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Balloon Aortic Valvuloplasty as Bridge-to-Decision in High Risk Patients with Severe Aortic Valve Stenosis

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Abstract

Background. A sizable group of patients with symptomatic aortic stenosis (AS) can undergo neither surgical aortic valve replacement (AVR) nor transcatheter aortic valve implantation (TAVI) because of clinical contraindications. The aim of this study was to assess the potential role of balloon aortic valvuloplasty (BAV) as a “bridge-to-decision” in selected patients with severe AS and potentially reversible contraindications to definitive treatment.

Methods. We retrospectively enrolled 645 patients who underwent first BAV at our Institution between July 2007 and December 2012. Of these, the 202 patients (31.2%) who underwent BAV as bridge-to-decision (BTD) requiring clinical re-evaluation represented our study population. BTD patients were further subdivided in 5 groups: low left ventricular ejection fraction; mitral regurgitation grade ≥3; frailty; hemodynamic instability; comorbidity. The main objective of the study was to evaluate how BAV influenced the final treatment strategy in the whole BTD group and in its single specific subgroups.

Results. Mean logistic EuroSCORE was 23.5±15.3%, mean age was 81±7 years. Mean transaortic gradient decreased from 47±17 mmHg to 33±14 mmHg. Of the 193 patients with BTD-BAV who received a second heart team evaluation, 72.5% were finally deemed eligible for definitive treatment (25.4%for AVR; 47.2% for TAVI): respectively, 96.7% of patients with left ventricular ejection fraction recovery; 70.5% of patients with mitral regurgitation reduction; 75.7% of patients who underwent BAV in clinical hemodynamic instability; 69.2% of frail patients and 68% of patients who presented relevant comorbidities. 27.5% of the study population was deemed ineligible for definitive treatment and treated with standard therapy/repeated BAV. In-hospital mortality was 4.5%, cerebrovascular accident occurred in 1% and overall vascular complications were 4% (0.5% major; 3.5% minor).

Conclusions. Balloon aortic valvuloplasty should be considered as bridge-to-decision in high-risk patients with severe aortic stenosis who cannot be immediate candidates for definitive percutaneous or surgical treatment.

Keywords: Aortic valve stenosis, transcatheter aortic valve replacement, mortality, complications, long-term

Introduction

A sizable proportion of patients with severe aortic stenosis (AS) have clinical conditions that may preclude definitive treatment with surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR)[1-3]. With the possible exception of haemodynamically unstable patients or symptomatic patients who require urgent major non-cardiac surgery, current guidelines do not support the use of percutaneous balloon aortic valvuloplasty (BAV) as a bridge to SAVR or TAVR[4,5]. Of interest, a possible role for BAV and subsequent clinical re-evaluation has been proposed in selected patients with severe AS and clinical conditions generating uncertainty within the heart team [6], but there are virtually no data supporting such a strategy.

With the present study we sought to evaluate the role of BAV as a “bridge-to-decision” in selected patients with severe AS and potentially reversible contraindications to definitive surgical or transcatheter treatment.

Methods

Patient population. All consecutive patients who underwent BAV at our institutions were entered in a prospective BAV registry. Indications to BAV, always discussed within the heart team, were the following: 1) Destination therapy, i.e. palliation of symptoms in patients without other therapeutic options; 2) bridge-to-TAVR, in patients who are candidates for TAVR with the aim of improving clinical conditions before the procedure; 3) bridge-to-AVR, in patients who were candidates for AVR in order to improve clinical status or reduce surgical risk; 4) bridge-to-decision BAV (BTD), when there was either severe clinical instability or initial heart team evaluation was not conclusive and indicated the necessity of a subsequent clinical or instrumental re-evaluation. The present study focuses on this last patients’ group. Based on the main reason for postponing the final decision-making, patients were further (and retrospectively) subdivided into 5 subgroups of interest: a) low left ventricular ejection fraction (LVEF≤30%); b) mitral valve regurgitation (MVR) grade ≥3; c) frailty, ie patients with a Rockwood Frailty Index =3 or frailty index=2 with at least another severe comorbidity between COPD, renal failure (GFR< 30 ml/min), BMI <20 o >30 Kg/m^2, serum albumin <3.5 g/dL and liver cirrhosis; d) hemodynamic instability, either cardiogenic shock or acute pulmonary edema or NYHA class IV; e) comorbidity, representing a potentially reversible contraindication for definitive treatment *per se* or in combination with other risk factors (including pulmonary hypertension, multiple comorbidities, need for urgent non cardiac surgery).

