Utility of balloon aortic valvuloplasty in the transcatheter aortic valve implantation era

Luke Dawson,1,2 Alex Huang,1,3 Laura Selkrig,1 James A Shaw,1 Dion Stub,1,3 Antony Walton,1 Stephen J Duffy1,3

ABSTRACT

Background Balloon aortic valvuloplasty (BAV) has seen renewed interest since the advent of transcatheter aortic valve implantation (TAVI). The study aimed to characterise a contemporary BAV cohort and determinants of clinical outcomes.

Methods Patients undergoing BAV at a single tertiary centre were retrospectively reviewed over a 10-year period, and functional and mortality outcomes were reported with up to a 2-year follow-up.

Results 224 patients (aged 82.5±8.3 years; 48% female) underwent BAV over the study period. Indications were either destination treatment (39%) or bridge-to-valve replacement (61%)—including bridge-to-decision (29%), symptom relief while on the waiting list (27%), and temporary contraindications to TAVI/aortic valve replacement (AVR) (5%). The mean reduction of aortic mean pressure gradient was 38%. Procedural mortality occurred in 0.5%, stroke in 1.3%, and major bleeding in 0.9%. Twelve-month mortality was 36% overall, and 26% and 50% in the bridging and destination groups, respectively. New York Heart Association (NYHA) class improved by ≥1 at 30 days in 50%. Among the bridge-to-TAVI/AVR group, 40% proceeded to TAVI/AVR within 12 months following BAV. In multivariate analysis, active malignancy at baseline (OR: 4.4, 95% CI: 1.3 to 15.1, p=0.02), smoking history (OR: 3.3, 95% CI: 1.3 to 7.9, p<0.01), LVEF ≤30% at baseline (OR: 3.2, 95% CI: 1.3 to 7.6, p<0.01), destination treatment (OR: 2.2, 95% CI: 1.0 to 4.9, p=0.04) were all associated with 12-month mortality.

Conclusions BAV remains a useful procedure with relatively low rates of complications, however, 1-year mortality rates are high. Contemporary indications for BAV include a bridge to definitive valve replacement or destination treatment.

INTRODUCTION

Aortic stenosis (AS) is the most common valvular pathology in the elderly population and the preferred treatment in higher-risk populations has undergone major changes over the last 10 years with the development of transcatheter aortic valve implantation (TAVI).1-3 In this setting, there has been renewed interest in balloon aortic valvuloplasty (BAV), with increasing procedural numbers both in the USA4,5 and other countries,6,7 which is a marked change from the previous steady decline since its early peak in the 1990s.8 Initially proposed as an alternative to surgical aortic valve replacement (AVR),9 BAV was shown to improve symptoms, although with significant complication rates and no long-term survival benefits.9-12 Traditional indications for BAV have been limited to poor surgical candidates and have included cardiogenic shock,9,13 preoperative optimisation14 and symptomatic improvement with palliative intent.9,11,12,15 Recently, a

