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Optimal Balloon Size in Balloon Aortic Valvuloplasty: Results from a Retrospective Analysis of Multi-slice Computed Tomography

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Abstract Balloon aortic valvuloplasty (BAV) is a bridging therapy for surgical aortic valve replacement and transcatheter aortic valve implantation. Multi-slice computed tomography (MSCT) area-derived aortic annulus diameter was measured retrospectively to determine whether its use can improve the acute gain of aortic valve area compared to echo-derived annulus diameter during BAV. Patients with symptomatic severe aortic stenosis who underwent BAV following MSCT were included in the analyses. All patients underwent evaluations by transthoracic echocardiography before and after BAV. To assess aortic stenosis severity, peak transaortic valve velocity, mean pressure gradient, effective orifice area (EOA), and the Doppler velocity index (DVI) were measured. To assess post-BAV improvement, the ratios of the post-procedural parameters to the pre-procedural parameters, the acute gain ratios, were calculated. Twenty-two patients were analyzable for this study. EOA and DVI improved significantly post-BAV. The optimal cut-off value of the ratio of final balloon size to the MSCT area-derived diameter (B/AREAd) for an adequate DVI increase was >0.936. Frequency of patients with adequate DVI improvement was significantly higher in B/AREAd>0.936 group than that in B/AREAd≤0.936 group (88% vs 43%, p=0.04), with few showing worsening aortic regurgitation. Safe and effective BAV appears feasible using the B/AREAd cut-off value.

Key words: aortic stenosis, balloon aortic valvuloplasty, echocardiography, multi-slice computed tomography

Introduction

Balloon aortic valvuloplasty (BAV) has been used as a palliative strategy for high-risk patients with severe aortic stenosis (AS),[1] and it has been recognized as a bridging therapy for surgical aortic valve replacement.[1,2] In the transcatheter aortic valve implantation (TAVI) era, BAV has been performed as a bridging therapy for TAVI and as a diagnostic tool to assess therapeutic response by a significant reduction in the transaortic pressure gradient. In general, the aortic annulus diameter is measured by two-dimensional (2D) transthoracic echocardiography (TTE), and the balloon is sized up to a 1:1 ratio compared with the aortic annulus diameter.[2] Aggressive balloon dilatation may lead to larger acute gain, but the risk of aortic regurgitation (AR) and annulus rupture sometimes tends to increase. In our hospital, we have performed the BAV procedure using the step-up strategy (details are described in the methods section) up to the echo-derived

diameter without AR deterioration; therefore, there are several patients with an inadequate acute gain of aortic valve area (AVA). In the TAVI era, annulus area measured by multi-slice computed tomography (MSCT) has been used for optimal device sizing. It has been reported that 2D echo-derived annulus diameter is theoretically underestimated compared to the area-derived annulus diameter on MSCT images.[4] We hypothesized that a greater acute gain can be obtained safely with BAV when we determine the balloon size of BAV based on the area-derived annulus diameter by MSCT. Therefore, the MSCT area-derived annulus diameter was retrospectively measured, and whether it can lead to a greater acute gain of AVA compared to echo-derived annulus diameter during BAV was subsequently investigated.

Methods

Inclusion and exclusion criteria

Seventy-five patients with symptomatic severe AS who underwent BAV in our institution from December 2012 to March 2017 were included in the present study. Of the 75 patients, those who underwent MSCT to determine the area-derived diameter were finally included in the following analyses.

BAV procedure

The femoral vein was accessed and dilated with a 6-Fr dilator. The puncture site was pre-closed with a percutaneous suture closure device (Proglide, Abbott Corporation, Santa Clara, CA, USA), and a 25-cm, 14-Fr sheath (MEDIKIT catheter introducer kit, MEDIKIT, Tokyo, Japan) was placed. The suture knot was closed when the sheath was removed at completion of the procedure based on an established method. An 8-Fr Lamp 135° sheath (Mullins introducer set, Medtronic, Dublin, Ireland) was inserted into the left atrium (LA) via a transseptal approach. Two arterial accesses were obtained at the common femoral artery or upper limb arteries to insert a 25-cm, 4-Fr sheath for the placement of a 10-mm gooseneck snare catheter (Goose Neck™ Snare, COVIDIEN, Dublin, Ireland) and a pig-tail catheter above the aortic valve. Using this pig-tail catheter, aortic pressure was measured.

