Clinical Investigation

Staged Balloon Aortic Valvuloplasty before Standard Aortic Valve Replacement

in Selected Patients with Severe Aortic Valve Stenosis

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This study evaluated preoperative balloon aortic valvuloplasty (BAV) as a technique to decrease aortic valve replacement (AVR) risk in patients who have severe symptomatic aortic valve stenosis with substantial comorbidity.

We report the outcomes of 18 high-risk patients who received BAV within 180 days before AVR from November 1993 through December 2011. Their median age was 78 years (range, 51–93 yr), and there were 11 men (61%). The pre-BAV median calculated Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) was 18.3% (range, 9.4%–50.7%). Preoperative left ventricular ejection fraction measured a median of 0.23 (range, 0.05–0.68), and the median aortic valve area index was 0.4 cm^2/m^2 (range, 0.2–0.7 cm^2/m^2). The median interval from BAV to AVR was 28 days (range, 1–155 d). There were no strokes or deaths after BAV; however, 4 patients (22%) required mechanical circulatory support, 3 (17%) required femoral artery operation, and 1 (6%) developed severe aortic valve regurgitation. After BAV, the median STS PROM fell to 9.1% (range, 2.6%–25.7%) (compared with pre-BAV, P <0.001). Echocardiography before AVR showed that the median left ventricular ejection fraction had improved to 0.35 (range, 0.15–0.66), and the aortic valve area index to 0.5 cm^2/m^2 (range, 0.3–0.7 cm^2/m^2) (compared with pre-BAV, both P <0.05). All patients received AVR. Operative death occurred in 2 patients (11%), and combined operative death and morbidity in 7 patients (39%).

Staged BAV substantially reduces the operative risk associated with AVR in selected patients. ***(Tex Heart Inst J 2014;41(2):152-8)***

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Some patients who present with severe symptomatic aortic valve stenosis have substantial comorbidity and are at high risk for aortic valve replacement (AVR). Often, the patient, the cardiologist, and the surgeon accept the high-risk nature of the valve procedure and make a collective decision to move ahead with either surgical or transcatheter aortic valve replacement (TAVR). Although not well established, another option is to perform balloon aortic valvuloplasty (BAV) to improve valvular function, cardiac function, and clinical status as a bridge to more satisfactory therapy.[1,2] Surgery can then be performed with reduced risk. The present study evaluates our experience with BAV as a measure to improve clinical status and reduce operative risk before AVR in a selected group of patients who were deemed to be at high risk for operation.

Patients and Methods

The Institutional Review Board, Mayo Clinic, approved this study. All patients (or their families when applicable) gave informed consent to participate in the study. At Mayo Clinic, the Division of Cardiovascular Medicine and the Division of Surgery each maintains its own database of prospectively collected data on all patients treated with BAV and AVR. To identify patients for this study, we retrospectively queried and cross-referenced the 2 databases.

We used the Society of Thoracic Surgeons (STS) Risk Calculator to estimate predicted risk of operative death, morbidity, operative death and morbidity, and length of stay. Morbidity estimates included permanent stroke, prolonged ventilation, deep sternal wound infection, renal failure, and reoperation. Length of stay was reported

as long length of stay (>14 d) and as short length of stay (<7 d).

For the purposes of this study, we limited the proposed operative procedure during the risk calculation to AVR with or without coronary artery bypass grafting (CABG). We defined high risk for operation as an estimated STS Predicted Risk of Mortality (PROM) of >8%. Furthermore, we limited our study to those patients who received BAV within 180 days before AVR. The decision to proceed with BAV before AVR was made at the discretion of the treating surgeon. There was no formal decision process, and at the time the patients were not candidates for the Placement of Aortic Transcatheter Valves (PARTNER) Trial.

From November 1993 through December 2011, we identified 233 patients who had received BAV and 8,699 patients who had received AVR. Of the AVR group, 5,434 were eligible for the STS PROM; and of this group, 792 patients (15%) had a STS PROM of 8% or greater. There were 18 patients with a pre-BAV STS PROM of 8% or greater who also had received BAV within 180 days before AVR; they formed the study group for this report.