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| Table 1  Baseline characteristics |
|---------------------------------|
|                                | All Patients | Bridge-to-TAVI/AVR | Destination | P value |
|                                | n=224        | n=136              | n=88        |         |
| **Demographics:**              |              |                    |             |         |
| Age (years), mean ± SD         | 82.5±8.3     | 82.8±7.4           | 82.0±9.5    | 0.51    |
| Male, n (%)                    | 117 (52.2)   | 70 (51.5)          | 47 (53.4)   | 0.78    |
| BMI, mean ± SD*                | 26.7±6.0     | 27.1±6.1           | 26.1±5.8    | 0.24    |
| **Comorbidities:**             |              |                    |             |         |
| Hypertension, n (%)            | 145 (64.7)   | 90 (66.2)          | 55 (62.5)   | 0.57    |
| Hypercholesterolemia, n (%)    | 122 (54.5)   | 80 (58.8)          | 42 (47.7)   | 0.1     |
| Diabetes, n (%)                | 68 (30.4)    | 42 (30.9)          | 26 (29.6)   | 0.83    |
| Smoking history, n (%)         | 97 (43.3)    | 58 (42.7)          | 39 (44.3)   | 0.81    |
| COPD, n (%)                    | 45 (20.1)    | 26 (19.1)          | 19 (21.6)   | 0.65    |
| Active malignancy, n (%)       | 23 (10.3)    | 11 (8.1)           | 12 (13.6)   | 0.18    |
| Atrial fibrillation, n (%)     | 78 (34.8)    | 42 (30.9)          | 36 (40.9)   | 0.12    |
| eGFR<30                        | 32 (14.3)    | 16 (11.8)          | 16 (18.2)   | 0.18    |
| **Baseline Functional Status:**|              |                    |             |         |
| Baseline NYHA score, mean ±SD  | 2.9±0.7      | 2.9±0.7            | 3.0±0.8     | 0.24    |
| NYHA 1, n (%)                  | 7 (3.1)      | 3 (2.2)            | 4 (4.6)     | 0.06    |
| NYHA 2, n (%)                  | 50 (22.3)    | 32 (23.5)          | 18 (20.5)   |         |
| NYHA 3, n (%)                  | 124 (55.4)   | 82 (60.3)          | 42 (47.7)   |         |
| NYHA 4, n (%)                  | 43 (19.2)    | 19 (14.0)          | 24 (27.3)   |         |
| Syncope, n (%)                 | 21 (9.4)     | 17 (12.5)          | 4 (4.6)     | 0.05    |
| Cardiogenic shock, n (%)       | 6 (2.7)      | 0 (0)              | 6 (6.8)     | <0.01   |
| STS Risk Score, mean ±SD       | 7.3±0.3      | 6.4±0.3            | 8.7±0.7     | <0.001  |
| **Baseline Echocardiogram2:**  |              |                    |             |         |
| LVEF (%), mean ± SD            | 47.7±16.9    | 50.3±15.3          | 43.6±18.5   | <0.01   |
| LVEF ≤40%, n (%)               | 77 (35.2)    | 40 (29.6)          | 37 (44.1)   | 0.03    |
| LVEDD (mm), mean ± SD          | 49.1±8.4     | 48.7±7.8           | 49.9±9.5    | 0.34    |
| **Aortic Valve:**              |              |                    |             |         |
| Aortic valve area (cm2), mean ± SD | 0.6±0.2   | 0.6±0.2            | 0.7±0.2     | 0.79    |
| Mean gradient (mmHg), mean ± SD | 46.1±19.0   | 47.5±19.8          | 43.8±17.4   | 0.16    |
| Low-gradient AS                | 44 (20.4)    | 22 (16.4)          | 22 (26.8)   | 0.07    |
| **Mitral Regurgitation:**      |              |                    |             |         |
| None, n (%)                    | 48 (23.4)    | 35 (28.0)          | 13 (16.3)   | 0.25    |
| Mild, n (%)                    | 93 (45.4)    | 55 (44.0)          | 38 (47.5)   |         |
| Moderate, n (%)                | 58 (28.3)    | 32 (25.6)          | 26 (32.5)   |         |
| Severe, n (%)                  | 6 (2.9)      | 3 (2.4)            | 3 (3.8)     |         |
| E/e’, mean ± SD                | 23.0±11.5    | 20.5±8.9           | 27.0±14.0   | <0.001  |

*207 BMI measures available.
†219 TTE measures prior to BAV available.
AS, aortic stenosis; BAV, balloon aortic valvuloplasty; BMI, body mass index; CABG, coronary artery bypass grafts; COPD, chronic obstruction pulmonary disease; eGFR, estimated glomerular filtration rate; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgery.
more contemporary indication for BAV has included its utilisation as a bridge to either surgical or transcatheter AVR in patients who may have a temporary contraindication,16,19 who may derive uncertain benefit from TAVI or AVR,16–19 or when valve replacement is not immediately available.6 7 16 19–23 Recent data suggest that emergency TAVI has a poor outcome, whereas BAV treatment may give time to prognosticate more accurately.24 Timely TAVI availability remains an important concern among this population given the high mortality among patients with severe AS and the potential for death among wait-listed patients,25 which may potentially be reduced with bridging BAV given its effect on initial improvement in survival.26 This study aimed to assess contemporary indications and outcomes for BAV, as well as to identify factors that predict functional, haemodynamic and mortality benefits to highlight select patient groups that may benefit most from BAV procedures in the TAVI era.

MATERIALS AND METHODS
Consecutive patients undergoing BAV for severe aortic stenosis from February 1, 2008 to September 1, 2017 at The Alfred Hospital, a large tertiary referrals centre in Melbourne, Australia, were retrospectively identified from the hospital cardiac database. Severe aortic stenosis was determined by transthoracic echocardiography prior to the procedure and was defined as either aortic valve area (AVA) <1.0 cm², Dimensionless Performance Index (DPI)<0.25 or mean gradient ≥40 mm Hg in the setting of normal left ventricular (LV) function on transthoracic echocardiography. Severe aortic stenosis in the setting of abnormal LV function was determined by an increase in mean gradient to ≥40 mm Hg with dobutamine stress transthoracic echocardiogram (TTE) or by Heart Team assessment. Patients with mixed aortic valve disease (moderate or severe aortic regurgitation in addition to AS) are not assessed for BAV at our centre and are not included in the study. The project was approved by the Alfred Hospital Ethics Committee.