A 6-Fr Swan-Ganz catheter (Edwards Lifesciences Corporation, Irvine, CA, USA) was used to measure cardiac output by the thermodilution method. A 6-Fr end-hole wedge-balloon catheter (ARROW Wedge Pressure Catheters, Teleflex Medical Japan, Tokyo, Japan) was inserted through a Lamp catheter into the LA, across the mitral valve, and into the left ventricle (LV). The simultaneous pressure gradient (ΔP) was measured between the aorta and LV to calculate the mean transaortic valve pressure gradient (mean LV-Ao ΔP). AVA was calculated based on Gorlin's formula using mean LV-Ao ΔP and cardiac output. The tip of a 0.032˝ spring-tip guidewire (Toray Medical, Tokyo, Japan) was manually shaped, creating 4 to 5 coil turns with a radius of 5-10 mm, and it was used as a stylet to facilitate directing the inflated wedge-balloon catheter from the LV apex to the LV outflow. The tip of the wedge catheter was directed in the antegrade direction from the LV to the aorta, crossed by blood flow across the aortic valve, and it was further advanced into the aorta. A 0.032˝ extra-stiff wire (Cook Corporation, Bloomington, IN, USA) was inserted through the inner lumen of the wedge catheter, and its distal end was fixed using a gooseneck snare catheter in the descending aorta. Both the wedge catheter and Lamp sheath were removed, leaving the extra-stiff wire alone as an intracardiac wire loop. The Inoue balloon (Toray Medical) was inserted from the right femoral venous sheath into the right atrium and advanced over the wire loop across the aortic valve. The valvuloplasty was performed by applying multiple manual inflations (usually 5 times) with stepwise increases of balloon size, starting from the aortic annulus diameter measured by TTE minus 5 mm and ending up at the aortic annulus diameter. TTE evaluation for acute AR was performed after every size dilatation. When acute AR was significantly increased, no further dilatation was performed. After completion of valvuloplasty, the hemodynamic parameters (mean LV-Ao ΔP and AVA) were re-evaluated and compared with the baseline value.[5,6]

Echocardiography

All patients underwent comprehensive measurement by TTE before and after the BAV procedure based on the ASE/ESE guideline.[7] To assess the severity of AS, peak transaortic valve velocity, mean pressure gradient, effective orifice area (EOA), and the Doppler velocity index (DVI) were measured.[6] DVI <0.25 was defined as severe AS.[7] For assessment of improvement after BAV, the ratio of the post-procedural parameters to the pre-procedural parameters, the "acute gain ratio," was calculated.

Aortic annulus diameter between the hinge points of the cusps was measured on the parasternal long axis view on preprocedural TTE images.[8] The ratio of the final balloon size to the aortic annulus diameter measured by TTE was defined as "B/TTEd." To assess the severity of AR and to evaluate the change between pre- and post-procedure, the distribution of the regurgitant jet into the LV (I, II, III, and IV)[9] was evaluated before and after the BAV procedure.

Measurement on MSCT

The area-derived annulus diameter and minimum/maximum annulus diameter were measured using dedicated software[10,11] (3 Mensio Structural Heart, 3 Mensio Imaging BV, Bilthoven, The Netherlands). On the 3-dimensional reconstructed MSCT images, the annular plane was defined as the plane connecting the nadirs of 3 cusps, and the annulus area was measured in mid-systole. Each diameter was calculated. The ratio of the final balloon size to the area-derived diameter measured by MSCT was defined as "B/AREAd," and the minimum diameter was defined as "B/MINd."

Statistical analysis

Continuous data are presented as means ± standard deviation (SD) if normally distributed, or as medians and interquartile ranges (IQRs) if not normally distributed. Continuous variables were assessed by Student's *t*-test. Paired tests were analyzed by the paired *t*-test

Categorical variables are presented as numbers and percentages, and they were tested using the chi-squared test. In addition, receiver operating characteristic (ROC) analysis was performed to identify the optimal cut-off of B/AREAd for a post-procedural DVI to pre-procedural DVI ratio of 1.3. All analyses were done using JMP software (version 13, JMP Pro, SAS Institute Japan, Tokyo, Japan). All statistical tests were two-sided, and a p-value <0.05 was considered significant.