Excluded from the study were 215 patients who did not meet the inclusion criteria. Patients in this group received isolated BAV (126 procedures), TAVR (107 procedures), or AVR (16 procedures).

Treatment of those patients who met inclusion criteria for the study took place in the following years: one patient in 1993, one in 2000, one in 2002, one in 2007, 4 in 2008, 4 in 2009, 3 in 2010, and 3 in 2011. We collected data required to calculate the STS PROM. During a single session, we entered the data into the STS Risk Calculator and recorded the pre-BAV and pre-AVR STS PROM. We collected echocardiographic data and all operative morbidity and mortality data as defined by STS criteria.

Statistical Analysis

We report descriptive statistics for categorical variables as count and percentage, and for continuous variables as median (range). We compared categorical variables by means of the Fisher exact test and continuous variables by means of the 2-sample *t* test or Wilcoxon rank sum test, where appropriate. We used logistic regression models to identify univariate and multivariate predictors of perioperative death. All statistical tests were 2-sided, with the α level at 0.05 for statistical significance. We compared pre-BAV data and pre-AVR data, and we report actual outcome data.

Results

The median age of the 18 patients was 78 years (range, 51–93 yr); there were 11 men (61%). All patients presented with New York Heart Association functional class III or IV heart-failure symptoms. We report the pre-BAV and pre-AVR STS Risk Calculator variables in Table I and the STS PROM in Table II. The median pre-BAV STS PROM risk was 18.3% (range, 9.4%–50.7%) and the Mortality or Morbidity risk was 63.7% (range, 34.5%–90.4%). Pre-BAV echocardiography revealed a median left ventricular ejection fraction (LVEF) of 0.23 (range, 0.05–0.68) and a median aortic valve area index of 0.4 cm^2/m^2 (range, 0.2–0.7 cm^2/m^2). Aortic regurgitation was present in 15 patients and was trivial in 6, mild in 6, and moderate in 3.

The median interval from hospital admission to BAV was 1 day (range, 0–5 d). Two patients received percutaneous coronary intervention during the BAV intervention. Substantial complications occurred in 7 of the 18 patients (39%) after the BAV, and 2 of those patients experienced multiple complications. Four patients (22%) required mechanical circulatory support that included an intra-aortic balloon pump (IABP) in 3 and TandemHeart® (CardiacAssist, Inc.; Pittsburgh, Pa) support in 2. In addition, 3 patients (17%) required repair of the femoral artery (2 after mechanical circulatory support), 2 (11%) developed respiratory failure, 1 (6%) developed severe aortic regurgitation, and 1 (6%) experienced ventricular fibrillation and was successfully resuscitated. There was no death directly related to the BAV. Ten patients (56%) received hospital discharge after BAV at 5.5 days (range, 2–34 d).

The median pre-AVR STS PROM was 9.1% (range, 2.6%–25.7%) and the overall Mortality or Morbidity risk was 39.5% (range, 16.3%–73.1%). We compare the specific STS estimated risks in Table II. One patient did not undergo echocardiography before the AVR. In the remaining patients, pre-AVR echocardiography showed a median LVEF of 0.35 (range, 0.15–0.66) and a median aortic valve area index of 0.5 cm^2/m^2 (range, 0.3–0.7 cm^2/m^2). Table III shows comparative pre-BAV and pre-AVR echocardiographic data. The median time from post-BAV echocardiography to AVR was 19 days (range, 0–156 d). Pre-AVR aortic regurgitation, present in 15 patients (83%), was trivial in 6 (33%), mild in 5 (28%), moderate in 3 (17%), and severe in 1 (6%).

The median interval from BAV to AVR was 28 days (range, 2–155 d). No patient received dobutamine stress echocardiography to evaluate contractile reserve. Operations included AVR in all patients and an additional procedure in 11 (61%) that included CABG in 4 (22%), aortic root enlargement in 4 (22%), IABP support in 3 (17%), mitral valve replacement in 2 (11%), mitral valve repair in 2 (11%), left atrial appendectomy in 2 (11%), extracorporeal membrane oxygenation in 1 (6%), tricuspid valve replacement in 1 (6%), and repair of femoral vessels in 1 (6%).