Demographic data were obtained through a detailed review of the hospital electronic medical records to determine patient demographics, comorbidities, cardiovascular risk factors, cardiac symptoms and presence of cardiogenic shock prior to the procedure. Functional status was determined from medical records by trained medical personnel by applying New York Heart Association (NYHA) criteria to the nearest clinical encounter describing functional ability within 30 days preceding BAV procedure. Indication for BAV was determined by clinician intent at the time of BAV procedure (eg, bridge-to-TAVI/AVR) and patients remained in their intention-to-treat grouping irrespective of the eventual outcome (ie, bridge-to-TAVI and bridge-to-AVR patients did not necessarily receive a valve replacement procedure). Throughout the study period, over 300 TAVI procedures were performed at our institution, with 70 TAVIs performed in 2016 and >90 procedures projected for 2017.

BAV procedures were performed by three individual operators (SD, AW, DS) using standard techniques via the retrograde femoral approach in all patients. Peak and mean gradient measures were confirmed with simultaneous catheter gradient measures. NuMED NuCLEUS and Pyramed Cristal aortic balloons are used at our institution. Sheath size, balloon size, preprocedural and post-procedural haemodynamics, immediate complications and in-hospital mortality were determined from the electronic procedural and clinical records. In-hospital complications, including myocardial infarction and stroke, were defined according to the Academic Research Consortium definitions.27 Significant bleeding was defined as Bleeding Academic Research Consortium Classification Type 3 or 5.28 Acute kidney injury (AKI) following BAV was defined as increase in serum creatinine ≥26.5 μmol/L within 48 hours or increase in creatinine to ≥1.5 times baseline taken within the prior 7 days according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria.29

Patient outcomes were assessed at 30 days, 6 months and 12 months post procedure. Clinic notes and subsequent admissions were used to determine NYHA functional status and hospital readmission rates. TTE reports were reviewed to determine LV ejection fraction (LVEF), AVA, LV end-diastolic diameter (LVEDD), E/e’ and severity of mitral regurgitation (trivial, mild, moderate or severe). Patient mortality was assessed to at least 12 months using clinical records and telephone follow-up, with days from procedure to death used to generate Kaplan-Meier survival curves. If a patient received TAVI or AVR during the 12 months post BAV, then they were no longer included in functional or TTE response after

Figure 1  Procedural numbers by indication – procedural numbers at a single institution over a 9-year period. *2017 data only includes up to September 2017 (with projected numbers for the 2017 calendar year being 45 bridge-to-TAVI/AVR procedures and 8 destination procedures). AVR, aortic valve replacement; TAVI, transcatheter aortic valve implantation.
this point, however, continued to be followed for post-procedural mortality to at least 12 months. If a patient received a repeat BAV within 12 months, then the patient was censored from follow-up at the time of repeat BAV and included as a new procedure.

Statistical analysis was performed using Stata V.14.2 for Macintosh. All categorical variables are presented as frequencies and percentages and continuous variables are presented as mean±SD. Comparisons between groups were performed with the χ² test for categorical variables and Student t test for continuous variables. Multivariate analysis was performed using logistic regression to determine independent predictors of 12 month mortality, functional response (defined by NYHA score improvement ≥1 at 30 days) and haemodynamic response (defined by improvement in LV EF by ≥20% at 30 days). Variables with a p<0.10 in univariate analysis were considered for inclusion in multivariate analysis. The cumulative probability of survival was estimated by Kaplan-Meier curves, with survival between indication groups compared using the log-rank test. All calculated p values were two-sided and p values of <0.05 were considered statistically significant.

RESULTS

Two hundred and twenty-four patients were included in the cohort; the mean age was 82.5±8.3 years, and 47.8% were female (table 1). Procedural numbers increased across the study period, mainly driven by an increase in the number of bridge-to-TAVI/AVR procedures performed, in line with an increase in TAVI procedural numbers across the same period (figure 1).

Baseline clinical characteristics were similar in the bridge-to-TAVI/AVR and destination indication groups, however, there was a higher rate of prior BAV in the destination group (15.9% vs 5.9%, p<0.01). Syncope was more common among the bridge-to-TAVI/AVR group (p=0.05), whereas cardiogenic shock was more common in the destination group (p<0.01). Mean Society of Thoracic Surgery (STS) Risk Score was lower in the bridge-to-TAVI/AVR group (6.4±0.3% vs 8.7±0.7%, p<0.001). Baseline echocardiographic data are presented in table 1, with the destination group having lower mean LVEF (43.6±18.5% vs 50.3±18.5%, p<0.01), and higher mean E/e' ratios (27.0±14.0 vs 20.5±8.9, p<0.001) compared with the bridge-to-TAVI/AVR group. Indications for BAV are presented in table 2.

Procedural characteristics are presented in table 3. One hundred and nine procedures (48.7%) were performed electively, with 84 of these (37.5%) performed at the time of TAVI workup with coronary and peripheral angiography. The mean gradient reduction was 15.9±9.5 mm Hg, with 144 procedures (66.4%) reducing the gradient by ≥30%. Balloon size used was 18 mm in 56.6%, 20 mm in 23.7% and 22 mm in 11.4%, with other sizes being less common.