Study objectives and definitions. All patients had ambulatory visit and echocardiography scheduled 1 month after BAV. The main objective of the study was to evaluate how BAV influenced the final heart team decision-making in the whole BTD group and in its single specific subgroups. The impact of BAV was also evaluated in specific subgroups of interest: in patients with low LVEF a significant improvement was considered as an improvement > 5% or a final LVEF>30% in conjunction with subjective clear clinical benefit; in patients with MVR grade ≥3, significant improvement was defined by a final MVR ≤2 using standard definitions[7]. Final therapeutic decision formulated by the heart team did not rely only on these changes but took into account the whole patient status and life expectancy. Based on this second evaluation, patients were candidates for TAVI, AVR or medical treatment with possible repeat palliative BAV (MT/BAV).

Symptomatic status was classified based on the presence of syncope, stable angina, acute coronary syndrome, dyspnea (New York Heart Association class), or cardiogenic shock. Coronary artery disease included previous percutaneous coronary intervention (PCI), previous coronary artery bypass graft (CABG), or documented stenosis ≥70% of a major coronary vessel by visual estimate at angiography. Chronic kidney disease (CKD) was identified by a glomerular filtration rate (GFR) calculated by the MDRD (Modification of Diet in Renal Disease) formula <60 ml/min/1.73 m^2. Severe CKD was defined as a GFR <30 ml/min/1.73 m^2. Chronic obstructive pulmonary disease was identified by forced expiratory volume in 1 second<1 liter or long-term use of bronchodilators, steroids or oxygen for lung disease. Pulmonary hypertension was defined as an estimated systolic pulmonary pressure ≥60 mmHg with echocardiography. The surgical risk was estimated with the logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation).[8]

In-hospital events measured were: all-cause death, cardiac death (including deaths not clearly due to extra-cardiac causes), cerebrovascular events (stroke, transient ischemic attack), myocardial infarction, acute aortic regurgitation, and vascular complications (local hematoma, retroperitoneal hematoma, artero-venous fistula, dissection, femoral pseudo-aneurysm, thrombosis). Stroke was classified as disabling or not disabling based on the use of the modified Rankin Scale.[9] Vascular complications were defined major (leading to death, life-threatening or major bleeding, permanent damage or requiring surgery) or minor (including percutaneous closure device failure).

All patients signed written informed consent for the procedure and for enrollment in the local BAV registry.

Statistical analysis. Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were presented as frequencies and percentages. For comparisons between groups, the Chi-square test for categorical variables was used. Student t test was used to compare continuous variables. Multivariable Cox regression was used to identify predictors of definitive treatment of aortic stenosis. Dichotomous variables with a frequency greater than 1% and all continuous variables were selected for the analysis. A stepwise model was used to select variables for the final model (probability to enter the model = probability to exit from the model = 0.15). All tests were 2-sided and statistical significance was defined as $p<0.05$. All analyses were performed with the SPSS 17.0 software (SPSS Inc., Chicago, Illinois).