Operative death occurred in 2 patients (11%) after AVR and combined operative death and morbidity in 7 (39%). One patient died of a hemorrhagic stroke dur-

TABLE I. Society of Thoracic Surgeons Risk Calculation Variables

Variable	Pre-BAV	Pre-AVR	*P* Value
Continuous			
Age (yr)	74 (52–94)	74 (52–94)	1.00
Weight (kg)	82 (36–125)	81 (39–115)	1.00
Height (cm)	171 (149–189)	170 (141–189)	1.00
Creatinine (mg/dL)	1.7 (0.5–6.5)	1.6 (0.6–4.5)	0.46
Left ventricular ejection fraction	0.23 (0.05–0.68)	0.35 (0.15–0.66)	0.03
Categorical			
Diabetes mellitus	—	—	1.00
None	13	13	—
Oral medication	1	1	—
Insulin	4	4	—
Dialysis	3	3	1.00
Hypertension	9	9	1.00
Infective endocarditis	0	0	1.00
Chronic lung disease	—	—	1.00
None	8	8	—
Mild	3	3	—
Moderate	4	4	—
Severe	3	3	—
Immunosuppression	3	3	1.00
Peripheral vascular disease	8	8	1.00
Cerebrovascular disease	5	5	1.00
Previous CABG	6	6	1.00
Previous valve replacement	1	1	1.00
Previous percutaneous coronary intervention	3	5	0.69
Previous myocardial infarction	6	6	1.00
Cardiac presentation	—	—	—
1	7	9	Unable to evaluate
2	5	6	—
3	3	3	—
4	3	0	—
5	1	0	—
NYHA functional class	—	—	0.05
I, II	0	4	—
III, IV	18	14	—
Cardiogenic shock	6	2	0.1
Resuscitation	0	0	1.00
Arrhythmia	5	5	1.00
Inotropic agents	5	1	0.1

AVR = aortic valve replacement; BAV = balloon aortic valvuloplasty; CABG = coronary artery bypass grafting; NYHA = New York Heart Association

Data are presented as median and range or as count. All statistical tests were 2-sided with the α level at 0.05 for statistical significance.

TABLE I (continued). Society of Thoracic Surgeons Risk Calculation Variables

Variable	Pre-BAV	Pre-AVR	*P* Value
No. diseased coronary vessels	—	—	1.00
0	7	7	—
1–3	11	11	—
Left main disease	3	3	1.00
Mitral stenosis	3	3	1.00
Aortic regurgitation	—	—	0.57
None or trivial	9	8	—
Mild, moderate, or severe	9	9	—
Mitral regurgitation	—	—	1.00
None or trivial	1	1	—
Mild, moderate, or severe	17	16	—
Tricuspid regurgitation	—	—	0.32
None or trivial	3	2	—
Mild, moderate, or severe	15	13	—
Operative incidence	—	—	1.00
First operation	11	11	—
First reoperation	7	7	—
Status	—	—	0.06
Elective	6	11	—
Urgent/emergent	12	7	—
Intra-aortic balloon pump	—	—	0.65
None	13	14	—
Intraoperative/postoperative	4	1	—

AVR = aortic valve replacement; BAV = balloon aortic valvuloplasty; CABG = coronary artery bypass grafting; NYHA = New York Heart Association

Data are presented as median and range or as count. All statistical tests were 2-sided with the α level at 0.05 for statistical significance.

ing a single hospital stay, 52 days after the BAV and 23 days after the AVR; the patient's pre-BAV risk of death was 23.5% and the pre-AVR risk was 22.2%. A second death, from multisystem organ failure, occurred 95 days after the BAV and 26 days after the AVR; the patient's pre-BAV risk was 16.5% and the pre-AVR risk was 23.1%. Additional operative complications after AVR included respiratory failure with need for prolonged ventilation in 4 patients (25%), acute renal failure in 1 (6%), and need for reoperation in 1 (6%). The median hospital stay after AVR was 12 days (range, 5–51 d).