Major vascular complications occurred in 3.1%, stroke in 1.3%, major bleeding in 0.9% and in-hospital mortality was 2.2%. Procedural mortality occurred in only one patient due to acute aortic regurgitation, while undergoing urgent inpatient BAV for intractable NYHA class 4 symptoms in the setting of low-flow AS. An 18 mm balloon size was used with single inflation, and no clear precipitant for acute aortic regurgitation was identified. There were no significant differences in procedural characteristics or in-hospital complications between the bridge-to-TAVI/AVR cohort and the destination cohort.

For destination and bridge-to-TAVI/AVR groups, mortality was 50.0% and 26.3% at 12 months (p<0.01), respectively (table 4). Eighty-six patients had a repeat aortic procedure: 18 patients had repeat BAV (median time to BAV 357 days), 56 patients proceeded to TAVI (median time to TAVI 135 days) and 12 patients proceeded to AVR (median time to AVR 128 days). Of the 136 patients receiving BAV for bridge-to-TAVI/AVR, only 54 patients (39.7%) proceeded to TAVI or AVR within 12 months following BAV, with many patients (60.3%) not proceeding to TAVI due to either death or Heart Team decision that they were unlikely to benefit. Twelve-month mortality was 7.0% among those proceeding to TAVI or AVR.

NYHA functional response to BAV is presented in figure 2. Of the cohort, 74.6% were NYHA grade 3 or 4 at baseline, compared with 34.8% at 30 days, 55.4% at 6 months, and 68.9% at 12 months (p<0.001). Multivariate analysis demonstrated NYHA 4 at baseline, NYHA 3 at baseline, body mass index (BMI) ≥30 kg/m², female gender, and bridge-to-TAVI/AVR as the indication for the BAV, which were all associated with NYHA grade improvement of ≥1 at 30 days post BAV (table 5).

The mean aortic valve area was 0.65±0.2 cm² at baseline, 0.79±0.3 cm² at 30 days, 0.73±0.2 cm² at 6 months, and 0.66±0.2 cm² at 12 months. The mean aortic mean gradient was 46.1±19.0 mm Hg at baseline (pre-BAV), 40.4±0.2 mm Hg at 30 days (p<0.001 compared with
Table 3 Procedural characteristics and complications

|                  | All patients | Bridge-to-TAVI/AVR | Destination | P value |
|------------------|--------------|--------------------|-------------|---------|
|                  | n=224        | n=136              | n=88        |         |
| Procedural features |              |                    |             |         |
| Elective procedure, n(%) | 109 (48.7) | 65 (47.8) | 44 (50.0) | 0.75    |
| During TAVI workup angiogram, n (%) | 84 (37.5) | 84 (61.8) | 0 (0) | <0.001 |
| Balloon size, mean±SD | 19±2         | 19±2               | 19±2     | 0.11    |
| Sheath size, mean±SD | 10±2         | 10±2               | 10±1     | 0.17    |
| Inflations, n (%) |              |                    |            |         |
| 1                | 73 (79.7)    | 107 (81.7)         | 66 (76.7)  | 0.47    |
| 2                | 36 (16.6)    | 18 (13.7)          | 18 (21.0)  |         |
| ≥3               | 8 (3.6)      | 6 (4.6)            | 2 (2.3)    |         |
| LVEDP (mm Hg), mean±SD | 18.0±20.2 | 18.6±22.9          | 16.7±11.4  | 0.67    |
| Mean gradient (mm Hg) |              |                    |            |         |
| Pre-BAV, mean±SD | 41.6±18.1    | 42.2±18.1          | 40.8±18.0  | 0.57    |
| Post-BAV, mean±SD | 26.2±13.4    | 26.2±13.3          | 26.1±13.5  | 0.97    |
| Reduction, mean±SD | 15.9±9.5    | 16.5±9.4           | 14.9±9.7   | 0.23    |
| Reduced by ≥30%, n (%) | 144 (66.4) | 93 (69.9)          | 51 (60.7)  | 0.16    |
| In-hospital complications |              |                    |            |         |
| Any complication, n (%) | 18 (8.0)    | 11 (8.1)           | 7 (8.0)    | 0.59    |
| Vascular complications, n (%) | 7 (3.1)     | 5 (3.7)            | 2 (2.3)    | 0.56    |
| Myocardial infarction, n (%) | 1 (0.5)    | 1 (0.7)            | 0 (0)      | 0.42    |
| Major bleeding (BARC ≥3), n (%) | 2 (0.9)     | 1 (0.7)            | 1 (1.1)    | 0.76    |
| Acute kidney injury, n (%) | 2 (0.9)     | 1 (0.7)            | 1 (1.1)    | 0.76    |
| Stroke, n (%) | 3 (1.3)      | 1 (0.7)            | 2 (2.3)    | 0.33    |
| Acute aortic regurgitation, n (%) | 1 (0.5)    | 0 (0)              | 1 (1.1)    | 0.21    |
| Pacemaker insertion, n(%) | 2 (0.9)     | 2 (1.5)            | 0 (0)      | 0.25    |
| In-hospital mortality n (%) | 5 (2.2)     | 1 (0.7)            | 4 (4.6)    | 0.06    |
| Procedural mortality, n (%) | 1 (0.5)     | 0 (0)              | 1 (1.1)    | 0.21    |