Results

Study population

Of the 75 patients who underwent BAV, 66 underwent BAV with the trans-atrial septum approach (antegrade approach), and 9 patients underwent BAV with the trans-aortic valve approach (retrograde approach). Of the 66 patients who underwent the antegrade approach, 24 (33.3%) underwent pre-procedural MSCT to evaluate aortic root anatomy. Two of the 24 patients were excluded due to non-analyzability of EOA; thus, 22 patients were defined as analyzable for this study, and their profile is shown in Figure 1. Baseline characteristics and pre-procedural echocardiographic parameters are tabulated in Table 1.

Post-procedural evaluation

After the BAV procedure, post-procedural EOA and DVI improved significantly compared to the pre-procedural values [EOA (cm^2) 0.55 ± 0.11 vs. 0.80 ± 0.20, p<0.001; DVI 0.20 ± 0.06 vs. 0.27 ± 0.12, p<0.001; pre- vs. post-, respectively)].

Figure 2 shows the relationship between post-procedural EOA and DVI. There was only a weak correlation between the two parameters (R=0.46, p=0.03), possibly because there was greater variability in EOA measurement than in DVI measurement. Therefore, in this study, DVI was chosen as a procedural performance index, because of its lesser variability.

Although it was arbitrary, this population was divided based on the median value of the acute gain ratio of DVI (1.3). Subsequently, these two groups were defined as: one group whose acute gain ratio was >1.3, which was defined as the "improvement group"; and the other group whose acute gain ratio was ≤1.3, which was defined as the "non-improvement group."

Table 2 shows the differences in B/AREAd,

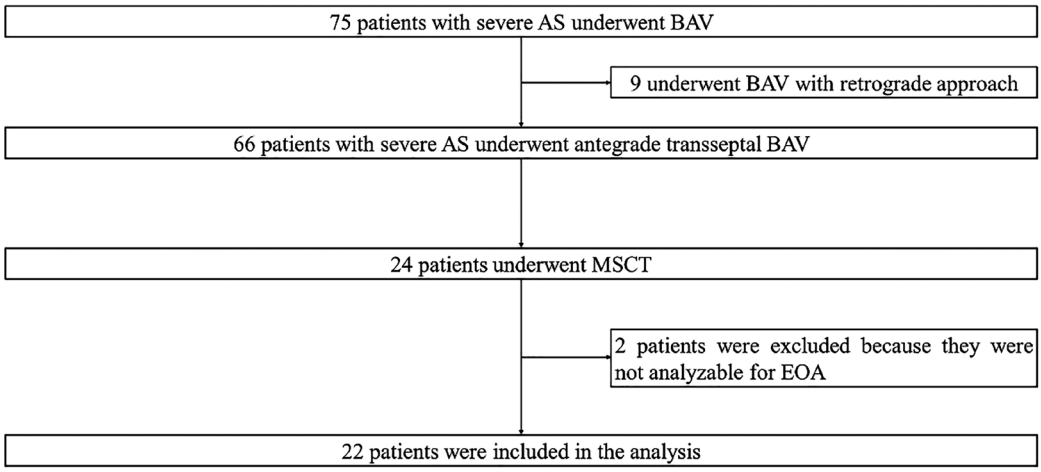

Fig. 1 Study profile
AS = aortic stenosis, BAV = balloon aortic valvuloplasty, MSCT = multi-slice computed tomography, EOA = Effective orifice area

Table 1 Patients' baseline characteristics

Variable	Mean ± SD or Number (%)
Number of patients	22
Age, years	85 ± 5
Male sex	7 (32)
Body surface area, m^2	1.42 ± 0.17
Hypertension	18 (82)
Diabetes mellitus	7 (32)
Dyslipidemia	8 (36)
Chronic kidney disease	8 (36)
NYHA grade	
I	4 (18)
II	14 (64)
III	1 (5)
IV	3 (14)
EuroSCORE II	4.9 (4.0 - 5.4)
STS PROM	7.0 ± 2.9
Left ventricular diastolic dimension, mm	45.9 ± 5.9
Left ventricular ejection fraction, %	59.2 ± 13.3
Transaortic peak valve velocity, m/s	5.0 ± 0.8
Transaortic mean pressure gradient, mmHg	54.0 (46.8 - 73.5)
Effective orifice area, cm^2	0.55 ± 0.11
Doppler velocity index	0.20 ± 0.06
Aortic annulus diameter, mm	20.5 ± 1.5
Pre-procedural AR	
None	1 (5)
I	13 (59)
II	8 (36)
III	0 (0)
IV	0 (0)