Results

Between July 2007 and December 2012, 645 patients underwent first BAV at our institutions. In 202 cases (31.2%), indication for the procedure was bridge-to-decision, which represents the focus of this study. Study flow is reported in figure 1. Demographics, clinical history and baseline characteristics are reported in Table 1. High-risk profile is confirmed by advanced age (81±7 years) and high prevalence of comorbidity, including coronary artery disease (43.1%), previous cardiac surgery (9.9%), severe renal disease (27.2%), COPD (29.2%) and high logistic EuroSCORE (23.5±15.3%). Table 2 summarizes echocardiography data before and after BAV. Mean trans-valvular gradient decreased from 47±17 mmHg to 33±14 mmHg and AVA increased fron 0.66±0.17 mm^2 to 0.84±0.24 mm^2. Nine patients died before hospital discharge, the vast majority (8 patients) presented hemodynamic instability at admission. The incidence of other complications was overall low (table 3). All 193 surviving patients were re-evaluated at outpatient clinic and by the heart team around 1 month later.

Patients with low LVEF. A significant improvement in LVEF was observed in 30/44 surviving patients (63.8%). Average LVEF was 38±7% in patients who recovered vs. 26±4% ($p<0.01$) in those who did not. There were no significant differences in demographics and clinical history, including previous myocardial infarction, between patients who recovered LVEF and those who did not. Baseline LVEF was also similar between groups (28±4 mmHg vs 26±3 mmHg, respectively, p=0.27), as well as baseline AVA (0.65±0.17 mm^2 vs. 0.64±0.15 mm^2, p=0.83). Conversely, there was a significant difference in baseline transvalvular gradients (mean gradient 42±16 mmHg vs. 31±8 mmHg, p=0.03). After 1 month, patients who recovered showed similar AVA (0.80±0.23 mm^2 vs. 0.88±0.21 mm^2, p=0.30) but higher gradients (mean gradient 33±15 mmHg vs. 22±7 mmHg, $p<0.01$). Among patients with LVEF recovery 96.7% were candidates for definitive treatment (53.4% TAVI, 43.3% AVR) vs. 21.4% (all TAVI) in patients who did not show LVEF recovery ($p<0.001$)(figure 2).

Patients with MVR. Within the 33 patients with MVR grade ≥3, a significant reduction of MVR grade was observed in 17 (51.5%), whereas in 16 patients (48.5%) there were no relevant changes. There were no significant differences between patients who improved MVR grade and those who did not, with the notable exception of AVA after BAV (0.89±0.21mm^2 vs. 0.72±0.17 mm^2, p=0.045). Changes in MVR grade and final heart team decision is illustrated in figure 3. Overall, 70.5% of patients with MVR grade reduction were addressed to definitive treatment (52.9% TAVI, 17.6% AVR) vs. 31.3% of patients whitout MVR grade improvement (p=0.02).

Patients with hemodynamic instability. Among 103 patients, 9 (8.7%) presented with cardiogenic shock, 44 (42.7%) with acute pulmonary edema at the time of BAV, and 50 (48.6%) with NYHA class IV. Eight patients (7.8%) died in-hospital. Among the 95 remaining patients, 21 (22.1%) were candidates for AVR, 57 (60%) for TAVI and 17 (17.9%) for MT/BAV.

Frailty. Thirteen patients were classified as fragile according to previously mentioned criteria. They must be fragile enough to be considered ineligible for definitive treatment at the time of BTD but not so fragile to be directly addressed to a MT/BAV strategy. Among them, 6 patients (46.1%) finally underwent TAVI, 3 AVR (23.1%) and 4 (30.8%) MT/BAV.

Comorbidity. Among 47 patients with relevant comorbidity and potentially reversible conditions, 34 (72.3%) received BAV as bridge to urgent non cardiac surgery, 5 had severe pulmonary hypertension (10.6%), and 8 patients had multiple comorbidities (17%). After BTD BAV, 25 (53.2%) were addressed to MT/BAV, 7 to TAVI (14.9%), and 15 (31.9%) to AVR.

Whole BTD population. Of the 193 patients with BTD-BAV who received a second heart team evaluation, 49 (25.4%) were finally deemed eligible for AVR, 91 (47.2%) for TAVI, and the remaining 53 (27.5%) were deemed ineligible for definitive treatment and were candidates for MT/BAV (figure 4).

