri-procedural time point or at latest follow-up. There was one major adverse event seen during the procedure which involved transient ventricular fibrillation requiring direct current (DC) cardioversion. Nine (9) (15%) patients had minor adverse events, which included seven patients (11%) with partial femoral arterial occlusion requiring anti-coagulation. Other adverse outcomes were local groin haematoma (n = 1) and femoral venous thrombus (n = 1).

There was one significant post-procedural adverse event with bradycardia requiring chest compressions and extracorporeal cardiopulmonary resuscitation (ECPR) with post-procedural ischaemic changes on cerebral imaging.

Predictors of Freedom From Re-Intervention

The overall FFI rate was 75% (45 of 60) at 3-year mean follow-up. Of the 15 patients who required further intervention, three underwent secondary BAV with two of these progressing to surgical intervention (one undergoing subsequent Ross procedure and one having secondary SAV, with ultimate Ross valve replacement). After primary BAV, four patients had SAV as their second procedure, of which one went on to have a Ross procedure. The remaining eight patients who required further intervention post primary BAV all underwent a Ross procedure. Mean time to any re-intervention was 1.2 years. Overall mean time to valve replacement for those that ultimately underwent Ross procedure was 1.8 years (n = 11). Early re-intervention was performed on two patients with one patient requiring SAV within 24 hours due to unsuccessful BAV, and another at day 5 post-BAV due to significant AI.

Predictors of FFI for the 45 patients who had only a single BAV procedure were related to the morphological aortic valve type ($p = 0.01$) and the function of the valve post BAV (Figure 2). The function of the valve post BAV included post BAV catheter gradient ($p = 0.04$), the post BAV mean echo gradient ($p = 0.03$) and the degree of aortic insufficiency post BAV ($p < 0.01$). Of note, those patients who were shown to have a post-BAV mean echo gradient <30 mmHg and less than moderate regurgitation were all free from further intervention at latest follow-up. Balloon/annulus ratio was not significant, likely due to the narrow range

of values (0.96 ± 0.11). Freedom from re-intervention was not predicted by demographic factors, valve size or pre-BAV gradients (Table 1).

The Kaplan-Meier freedom from re-intervention for the entire cohort at 10 years was 0.58 (95% CI = 0.28, 0.80). Fifteen (15) of the patients who underwent primary BAV were neonates (<30 days). Ten (10) of the 15 were free from re-intervention at latest follow-up, compared to 35 of 45 children in which BAV was performed at >30 days of age (p = 0.19) (Figure 3).

Discussion

Balloon aortic valvuloplasty offers several potential advantages in the management of AS. It is a less invasive procedure than SAV or valve replacement and may safely delay surgery until patients reach an age where there may be fewer post-surgical re-interventions (i.e. effectively reducing the number of surgical interventions, particularly with reference to conduit changes required post-Ross procedure).

Surgical aortic valvotomy in the neonatal period has been shown to significantly increase the risk of re-intervention [7]. In our neonatal population, surgical re-intervention was safely delayed (no mortality and no major adverse events in this subgroup) beyond the neonatal period in all but one neonate. Importantly, the overall FFI in this age group was 66% (mean follow-up 2.06 yrs), which is comparable to the best reported primary surgical results [7,13,14].

Table 1 Variables investigated for association with freedom from re-intervention.

Independent Variable	value (range)	P-value
Gender	43 male	0.87
Age	135 (2–6872)	0.16
Weight	5.6 (2.5–86)	0.42
Height	60 (48–188)	0.33
BSA	0.29 (0.10–2.03)	0.36
AoV type	Uni/bi/tricuspid (6/44/3)	**0.01**
Date	2001–2015	0.11
No of Balloons	1 or 2	0.46
AoV annulus (mm)	9.85 (6–30)	0.22
AoV annulus (Z score)	1.52 (0.6–2.2, IQR)	0.39
Balloon/AoV ratio	0.96 (±0.11)	0.20
Cath Gradient (pre)	58.1 ((±15.9)	0.053
Cath Gradient (post)	22.9 (±13.1)	**0.04**
Peak Echo Gradient (pre)	103 (24.7)	0.53
Mean Echo Gradient (pre)	56 (±14.5)	0.42
AI (pre)	None/mild/mod./severe	0.87
Peak Echo Gradient (post)	49 (±21.9)	0.11
Mean Echo Gradient (post)	25 (±11.7)	**0.03**
AI (post)	None/mild/mod./severe	<**0.01**

Abbreviations: BSA, body surface area; AoV, aortic valve; AI, aortic insufficiency.