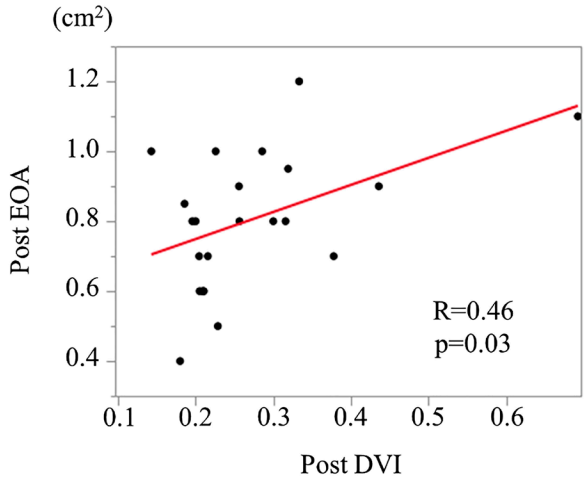

Fig. 2 The correlation between post-procedural EOA and DVI
There was only a weak correlation between post-procedural EOA and DVI (R=0.46, p=0.03). EOA = Effective orifice area, DVI = Doppler velocity index

Table 2 Differences in B/AREAd, B/MINd and B/TTEd between the improvement and non-improvement groups

Variable	Improvement group	Non-improvement group	p-value
B/AREAd	0.92 ± 0.04	0.89 ± 0.05	0.1608
B/MINd	1.06 ± 0.10	1.04 ± 0.07	0.6201
B/TTEd	1.01 ± 0.06	1.02 ± 0.08	0.7322

B/MINd, and B/TTEd between the improvement and non-improvement groups. In B/MINd and B/TTEd, there were no significant differences between the two groups, while B/AREAd tended to be larger in the improvement group than in the non-improvement group (0.92 ± 0.04 vs 0.89 ± 0.05, p=0.16). ROC curve analysis was performed to identify the optimal cut-off value of B/AREAd defined using Youden index for an acute gain ratio>1.3, and B/AREAd>0.936 (AUC 0.684, p=0.20, sensitivity 0.54, specificity 0.89, Fig. 3) was identified. Table 3 shows the baseline characteristics and echocardiographic parameters with patients divided into the two groups based on B/AREAd 0.936.

Based on this cut-off value, 6 patients with B/AREAd≤0.936 were included in the improvement group (6/14, 43%), with two showing worsening of AR after BAV (2/6, 33%), while 7 patients with B/AREAd>0.936 were included in the improvement group (7/8, 88%), with only two showing worsening of AR after BAV (2/7, 28%) (Fig. 4). There was no significant difference between two groups in the ratio of worsening AR (p=0.85). Although post procedural DVI tended to be numerically better in patients with B/AREAd>0.936 than in patients with B/AREAd≤0.936 (0.33 ± 0.17 vs. 0.24 ± 0.06, p=0.06), a frequency of the improvement group in B/AREAd>0.936 was significantly greater than that in B/AREA≤0.936 (88% vs 43%, p=0.04).

Discussion

The main findings of this study were that: 1) after a BAV procedure, post-procedural EOA and DVI improved significantly; 2) there was only a weak correlation between post-procedural EOA and DVI; 3) the optimal cut-off value of B/AREAd for an adequate increase of DVI (acute gain ratio>1.3) was B/AREAd>0.936; and 4) patients with B/AREAd>0.936 tended, though not significantly, to obtain greater DVI, with few showing

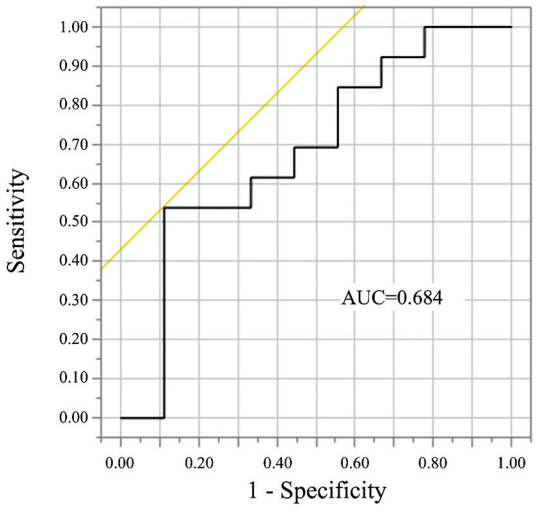

Fig. 3 Receiver operating curve analysis for B/AREAd to predict acute gain ratio>1.3
ROC curve analysis was performed to identify the optimal cut-off value of B/AREAd defined using Youden index for an acute gain ratio>1.3, and B/AREAd>0.936 (AUC 0.684, p=0.20, sensitivity 0.54, specificity 0.89).