LVEDP and mean gradient measured by catheter during procedure. Major vascular complications include false aneurysm, dissection or complication requiring surgery or percutaneous intervention (simple haematoma not included in major vascular complications unless meeting criteria for major bleeding, that is, BARC ≥3).

AVR, aortic valve replacement; BARC, Bleeding Academic Research Consortium; BAV, balloon aortic valvuloplasty; LVEDP, left ventricular end-diastolic pressure; TAVI, transcatheter aortic valve implantation.

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Table 4  BAV outcomes to 12 months

|                      | Bridge-to-TAVI/AVR | Destination | P value |
|----------------------|---------------------|-------------|---------|
| 30 days, n (%)       | n=130               | n=83        |         |
| NYHA improved ≥1*    | 71 (60.2)           | 32 (46.4)   | 0.07    |
| LVEF improved ≥10%†  | 8 (15.7)            | 7 (15.6)    | 0.99    |
| Readmission          | 22 (16.8)           | 9 (10.8)    | 0.23    |
| Mortality            | 2 (1.5)             | 9 (10.8)    | <0.01   |
| 6 months, n (%)      | n=111               | n=77        |         |
| NYHA improved ≥1*    | 39 (38.2)           | 21 (32.8)   | 0.48    |
| LVEF improved ≥10%†  | 11 (21.2)           | 1 (7.1)     | 0.23    |
| Readmission          | 41 (36.3)           | 31 (38.8)   | 0.73    |
| Mortality            | 17 (15.3)           | 25 (32.5)   | <0.01   |
| 12 months, n (%)     | n=95                | n=70        |         |
| NYHA improved ≥1*    | 18 (32.1)           | 9 (15.3)    | 0.03    |
| Readmission          | 49 (48.0)           | 31 (43.1)   | 0.52    |
| Mortality            | 25 (26.3)           | 35 (50.0)   | <0.01   |

*Functional data available for 187 patients at 30 days, 166 patients at 6 months and 115 patients at 12 months. Note functional scoring not performed for patients following a repeat aortic procedure (including TAVI, SAVR).
†TTE data for LVEF available for 96 patients at 30 days, and 66 patients at 6 months; 12-month data not included due to limited number of available TTEs.
AVR, aortic valve replacement; BAV, balloon aortic valvuloplasty; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SAVR, surgical aortic valve implantation; TAVI, transcatheter aortic valve implantation; TTE, transthoracic echocardiogram.

gradient immediately post BAV was associated with reduced 12 month mortality in univariate but not multivariate analysis, but was not associated with improvements in NYHA score. At 12 months, 76% had an NYHA score ≥2, consistent with severe symptomatic AS (figure 2).

**DISCUSSION**

This study focuses on the current indications, use and outcomes of BAV in the contemporary setting, where TAVI is commonly used. Among our cohort, 57% of procedures were performed as a bridge-to-TAVI/AVR (and is increasing year by year), demonstrating that this is increasingly becoming accepted as an indication for BAV. This is in line with current American College of Cardiology/American Heart Association guidelines stating BAV may be considered as a bridge to AVR or TAVI in patients with severe symptomatic AS (Class 2B; Level of Evidence C). Of note, in our cohort, BAV was used as a bridge-to-decision in 29% of the cases. Although procedural mortality for BAV is low (<1%) and there is significant symptomatic benefit following BAV, by 12 months there is a recurrence of severe, symptomatic AS in 76% of patients. Thus, definitive therapy such as TAVI or AVR should be offered in the first 6 months following BAV, where appropriate.