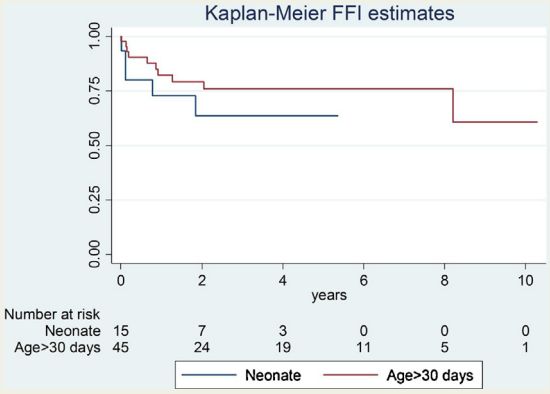

Figure 3 Freedom from re-intervention curve, based on age at intervention (p = 0.19).

Based upon re-intervention and complication rates, Moore et al. (2014), Prijic et al. (2015) and Pedra et al. (2004) [3,14,15] have all demonstrated BAV to be a valid alternative to surgery throughout the paediatric age group. Similarly, McCrindle et al. (2001) [13] found BAV to be a viable alternative to surgery in patients <30 days old. Systematic review of the combined surgical and interventional literature showed significant heterogeneity in results [9]. In this review no difference in post-intervention gradients were seen, and no difference in long-term survival or aortic replacement rates. It did show an increase in re-intervention with BAV compared to SAV. However, this was seen to be centre-dependent and interpretation was guarded based on seemingly arbitrary re-intervention criteria. Balloon aortic valvuloplasty offers additional benefits as it is a less invasive procedure, usually reduces admission duration, reduces intensive care and theatre costs [16], and reduces parental and family stress [17].

The available length of follow-up in our study is somewhat limited in comparison to previous BAV reports. However, throughout the study period the mean pre- and post- BAV haemodynamics are similar to large database publications [3]. Our patients achieved a reduction in stenosis with no mortality and a low number of adverse events, whilst achieving an overall rate of 75% FFI. It is likely some of the larger BAV reports and previously discussed comparative papers on BAV vs SAV include a significant sample from an earlier era in BAV. While surgical techniques have evolved, the current cohort of patients have largely undergone BAV using uniform techniques in the modern era utilising advanced balloon technology.

There has been recent interest in aortic valve morphology as a predictor of response to balloon dilation. Maskatia and colleagues showed in a large cohort that re-intervention was less likely to occur in bicuspid aortic valves while it was more likely to occur in all forms of unicuspid valve [18]. This trend was reiterated in the current series, with 66% of unicuspid

valves requiring re-intervention while only 16% of bicuspid valves went on to a further procedure. Further investigation on pre-procedure aortic valve morphology by Petit et al. [19] has examined leaflet fusion length, opening area and leaflet excursion angle as predictors of AI post BAV, however, this was not included in the scope of our study.

Of 15 patients who went on to have a secondary procedure, four had re-intervention due to aortic regurgitation. The development of regurgitation was independent of balloon/annulus ratio ($p = 0.74$). In the context of normal LV systolic function there were no patients who had a mean echo gradient post-procedure <30 mmHg who had re-intervention for restenosis. This suggests the relief of obstruction seen immediately post-BAV on echo is maintained over time.

The limitations of our study include that data are from a single centre and therefore total procedure numbers are limited, though the procedure is completely standardised. There was no scope for statistical comparison between SAV and BAV as BAV continues to be utilised as the first-line strategy.

Conclusions

Balloon aortic valvuloplasty is a safe and effective primary procedure in all age groups, with no significant difference in outcomes when performed in the neonatal period. Freedom from re-intervention was associated favourably with the bicuspid aortic valve type and post-BAV catheter and echo gradient. Even in those patients who required re-intervention (including those with unicuspid valve morphology) BAV safely delayed SAV, permitting growth and potentially improved surgical options. These findings support primary balloon dilation as the initial management of choice for patients with aortic valve stenosis.

Acknowledgements

We would like to acknowledge Janelle Johnson, Robert Ware and Kim Betts for their contribution to data collection and analysis.