Table 3 Baseline and echocardiographic characteristics with the patients divided into 2 groups based on B/AREAd 0.936

Variable	B/AREAd>0.936	B/AREAd≤0.936	p-value
Number of patients	8	14	
Age, years	83 ± 2	85 ± 1	0.37
Male sex, n (%)	6 (75)	9 (64)	0.60
Body surface area, m^2	1.40 ± 0.06	1.44 ± 0.05	0.62
Hypertension, n (%)	7 (88)	11 (79)	0.60
Diabetes mellitus, n (%)	3 (38)	4 (29)	0.67
Dyslipidemia, n (%)	5 (63)	3 (21)	0.05
Chronic kidney disease, n (%)	4 (50)	4 (29)	0.31
NYHA grade, n (%)			0.82
I	2 (25)	2 (14)	
II	5 (63)	9 (64)	
III	0 (0)	1 (7)	
IV	1 (13)	2 (14)	
EuroSCORE II	5.0 (3.5 - 6.5)	4.8 (4.1 - 5.4)	0.97
STS PROM	8.2 ± 1.0	6.3 ± 0.7	0.15
LVDd, mm	45.8 ± 2.1	46.0 ± 1.6	0.93
LVEF, %	61.3 ± 4.8	58.0 ± 3.6	0.58
Transaortic peak valve velocity, m/s	5.2 (4.3 − 5.5)	4.7 (4.5 - 5.4)	0.71
Transaortic mean PG, mmHg	53.5 (44.5 − 74.5)	54.0 (46.8 - 73.5)	1.00
Effective orifice area, cm^2	0.53 ± 0.04	0.55 ± 0.03	0.66
Doppler velocity index	0.22 ± 0.02	0.18 ± 0.02	0.16
Aortic annulus diameter, mm	21.1 ± 0.5	20.1 ± 0.4	0.14
Pre-procedural AR, n (%)			0.74
None	0 (0)	1 (7)	
I	5 (63)	8 (57)	
II	3 (38)	5 (36)	
III	0 (0)	0 (0)	
IV	0 (0)	0 (0)	

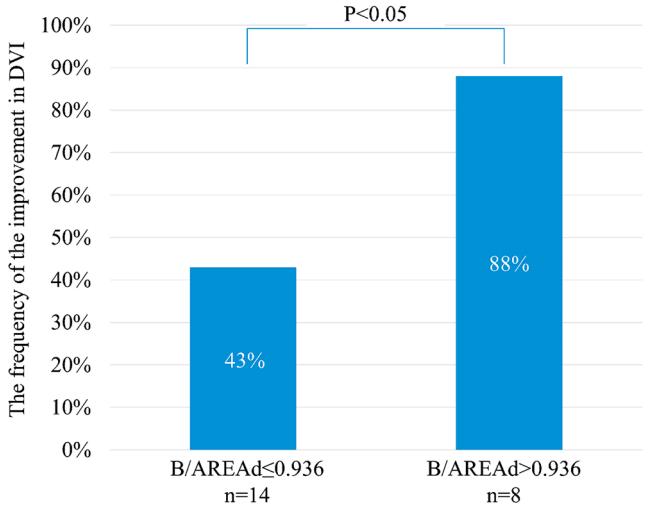

Fig. 4 The difference in the frequency of the improvement group between B/AREAd>0.936 and B/AREAd≤0.936
The frequency of the improvement group in B/AREAd>0.936 was significantly greater than that in B/AREA≤0.936. DVI = Doppler velocity index

worsening AR.