Frequently, given the age, frailty and multiple comorbidities of patients with severe aortic stenosis, potential benefits of TAVI or AVR may be uncertain, and with this uncertainty, it may be difficult to justify the procedural risks and costs associated with TAVI/AVR. BAV has utility in this context for two reasons. First, as proposed by previous studies, patient response to BAV can be used to delineate the contribution of aortic stenosis to patients’ symptoms and functional impairment, relative to other limiting comorbidities. It provides the clinical prediction of likely functional and haemodynamic response to a valve replacement and thus allows better patient selection. This indication accounted for 11% of our cohort. Second, patients with severe aortic stenosis often have complex medical histories that require further

Figure 2 Functional response to BAV – functional response to BAV assessed using NYHA scores to classify symptoms. BAV, balloon aortic valvuloplasty; NYHA, New York Heart Association.
evaluation of their comorbidities, prognosis and psycho-social support. BAV creates an opportunity for comprehensive patient assessment to be made. Indeed, only 40% of bridging patients proceeded to TAVI or AVR within 12 months following BAV, lending support to the discriminative power and clinical utility of BAV, as almost half of the patients originally considered for TAVI or AVR were subsequently deemed not suitable for these procedures. In this setting, BAV procedural numbers increased over the final few years of the study, mirroring the increase in TAVI procedural numbers as it becomes more frequently used among patients of lower risk.

Consistent with other studies, another important benefit of BAV is effective symptomatic relief. In our study, we have shown that in 30%–40% of all patients, the functional improvement (judged by the change in NYHA class of ≥1) lasts for 6 months. Although this may seem short lived, it could provide a meaningful improvement in the quality of life in the destination group, whose life expectancy may be severely limited by other comorbidities (eg, active cancer). Our finding also has implications for the bridging group, where waitlists for TAVI remain significant in many jurisdictions. Finally, recent data suggest that emergency TAVI has high rates of 30-day mortality, and bridging BAV in this setting may provide an opportunity to medically stabilise the patient with further assessment of suitability for TAVI once stabilised.24

Immediate postprocedural haemodynamic changes were comparable with previous studies (mean gradient reduction 13.2±13.5 mm Hg in the PARTNER Cohort B study vs 15.9±9.5 mm Hg in our study).26 Among our cohort, we describe low rates of major procedural complications and procedural mortality (0.5%) also consistent with prior data,16 19–21 and highlighting acceptable safety in this high-risk cohort. Twelve-month mortality was 50% among the destination treatment group, which is comparable with the 47% reported among the PARTNER Cohort B study for patients undergoing initial BAV.26 Twelve-month mortality was 26% in the bridge-to-TAVI/AVR group, which is also similar to previously reported rates.16 19 Active malignancy at baseline, smoking history, LVEF ≤30% at baseline and destination treatment as the indication for BAV were all associated with 12-month mortality in multivariate analysis, and therefore, careful consideration as to the likely benefit of a palliative BAV procedure in these patient groups should be made given their overall worsened prognosis.

Although numerous studies have reported BAV procedural outcomes,4–6 16 17 19 21–23 32–34 only one recent smaller study has assessed functional response following BAV,20 and none have assessed multivariate predictors of improvement in functional response post procedure. NYHA 4 at baseline, NYHA 3 at baseline, BMI ≥30 kg/m², female gender and bridge-to-TAVI/AVR as the indication for BAV were all associated with improvement in NYHA score at 30 days in our cohort. Our data highlight the benefit of using BAV as a bridge-to-TAVI/AVR, especially among more symptomatic patients (NYHA 3 and 4), and those of the female gender. The improved functional response and mortality benefit among obese patients has not previously been described but is consistent with the

### Table 5 Multivariate predictors of response to BAV

**Multivariate predictors of improvement of ≥10% in LVEF at 6 months post BAV**

| Predictor                              | OR   | 95% CI   | P value |
|----------------------------------------|------|----------|---------|
| LVEF ≤40% at baseline                  | 26.8 | 3.0–238.2| <0.01   |

**Multivariate predictors of NYHA score improvement of ≥1 at 30 days post BAV**

| Predictor                              | OR   | 95% CI   | P value |
|----------------------------------------|------|----------|---------|
| NYHA 4 at baseline                     | 14.2 | 4.4–45.1 | <0.001  |
| NYHA 3 at baseline                     | 4.8  | 2.0–11.4 | <0.001  |
| BMI ≥30 kg/m²                           | 3.0  | 1.3–6.8  | <0.01   |
| Female                                 | 2.1  | 1.0–4.3  | 0.04    |
| Indication: bridge-to-TAVI/AVR         | 1.9  | 0.9–3.9  | 0.08    |

**Multivariate predictors of 12-month mortality post BAV**

| Predictor                              | OR   | 95% CI   | P value |
|----------------------------------------|------|----------|---------|
| Active malignancy at baseline          | 4.4  | 1.3–15.1 | 0.02    |
| Smoking history                        | 3.3  | 1.3–7.9  | <0.01   |
| LVEF ≤30% at baseline                  | 3.2  | 1.3–7.6  | <0.01   |
| Non-elective procedure                 | 2.3  | 1.0–5.2  | 0.06    |
| Indication: destination                | 2.2  | 1.0–4.9  | 0.04    |
| BMI ≥30 kg/m²                           | 0.3  | 0.1–0.9  | 0.03    |

BAV, balloon aortic valvuloplasty; BMI, body mass index; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

**Figure 3** Kaplan-Meier survival estimates by indication – survival estimates for BAV over a 2-year follow-up. Groups compared using the log-rank test. AVR, aortic valve replacement; BAV, balloon aortic valvuloplasty; TAVI, transcatheter aortic valve implantation.
notion of the ‘obesity paradox’ described in TAVI and percutaneous coronary intervention (PCI) outcomes, whereby obesity is associated with improved post-TAVI and post-PCI survival. However, this observation may be at least partially driven by frail patients having lower BMI, which is not captured by our study.