At multivariable analyses, the independent predictors for definitive treatment of aortic stenosis were age (HR 0.93; 95% CI 0.88-0.99), body mass index (HR 1.09; 95% CI 1.01-1.18), coronary artery disease (HR 3.37; 95% CI 1.58-7.21), mean gradient before BAV (HR 1.03; CI 95% 1.00-1.05) and hemodynamic instability (HR 2.54; CI 95% 1.21-5.33).

Discussion

This study explored the role of BAV as bridge-to-decision in high-risk patients with severe aortic stenosis who presented cardiac or extra-cardiac conditions necessitating further evaluation by the heart team. The rationale behind such a strategy is twofold: helping the heart team to choose the best therapeutic option for each patient; avoiding futile procedures in patients who would probably not have prognostic benefit from definitive treatment of aortic stenosis. Our investigation suggests that, in this patient population, BTD BAV is safe and might have relevant impact on final decision-making.

Whilst many high-risk patients can be safely addressed to AVR[10] or TAVI[11-13] following accurate multidisciplinary evaluation, in some instances additional information may be needed to complete the diagnostic workout. Indeed multiple factors influence symptoms, life expectancy and final outcomes of invasive procedures in elderly patients with severe aortic stenosis and relevant comorbidity. Thus, not surprisingly, our study population was quite heterogeneous. In this context, the second heart team evaluation around 1 month after BTD BAV generated a true differentiation of final therapeutic decision between TAVI, AVR and MT/BAV, and our data show that clinical and/or laboratory changes occurred after BTD BAV were actually meaningful for decision-making. For example, patients who showed significant LVEF recovery and/or MVR grade reduction after BTD-BAV were significantly more likely to be candidates for definitive AS treatment in comparison with patients not showing significant changes. Likewise, BTD-BAV was very helpful in patients with hemodynamic instability, with the vast majority of patients (75.7%) successfully stabilized and candidates for definitive treatments. More challenging is the interpretation of results in patients classified as fragile or with relevant comorbidity, maybe because this post-hoc classification could only partially rely on objective data. Yet, 69.2% of very fragile patients and 46.8% of the patients with severe or multiple comorbidity were finally recommended for definitive AS treatment, mainly on the grounds of some clinical improvement.

There is growing utilization of BAV as a bridge to TAVI or AVR[14-19]. However, within this patient group, roughly 2 additional subgroups can be distinguished: 1) patients undergoing BAV to palliate symptoms and reducing operative risk while they are screened and await definitive therapy, which has been already planned ("true" bridge-to-TAVI or bridge-to-AVR); 2) patients undergoing BAV as a preliminary treatment strategy to choose the best therapeutic option, because there is the need to assess the potential benefit of valve replacement before committing to the procedural risk (bridge-to-decision). Our study is the first investigation specifically focused on this last peculiar BAV indication.

Previous studies have shown an improvement of LVEF after BAV[20], and an association between LVEF recover after BAV and prognosis post-TAVI[21,22]. Dobutamine stress echocardiography is commonly recommended to evaluate contractile reserve in patients with severe AS and reduced LVEF undergoing surgical or percutaneous aortic valve replacement. Nevertheless, BAV may provide complimentary information beyond contractile reserve[21]. In our view, this is particularly evident when there are other concomitant conditions potentially associated with adverse prognosis or lack of symptoms relief. It has been previously reported that nearly half of patients with severe AS and coexistent MVR showed a reduction in the magnitude of MVR after BAV[23]; our study reproduced very closely those figures (51.5% significant MVR reduction). A reduction in pulmonary artery systolic pressure can be observed in around half of the patients[24]. Additional insights can be provided by BTD BAV when an unstable hemodynamic state may preclude a thorough patient evaluation. Finally, in patients with very advanced age or serious comorbid disease, including frailty, cognitive impairment, severe lung disease, BTD BAV may be important to estimate the potential benefit of valve replacement. In fact, severe comorbidity is often determinant to deny AVR, but is also strongly affecting mid- and long-term prognosis after TAVI [22,25,26], and BTD BAV may be a useful tool to improve risk stratification.