Seventeen patients (94%) experienced a reduction in STS PROM after BAV (Table II). The group's STS PROM after the BAV fell from 18.3% to 9.1% (49.7% reduction; $P=0.0003$), and its risk of death or morbidity fell from 63.7% to 39.5% (62% reduction; $P=0.0007$).

There were 7 late deaths, which included myocardial infarction (1), non-Hodgkin lymphoma (1), mesenteric ischemia (1), chronic dialysis-dependent renal failure (1), and unknown cause (3). Survival at 6 months was 15 of 18 patients (83%), at 1 year was 13 of 18 (72%), and at 2 years was 9 of 18 (50%). At last follow-up of 2.7 years (range, 1.1–12 yr), 8 patients were alive.

Discussion

The present study reports the outcome of a group of selected patients deemed to be at high risk for AVR on the basis of the STS PROM. The measure of high risk in our study group was an STS PROM of 18.3%. No patient died after BAV, but there was considerable morbidity. Seventeen of the 18 patients (94%) experienced reduction in their STS PROM after BAV, a difference that we think was both statistically and clinically significant. The actual occurrence of death or morbidity after AVR was not much different from that predicted by the STS risk calculator.

We used the STS PROM because we considered it the best predictor of operative death after high-risk AVR. Studies from Dewey,[3] Basraon,[4] and their colleagues support that choice. The patients in our study were at high risk of death after AVR. Indeed, the group's STS

TABLE II. Estimated Pre-BAV and Pre-AVR Society of Thoracic Surgeons Predicted Risks

Variable	Pre-BAV (%)	Pre-AVR (%)	*P* Value
Mortality	18.3 (9.4–50.7)	9.1 (2.6–25.7)	0.0003
Morbidity or mortality	63.7 (34.5–90.4)	39.8 (16.3–73.1)	0.0007
Long stay (>14 d)	36.0 (19.3–74.9)	22.6 (6.9–50.8)	0.0008
Short stay (<7 d)	4.5 (1.6–16.3)	10.0 (2.9–36.2)	0.0005
Permanent stroke	3.4 (1.4–9.3)	2.7 (1.0–8.8)	0.02
Prolonged ventilation	56.5 (24.7–88.9)	31.2 (9.3–64.6)	0.0005
Deep sternal wound infection	0.8 (0.2–3.7)	0.5 (0.2–3.2)	0.55
Renal failure	14.0 (7.8–45.1)	9.0 (2.3–31.6)	<0.0001
Reoperation	21.9 (11.2–32.2)	13.5 (8.6–28.1)	0.0009

AVR = aortic valve replacement; BAV = balloon aortic valvuloplasty

Data are presented as median and range. All statistical tests were 2-sided with the α level at 0.05 for statistical significance.

TABLE III. Comparison of Pre-BAV and Pre-AVR Echocardiographic Data

Variable	Pre-BAV (%)	Pre-AVR (%)	*P* Value
Left ventricular ejection fraction	0.23 (0.05–0.68)	0.35 (0.15–0.66)	0.03
Mean aortic valve gradient (mmHg)	46 (19–73)	43 (15–66)	0.13
Aortic valve area index (cm^2/m^2)	0.4 (0.2–0.7)	0.5 (0.3–0.7)	0.03

AVR = aortic valve replacement; BAV = balloon aortic valvuloplasty

Data are presented as median and range. All statistical tests were 2-sided with the α level at 0.05 for statistical significance.