Determining patients who may show improvement in LV function following BAV or TAVI/AVR is clinically important to allow the selection of patients that may maximally benefit from the procedure. Among patients with low-gradient AS, we found that 47% had improved LVEF ≥10% at 6 months. In our study, the only factor associated with improvement in LVEF by ≥10% at 6 months was LVEF ≤40% at baseline in our study, suggesting a higher gain in patients with more advanced disease. This may support the role of using the improvement of LV function post BAV to identify patients that may benefit most from TAVI/AVR.

Limitations of this study include its retrospective cohort design at a single metropolitan centre, which may be susceptible to selection bias and reduced generalisability to the broader Australian and international populations. As with any retrospective study, there is the potential for unmeasured confounders and findings need to be interpreted as observational. The decision regarding whether a patient underwent BAV as a destination treatment or as a bridge-to-TAVI/AVR is partially explained by the difference in STS score between groups, but generally, baseline characteristics were surprisingly similar between the groups. Frailty and cognitive function play an important role in the selection of patients for BAV and TAVI and could not be captured by this study due to the retrospective design. These factors may have assisted in explaining the difference in patient selection and outcome between the destination and bridge-to-TAVI/AVR groups.

CONCLUSIONS

BAV remains a useful clinical procedure with relatively low rates of procedural complications and mortality and has become increasingly utilised since the advent of TAVI. Contemporary indications include destination therapy, where it provides effective symptomatic relief over 6–12 months, or as a bridge-to-TAVI/AVR where it can be used as a stratifying tool for clinical decision making on valve replacement, as a measure to address issues that pose temporary contraindication to TAVI/AVR and to offer symptomatic improvement to patients who have prolonged waiting time for the TAVI/AVR. Highly symptomatic patients (NYHA 3 or 4), females and obese patients may be more likely to benefit symptomatically following BAV.

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REFERENCES

1 Eggebrecht H, Mehta RH. Transcatheter aortic valve implantation (TAVI) in Germany 2008-2014: on its way to standard therapy for aortic valve stenosis in the elderly? EuroIntervention 2016;11:1029–33.

2 Grover FL, Vemulapalli S, Carroll JD, et al. 2016 Annual Report of The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. J Am Coll Cardiol 2017;69:1215–30.

3 Meredith IT, Walton A, Walters DL, et al. Mid-Term outcomes in patients following transcatheter aortic valve implantation in the CoreValve Australia and New Zealand study. Heart Lung Circ 2015;24:281–90.

4 Alkhouli M, Zack CJ, Sarraf M, et al. Morbidity and mortality associated with balloon aortic valvuloplasty: a national perspective. Circ Cardiovasc Inter 2017;10.

5 Badhka AO, Patel NJ, Singh V, et al. Percutaneous aortic balloon valvotomy in the United States: a 13-year perspective. Am J Med 2014;127:744–53.

6 Saia F, Marrozzini C, Ciucu C, et al. Emerging indications, in-hospital and long-term outcome of balloon aortic valvuloplasty in the transcatheter aortic valve implantation era. EuroIntervention 2013;8:1388–97.

7 Jabbour RJ, Stub D, Walton A. Aortic valvuloplasty - is a revival merited? Br J Cardiol 2011;18:34–6.

8 Moreno PR, Jang IK, Newell JB, et al. The role of percutaneous aortic balloon valvuloplasty in patients with cardiogenic shock and critical aortic stenosis. J Am Coll Cardiol 1994;23:1071–5.

9 Cribier A, Savin T, Saoudi N, et al. Percutaneous transmesial valvuloplasty of acquired aortic stenosis in elderly patients: an alternative to valve replacement? Lancet 1986;1:63–7.

10 Berland J, Cribier A, Savin T, et al. Percutaneous balloon valvuloplasty in patients with severe aortic stenosis and low ejection fraction. Immediate results and 1-year follow-up. Circulation 1989;79:1189–96.

11 Lieberman EB, Bashore TM, Herrinber JB, et al. Balloon aortic valvuloplasty in adults: failure of procedure to improve long-term survival. J Am Coll Cardiol 1995;26:1522–8.