This is a retrospective, nonrandomized, single-center study, and all our findings should be interpreted cautiously. Study population was quite heterogeneous, and classification into subgroups of interest was arbitrarily done post-hoc. Even recognizing that more data occur, consistency with findings from other investigations and the relatively large number of patients included in the present analysis are noteworthy.

Conclusion

Balloon aortic valvuloplasty should be considered as bridge-to-decision in high-risk patients with severe aortic stenosis who cannot be immediate candidates for definitive percutaneous or surgical treatment.

Tables

Table 1. Baseline characteristics.

Variable	All patients (n=202)
Demographics	
Age, *yrs*	81 ± 7
Male gender	89 (44.1)
Body mass index, *kg/m^2*	24.9 ± 4.7
BMI≤20	25 (12.4%)
Risk Factors	
Diabetes	63 (31.2)
Hypertension	161 (79.7)
Dyslipidemia	109 (54.0)
Clinical history	
Previous myocardial infarction	51 (25.2)
Previous percutaneous coronary intervention	32 (15.8)
Previous coronary artery bypass graft	18 (8.9)
Previous cardiac surgery	20 (9.9)
Previous cerebrovascular accident	28 (13.9)
Comorbidity	
Coronary artery disease	87 (43.1 %)
Chronic kidney disease	163 (80.7 %)
GFR<30 *ml/min/1.73 m^2*	55 (27.2 %)
Chronic obstructive pulmonary disease	261 (29.2%)
Pulmonary hypertension	5 (13.9 %)
Clinical presentation	
Dyspnea	189 (93.6)
NYHA I- II	28 (14.8 %)
NYHA III-IV	161 (85.2%)
Stable angina	47 (23.3 %)
Syncope	21 (10.4 %)
Cardiogenic shock	9 (4.5)
Logistic EuroSCORE, *%*	23.4 ± 15.2

Data are shown as mean ± standard deviation for continuous variables and absolute numbers (%) for dichotomous variables.

BMI= body mass index; EuroSCORE= european system for cardiac operative risk evaluation; GFR= glomerular filtration rate;

NYHA=New York Heart Association

Table 2. Echocardiographic parameters before and after balloon valvuloplasty.

	Before-BAV (n=202)	After-BAV (n=148)	p
AVA, *cm*^{2}	0.66 ± 0.17	0.84 ± 0.24	<0.01
Mean transvalvular gradient, *mmHg*	47 ± 17	33 ± 14	<0.01
Max gradient, *mmHg*	76 ± 27	55 ± 23	<0.01
Aortic regurgitation			<0.01
≤1+	148 (73.3)	88 (59.4)	
2+	48 (24.7)	53 (35.8)	
≥3+	6 (3.0)	7 (4.7)	
Mitral valve regurgitation			0.51
≤1+	119 (58.9)	89 (60.1)	
2+	50 (24.7)	42 (28.4)	
≥3+	33 (16.3)	17 (11.5)	
LVEF, *%*	50 ± 17	51 ± 16	0.47

Table 3. In-hospital outcome.

	All patients
Death	9 (4.5)
Cardiac	8 (4.0)
Non cardiac	1 (0.5)
Acute myocardial infarction	0
Cerebrovascular accident	2 (1.0)
Transient ischemic attack	0
Stroke	2 (1.0)
Disabling	1 (0.5)
Non disabling	1 (0.5)
Vascular complications	8 (4.0)
Major	1 (0.5)
Minor	7 (3.5)
Vascular complication description	
Access-site hematoma	5 (2.5)
Retroperitoneal hematoma	0
Artero-venous fistula	0
Femoral dissection	1 (0.5)
Femoral pseudo-aneurysm	2 (1.0)
Thrombosis	0
Acute aortic regurgitation	2 (1.0)