In the literature, it has been recommended that the goal of BAV has been a reduction in mean pressure gradient of 50 mmHg or 40-50% of the original gradient.[2] To consistently achieve such a large reduction in transaortic pressure gradient, extremely aggressive dilatation is sometimes needed. BAV was performed more aggressively in Europe and the USA, where TAVI was introduced in the early stage compared with Japan. Bail-out TAVI could be performed even if hemodynamic collapse occurred due to acute AR during the BAV procedure. However, there was a large time lag in the introduction of TAVI between Japan and Europe/USA. Moreover, in Japan, there are hospitals in which TAVI cannot be performed. During the study period, TAVI was not available in our institute. Therefore, the BAV procedure was performed using the step-up strategy to echo-derived diameter using an Inoue balloon via a transatrial septum approach (antegrade approach), and the procedure was finished whether or not a significant reduction of mean pressure gradient was obtained. Based on this concept, the safety index of balloon size was explored to avoid fatal complications in the BAV procedure.

The present study showed that the median value of the acute gain was 0.23 cm^2 for EOA and 0.06 for DVI. A narrative review[2] showed that the median and IQR of the acute gain of EOA was 0.30 (0.28-0.40) in the pre-TAVI era, while it was 0.34 (0.21-0.43) in the TAVI era. In further detail, smaller (<0.30 cm^2) or larger (>0.30 cm^2) acute gain of EOA was found in the TAVI era, suggesting a difference in the concept of BAV. Our strategy seems to be less aggressive compared to the reported results, but it is closer to the result of the pre-TAVI era than that of the TAVI era. Our concept of the BAV procedure might be similar to that prior to TAVI introduction in Europe. The result of the present study is comparable to the results of previous papers without aggressive dilatation.

Based on less aggressive dilatation in terms of safety, a cut-off value of the final balloon size/CT area-derived diameter (B/AREAd>0.936) was identified in the present study. Of the 8 patients with B/AREAd>0.936, 7 (88%) achieved adequate increases of DVI after the BAV procedure, with few showing worsening of AR (Fig. 5). Only one patient did not achieve an adequate increase of DVI (pre-procedure 0.19 vs. pre-discharge 0.21, acute DVI gain ratio = 1.11) despite satisfying the cut-off value of B/AREAd>0.936. During the BAV procedure,

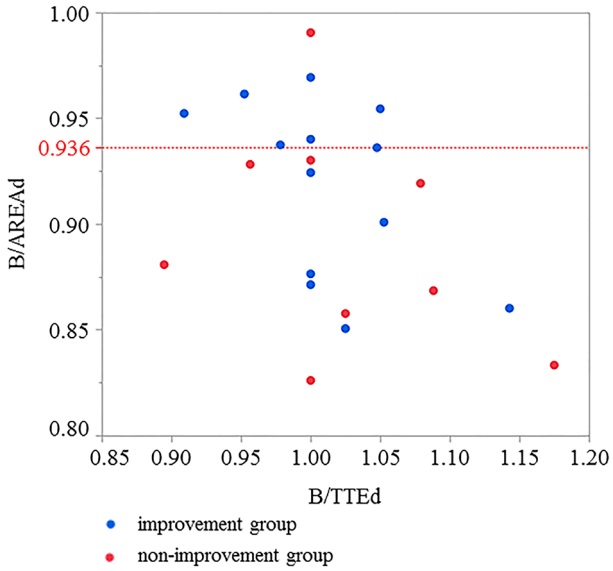

Fig. 5 Plot of B/TTEd against B/AREAd in 22 patients
Blue plots show the improvement group, and red plots shows the non-improvement group.

this patient had adequate improvement of the mean pressure gradient from 43 to 19 mmHg and an increase of left ventricular ejection fraction from 35% to 40%. The improvement of DVI was probably lost due to acute restenosis.

An aggressive strategy may lead to a large acute gain of EOA, but it may also lead to procedural complications, such as acute AR and annulus rupture. BAV with B/AREAd>0.936 would ensure safety and efficacy for patients who are not suitable for TAVI and/or in institutions where TAVI is not available.

Limitations

The present study was based on a retrospective data analysis of a small number of subjects who underwent BAV via the trans-atrial septum approach using an Inoue balloon in a single center. This small number might limit the interpretation of the study findings and could not lead to a significant p value in logistic regression analysis to identify the optimal cut-off of B/AREAd. The impact of this cut-off value on the clinical outcome was not assessed in the present study. Moreover, this study did not include patients who underwent retrograde BAV using conventional balloons. Therefore, further investigations are needed to clarify the usefulness of this cut-off value of B/AREAd >0.936.

Conclusions

Safe and effective BAV would be feasible using the cut-off value based on the ratio of the final balloon size to MSCT area-derived diameter.

Conflict of Interest

The authors declare no conflict of interest.

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