12 Otto CM, Mickel MC, Kennedy JW, et al. Three-year outcome after balloon aortic valvuloplasty. Insights into prognosis of valvular aortic stenosis. Circulation 1994;89:642–50.

13 Theiss HD, Greif M, Steinbeck G, et al. The role of percutaneous aortic balloon valvuloplasty for treatment of cardiogenic shock in the era of surgical valve replacement and TAVI. Intern Emerg Med 2014;9:345–7.

14 Kogoj P, Devjak R, Bunc M. Balloon aortic valvuloplasty (BAV) as a bridge to aortic valve replacement in cancer patients who require urgent non-cardiac surgery. Radiol Oncol 2014;48:62–6.

15 Safian RD, Berman AD, Diver DJ, et al. Balloon aortic valvuloplasty in 170 consecutive patients. N Engl J Med 1988;319:125–30.

16 Ben-Dor I, Maluenda G, Dvir D, et al. Balloon aortic valvuloplasty for severe aortic stenosis as a bridge to transcatheter/surgical aortic valve replacement. Catheter Cardiovasc Interv 2013;82:632–7.

17 Araque JC, Greason KL, Suri RM, et al. The Role of Balloon Aortic Valvuloplasty in Patients With Aortic Valve Stenosis and Society of Thoracic Surgeons Risk of 15% or Higher. Ann Thorac Surg 2016;101:592–6.
18 Dawkins S, Makkar RR. Balloon aortic valvuloplasty: is it still relevant? Circ 2017;10.
19 Moretti C, Chandran S, Vervueren P-L, et al. Outcomes of patients undergoing balloon aortic valvuloplasty in the TAVI era: a multicenter registry. J Invasive Cardiol 2015;27:547–53.
20 Daniec M, Nawrotte B, Sorysz D, et al. Acute and long-term outcomes of percutaneous balloon aortic valvuloplasty for the treatment of severe aortic stenosis. Catheter Cardiovasc Interv 2017;90:303–10.
21 Echchanis H, Durand E, Borz B, et al. Balloon aortic valvuloplasty in the era of transcatheter aortic valve replacement: acute and long-term outcomes. Am Heart J 2014;167:235–40.
22 Malkin CJ, Judd J, Chew DP, et al. Balloon aortic valvuloplasty to bridge and triage patients in the era of trans-catheter aortic valve implantation. Catheter Cardiovasc Interv 2013;81:358–63.
23 Saia F, Moretti C, Dall’Ara G, et al. Balloon aortic valvuloplasty as a bridge-to-decision in high risk patients with aortic stenosis: a new paradigm for the heart team decision making. J Geriatr Cardiol 2016;13:475–82.
24 Bongiovanni D, Küh R, Bleiziffer S, et al. Emergency treatment of decompensated aortic stenosis. Heart 2018;104:23–9.
25 Wijeyseewa HC, Wong WWL, Bennell MC, et al. Impact of wait times on the effectiveness of transcatheter aortic valve replacement in severe aortic valve disease: a discrete event simulation model. Can J Cardiol 2014;30:1162–9.
26 Kapadia S, Stewart WJ, Anderson WN, et al. Outcomes of inoperable symptomatic aortic stenosis patients not undergoing aortic valve replacement: insight into the impact of balloon aortic valvuloplasty from the partner trial (placement of aortic transcatheter valve trial). JACC Cardiovasc Interv 2015;8:324–33.
27 Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344–51.
28 Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the bleeding academic research Consortium. Circulation 2011;123:2736–47.
29 Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guidelines for acute kidney injury. Kidney Int Suppl 2012;2:1–138.
30 Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017;70:252–89.
31 Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.[Erratum appears in J Am Coll Cardiol. 2014 Jun 10;63(22):2489. Dosage error in article text]. J Am Coll Cardiol 2014;63:e57–185.
32 Christodoulidis G, Yu J, Kini A, et al. Gender-Specific outcomes after balloon aortic valvuloplasty: inhospital and long-term outcomes. Am Heart J 2015;170:180–6.
33 Jabbour RJ, Dick R, Walton AS. Aortic balloon valvuloplasty--review and case series. Heart Lung Circ 2008;17 Suppl 4:S73–81.
34 Khawaja MZ, Sohal M, Vail H, et al. Standalone balloon aortic valvuloplasty: indications and outcomes from the UK in the transcatheter valve era. Catheter Cardiovasc Interv 2013;81:366–73.
35 Konigstein M, Havakuk O, Arbel Y, et al. The obesity paradox in patients undergoing transcatheter aortic valve implantation. Clin Cardiol 2015;38:76–81.
36 Lancefield T, Clark DJ, Andrianopoulos N, et al. Is there an obesity paradox after percutaneous coronary intervention in the contemporary era? an analysis from a multicenter Australian registry. JACC Cardiovasc Interv 2010;3:660–8.