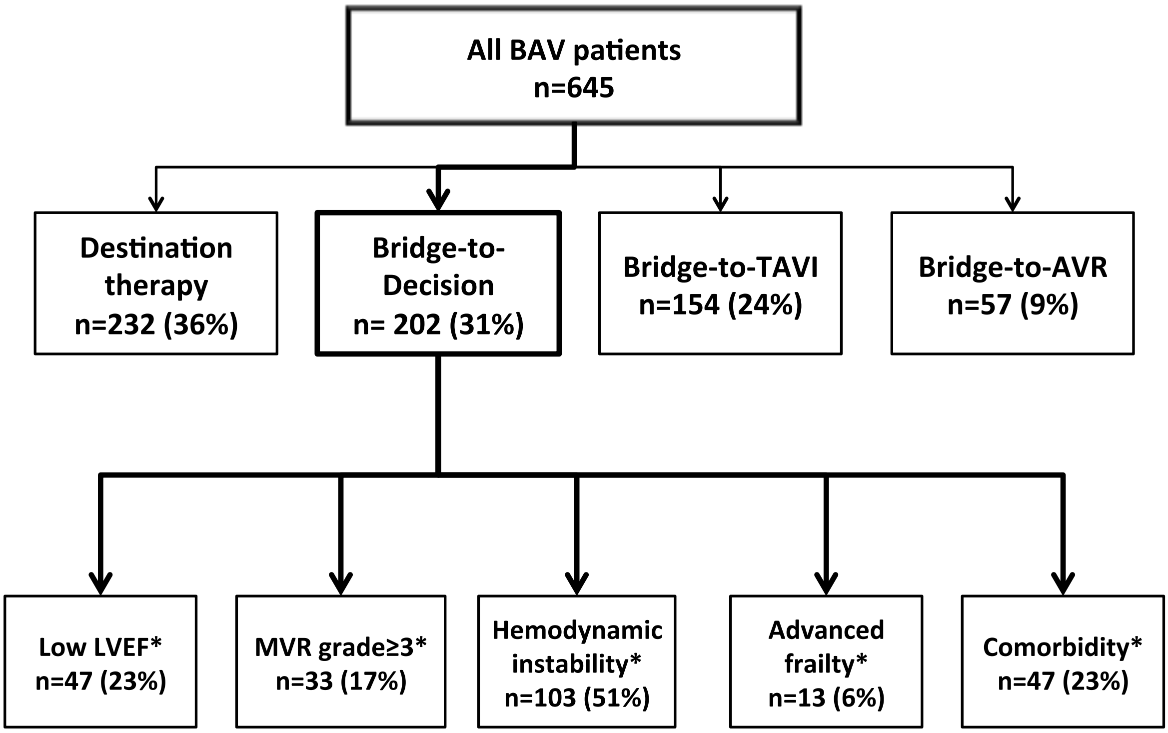
Table 4. Independent predictors for definitive treatment of aortic stenosis.

	Univariate analysis			Multivariate analysis†		
Variable	**HR**	**95% CI**	**p**	**HR**	**95% CI**	**p**
Age, *yrs*	0.95	0.90-0.99	0.02	0.93	0.88-0.99	0.021
Body mass index, *kg/m^2*	1.07	1.00-1.14	0.04	1.09	1.01-1.18	0.028
Coronary artery disease	3.74	1.89-7.38	0.0001	3.37	1.58-7.21	0.002
Chronic kidney disease	0.43	0.18-1.03	0.06			
Dyspnea	2.84	0.91-8.84	0.07			
Stable angina	2.19	0.99-4.88	0.05			
MVR grade≥3 (before BAV)	0.40	0.19-0.85	0.018			
MVR grade <3 (after BAV)*	5.28	1.20-23.31	0.028			
Mean gradient before BAV	1.02	1.00-1.04	0.09	1.03	1.00-1.05	0.017
Hemodynamic instability	1.86	1.01-3.42	0.05	2.54	1.21-5.33	0.014
LVEF recover*	15.5	3.76-63.5	<0.0001			

*Variables not tested in the multivariate analysis because they refer only to specific patient subgroups and are not applicable to the entire population; †C statistic=0.74; Hosmer and Lemeshow goodness-of-fit test p=0.23

BAV= balloon aortic valvuloplasty; LVEF=left ventricular ejection fraction; MVR= mitral valve regurgitation

Figures



*41 patients presented more than 1 condition

FIGURE 1.