References

[1] Lababidi Z. Aortic balloon valvuloplasty. Am Heart J 1983;106:751–2.
[2] Lababidi Z, Wu JR, Walls JT. Percutaneous balloon aortic valvuloplasty: results in 23 patients. Am J Cardiol 1984;53:194–7.
[3] Moore JW, Vincent RN, Beekman 3rd RH, Benson L, Bergersen L, Holzer R, et al. Procedural results and safety of common interventional procedures in congenital heart disease: initial report from the National Cardiovascular Data Registry. J Am Coll Cardiol 2014;64:2439–51.
[4] Soulatges C, Momeni M, Zarrouk N, Moniotte S, Carbonez K, Barrea C, et al. Long-Term Results of Balloon Valvuloplasty as Primary Treatment for Congenital Aortic Valve Stenosis: a 20-Year Review. Pediatr Cardiol 2015;36(6):1145–52.
[5] Petit CJ, Maskatia SA, Justino H, Mattamal RJ, Crystal MA, Ing FF. Repeat balloon aortic valvuloplasty effectively delays surgical intervention in children with recurrent aortic stenosis. Catheter Cardiovasc Interv 2013;82:549–55.
[6] ElZein C, Subramanian S, Polimenakos AC, Roberson D, Ilbawi MN. Systematic approach to aortic valvuloplasty in children and young adults. World J Pediatr Congenit Heart Surg 2013;4:412–7.
[7] Siddiqui J, Brizard CP, Galati JC, Iyengar AJ, Hutchinson D, Konstantinov IE, et al. Surgical valvotomy and repair for neonatal and infant congenital aortic stenosis achieves better results than interventional catheterization. J Am Coll Cardiol 2013;62:2134–40.
[8] Donald JS, Konstantinov IE. Surgical Aortic Valvuloplasty Versus Balloon Aortic Valve Dilatation in Children. World J Pediatr Congenit Heart Surg 2016;7:583–91.
[9] Hill GD, Ginde S, Rios R, Frommelt PC, Hill KD. Surgical Valvotomy Versus Balloon Valvuloplasty for Congenital Aortic Valve Stenosis: A Systematic Review and Meta-Analysis. J Am Heart Assoc 2016;5:e003931.
[10] Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802.
[11] Feltes TF, Bacha E, Beekman RH, Cheatham JP, Feinstein JA, Gomes AS, et al. Indications for Cardiac Catheterization and Intervention in Pediatric Cardiac Disease: A Scientific Statement From the American Heart Association. Circulation 2011;23:2607–52.
[12] Daubeney PE, Blackstone EH, Weintraub RG, Slavik Z, Scanlon J, Webber SA. Relationship of the dimension of cardiac structures to body size: an echocardiographic study in normal infants and children. Cardiol Young 1999;9:402–10.
[13] McCrindle BW, Blackstone EH, Williams WG, Sittiwangkul R, Spray TL, Azakie A, Jonas RA. Are outcomes of surgical versus transcatheter balloon valvotomy equivalent in neonatal critical aortic stenosis? Circulation 2001;104:I152–8.
[14] Prijic SM, Vukomanovic VA, Stajevic MS, Bjelakovic BB, Zdravkovic MD, Sehic IN, Kosutic J. Balloon dilation and surgical valvotomy comparison in non-critical congenital aortic valve stenosis. Pediatr Cardiol 2015;36(3):616–24.
[15] Pedra CA, Sidhu R, McCrindle BW, Nykanen DG, Justo RN, Freedom RM, Benson LN. Outcomes after balloon dilation of congenital aortic stenosis in children and adolescents. Cardiol Young 2004;14:315–21.
[16] Faraoni D, Nasr VG, DiNardo JA. Overall Hospital Cost Estimates in Children with Congenital Heart Disease: Analysis of the 2012 Kid's Inpatient Database. Pediatr Cardiol 2015.
[17] Utens EM, Versluis-Den Bieman HJ, Witsenburg M, Bogers AJ, Hess J, Verhulst FC. Does age at the time of elective cardiac surgery or catheter intervention in children influence the longitudinal development of psychological distress and styles of coping of parents? Cardiol Young 2002;12:524–30.
[18] Maskatia SA, Justino H, Ing FF, Crystal MA, Mattamal RJ, Petit CJ. Aortic valve morphology is associated with outcomes following balloon valvuloplasty for congenital aortic stenosis. Catheter Cardiovasc Interv 2013;81(1):90–5.
[19] Petit CJ, Gao K, Goldstein BH, Lang SM, Gillespie SE, Kim SI, Sachdeva R. Relation of Aortic Valve Morphologic Characteristics to Aortic Valve Insufficiency and Residual Stenosis in Children With Congenital Aortic Stenosis Undergoing Balloon Valvuloplasty. Am J Cardiol 2016;117:972–9.