PROM was 18.3% and that of STS PROM or Morbidity was 63.7%. The magnitude of these numbers placed our group of patients in the upper 90th percentile of mortality risk after AVR.[3,5] In fact, our group's risk of death was greater than that reported for either cohort A (11.8%) or B (11.6%) of the PARTNER trial.[5,6]

We found that BAV resulted in significantly improved valve function and cardiac function. This included LVEF (52% increase), mean aortic valve gradient (7% decrease), and aortic valve area index (25% increase). Our results are similar to those reported by Zhawaja and colleagues,[7] who found a significant reduction in peak aortic valve gradient (31%) and an increase in aortic valve area (38%). Furthermore, Saia and colleagues[8] noted a significant improvement in mean aortic valve gradient (25% decrease) and aortic valve area (40% increase).

We report a significant (49.7%) decrease in STS PROM after BAV. Because the STS Calculator is a proprietary algorithm, it is difficult to determine what factors contributed significantly to the differences. Similar results have been reported by Doguet and colleagues,[1] who noted a 30% reduction in the logistical EuroSCORE (from 18.6% to 13%) after BAV. In another study, Malkin and colleagues[2] reported that 58% of patients experienced significant clinical improvement after BAV.

The success of BAV is not guaranteed. In our series, morbidity occurred in 39% of patients and included the need for mechanical circulatory support in 22% and the development of respiratory failure in 11%. Doguet and

colleagues[1] reported that 29% of patients could not be discharged from the hospital after BAV because of heart failure. Kapadia and associates[9] reported access complications in 6% of their 90 patients. Although we had no deaths directly related to BAV, Kapadia and associates reported a 30-day mortality rate of 17%.

It is unlikely that aggressive medical management followed by surgical AVR in this situation would result in an acceptable outcome. Most of the patients in this group had attributes known to be associated with operative death after AVR. For example, cardiogenic shock and emergent operation remain significant predictors of increased mortality rates after AVR with an odds ratio of 3.77; 95% confidence interval, 2.75–5.16) in the most recent STS report.[10] There have been isolated reports of success with emergent AVR in the setting of cardiogenic shock, but low cardiac output, prolonged convalescence, and renal and respiratory failure are common.[11]

Transcatheter aortic valve replacement might be an alternative in this selected group of patients. However, the median STS PROM in our patients was over 18%, and Makkar and colleagues[12] report that TAVR in inoperable patients with an STS PROM of greater than 15% offers no advantage over medical therapy in the PARTNER 1B study.

It is important to note that the 2 deaths in our series were in patients whose STS risks did not significantly improve after BAV; these types of patients (the so-called "cohort C" patients) might not do well with any type of aortic valve operation. Another important point from the PARTNER Trial is that TAVR, for high-risk patients, does not result in any survival benefit (over surgical AVR) at 1 month, 1 year, or 2 years.[5,13] Furthermore, no data support emergent TAVR in acutely sick patients.

It is unclear how long one should wait to perform AVR after BAV. In our patients, the median number of days after BAV to AVR was 28 (range, 2–155 d). In Saia and colleagues' study,[8] all patients were re-evaluated for AVR one month after BAV; Doguet and colleagues[1] reported a median time interval of 61 days between BAV and AVR (range, 35–104 d). It is prudent to allow for clinical improvement after BAV before proceeding with AVR, and a period of 1 to 2 months seems reasonable. Clinical evaluation during follow-up visits should determine further treatment options.

Limitations. This study is limited by its small number of patients, probable selection bias, and retrospective design. Because most of these patients received treatment within the 4-year period during which we initiated our TAVR program, there probably is a selection bias. Many similar patients might have been nursed along and subsequently treated with TAVR under the auspices of the PARTNER trial. Finally, it can be difficult in a retrospective chart review to confidently establish why the surgeon chose to proceed with BAV. These limitations could be overcome only by a prospective study of a large number of patients, which would be time-consuming and costly.

Conclusion. There are patients with severe aortic stenosis who present with profound debility and who score high in overall STS PROM or mortality and morbidity risk associated with AVR. Surgery in this group might not provide a survival benefit. Balloon aortic valvuloplasty in selected patients serves as both a diagnostic and a therapeutic maneuver. Those patients who do not improve after BAV can avoid a nontherapeutic aortic valve operation. Selected patients who experience clinical improvement can undergo subsequent aortic valve surgery with less operative risk.

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