Study flow. Selection and classification of patients who underwent balloon aortic valvuloplasty (BAV) as bridge-to-decision. AVR= aortic valve replacement; LVEF= left ventricular ejection fraction; MVR= mitral valve regurgitation; TAVI=transcatheter aortic valve implantation.

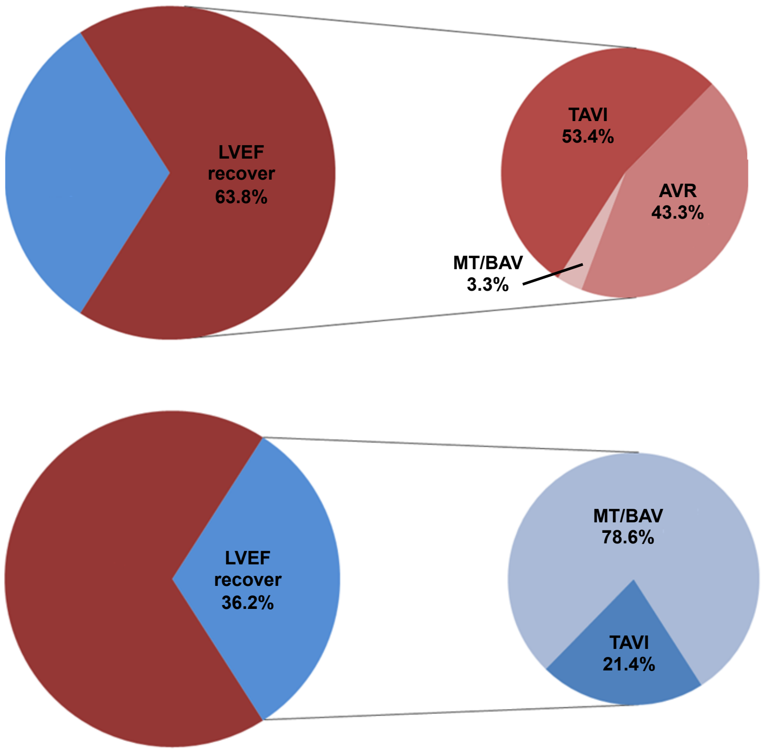


FIGURE 2.

Effect of bridge-to-decision balloon aortic valvuloplasty on decision making in patients with reduced left ventricular ejection fraction.

Proportion of patients with or without significant recover of left ventricular ejection fraction (LVEF) who were candidates for different definitive treatment of aortic stenosis after balloon aortic valvuloplasty. AVR= aortic valve replacement; MT/BAV= medical treatment/repeat balloon aortic valvuloplasty; TAVI=transcatheter aortic valve implantation

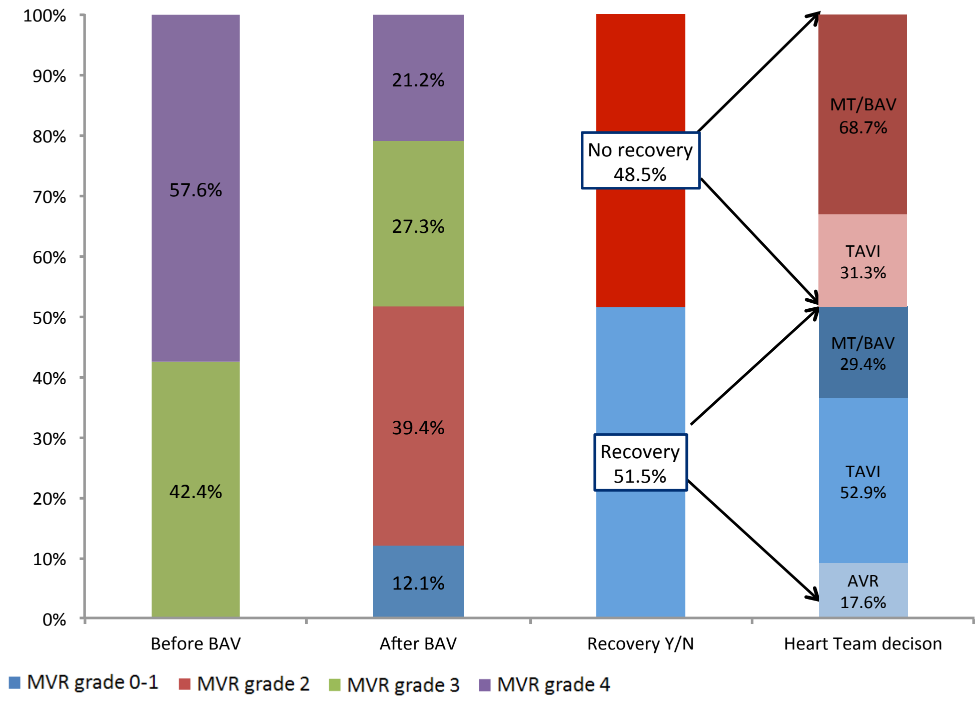


FIGURE 3.

Effect of bridge-to-decision balloon aortic valvuloplasty on decision making in patients with moderate to severe mitral valve regurgitation.

Changes in mitral valve regurgitation (MVR) grade after balloon aortic valvuloplasty and effect on final decision making by the heart team. AVR= aortic valve replacement; MT/BAV= medical treatment/repeat balloon aortic valvuloplasty; TAVI=transcatheter aortic valve implantation

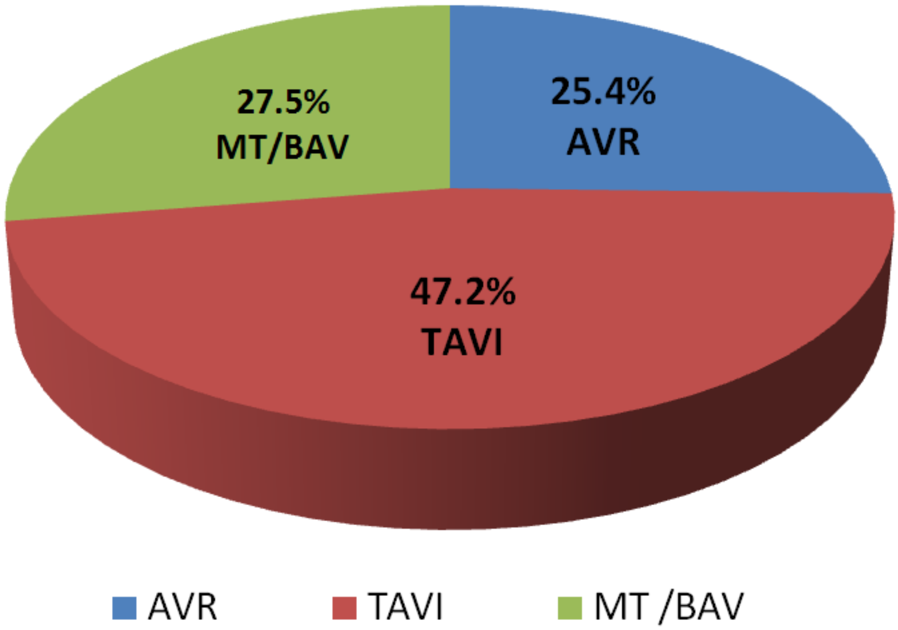


FIGURE 4.

Effect of bridge-to-decision balloon aortic valvuloplasty on decision making in the whole study population.

Outcome of the second heart team evaluation in patients who underwent bridge-to-balloon balloon aortic valvuloplasty. AVR= aortic valve replacement; MT/BAV= medical treatment/repeat balloon aortic valvuloplasty; TAVI=transcatheter aortic valve implantation.

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