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ORIGINAL ARTICLE

Impact of different degrees of computed tomography-based oversizing on clinical outcomes after transcatheter aortic valve implantation using the Portico system

Farklı derecelerde bilgisayarlı tomografi tabanlı büyük boyutlandırmanın Portico sistemi kullanarak transkateter aort kapak implantasyonu sonrası klinik sonuçlar üzerine etkisi

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ABSTRACT

Objective: This study aimed to evaluate the influence of different degrees of multidetector computed tomography (MDCT)-based perimeter oversizing on the incidence and severity of paravalvular aortic regurgitation (PAR) and conduction disturbances (CD) for the Portico device.

Methods: We retrospectively analyzed 63 patients who underwent transcatheter aortic implantation (TAVI) in our center from March 2017 to June 2019. The patients were divided into 2 groups (group I, below 13.9%; group II, above 13.9%) according to the degree of oversizing. Oversizing was calculated using the formula (device nominal perimeter/MDCT-derived annular perimeter-1)×100. Procedural and clinical data were evaluated using the valve academic research consortium definitions.

Results: Mild or moderate PAR was present in 76.4% of the patients in group I and 34.4% of the patients in group II (p=0.009). The rate of CD tended to be lower in the group I (p=0.034). A cutoff value of 13.9% was identified as the best predictive value for mild or moderate PAR. Multivariate analysis identified a lower percentage of oversizing (odds ratio 6.38; 95% confidence interval 2.00-20.33; p=0.002) as the most powerful independent predictor of PAR, whereas the implantation depth and severe oversizing were independent predictors of CD (p=0.003 and p=0.029, respectively). We demonstrated that the optimal acceptable perimeter-based oversizing range was between 10% and 15%.

Conclusion: Perimeter-based oversizing by MDCT inversely correlated with PAR after TAVI for the Portico device, and its preoperative evaluation could help in predicting PAR and CD.

ÖZET

Amaç: Çalışmanın amacı, Portico cihazı için paravalvüler aort yetersizliği (PAY) ve iletim bozukluklarının (İB) insidansı ve şiddetine çok dedektörlü bilgisayarlı tomografi (ÇDBT) ile üretilen çevre tabanlı 'oversizing' yüzdesinin etkisini değerlendirmektir.

Yöntemler: Mart 2017-Haziran 2019 tarihleri arasında merkezimizde transkateter aort kapak implantasyonu (TAKİ) uygulanan 63 hastayı retrospektif olarak inceledik. Hastalar 'oversizing' yüzdesine göre iki gruba ayrıldı (grup I, %13.9'un altında; grup II, %13.9'un üzerinde). 'Oversizing' (Cihaz nominal çevresi/ÇDBT'den türetilen dairesel çevre-1) * 100 olarak hesaplandı. Prosedür ve klinik veriler VARC-2 tanımlarıyla değerlendirildi.

Bulgular: Grup I'de ki hastaların %76.4'ünde ve II. Gruptaki hastaların %34.4'ünde hafif veya orta PAY mevcuttu (p=0.009). İB oranı hasta grubu I'de daha düşük olma eğilimindeydi (p=0.034). %13.9'luk bir kesme değerinin, hafif veya daha yüksek PAY için en iyi prediktif değere sahip olduğu belirlenmiştir. Çok değişkenli analizde, daha düşük 'oversizing' yüzdesi (odds oranı 6.38; %95 güven aralığı 2.00-20.33; p=0.002) PAY'ın en güçlü bağımsız öngörücüsü olarak ortaya çıkarken, implantasyon derinliği ve yüksek 'oversizing' yüzdesi İB'nin bağımsız göstergeleriydi (p=0.003 ve p=0.029, sırasıyla). Optimal kabul edilebilir çevre temelli büyük boy aralığının %10-15 arasında olduğunu gösterdik.

Sonuç: MDCT tarafından üretilen çevre temelli 'oversizing', Portico cihazı için TAKİ sonrası PAY ile ters korelasyon gösterdi ve preoperatif değerlendirilmesi PAY ve İB'in öngörülmesine yardımcı olabilir.

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Transcatheter aortic valve implantation (TAVI) is an alternative therapy for patients with valvular aortic stenosis (AS) who may be deemed intermediate- and high-risk for treatment with conventional surgical approaches.[1, 2] Despite a continuous improvement in TAVI technology, inappropriate device sizing may result in adverse outcomes such as mild-to-moderate paravalvular aortic regurgitation (PAR) or aortic annular rupture if an undersized device is used, and conduction disturbances (CD) if a severely oversized device is used.[3-5] To overcome these issues, the correct selection of prosthesis size is a crucial step for TAVI. The appropriate degree of oversizing based on aortic annulus measurements derived from multidetector computed tomography (MDCT) may help to reduce the implant-related risks attributable to severe oversizing while enabling exertion of control on PAR.

Previous studies have highlighted that the lower oversizing can lead to the occurrence of PAR, and conversely, severe oversizing can increase the rate of new permanent pacemaker (PPM) implantation.[6-8] Binder et al. [6] have established the best risk-benefit ratio, correlating oversizing with the occurrence of PAR and CD for Sapien XT. In another study with CoreValve, an insufficient oversizing under 11% significantly increased the incidence of PAR.[7] It is well recognized that sizing algorithms are device-specific, and improvements and different algorithms are necessary for sizing.

To the best of our knowledge, the benefit of oversizing strategies to prevent adverse clinical outcomes of TAVI with the Portico valve has not been discussed thus far. We aimed to evaluate the impact of different levels of oversizing on the post-procedural outcomes and the optimum device/annulus oversizing ratio that ensures the best risk-benefit ratio to reduce PAR and CD.

METHODS

Study population and data collection

This study included 63 patients who underwent transfemoral TAVI with Portico™ (Abbott Vascular, Santa Clara, CA, USA) in our institution between March 2017 and June 2019 owing to severe AS. Patients deemed intermediate- or high-risk according to the Society of Thoracic Surgery (STS) score or who were deemed inoperable had been refused for subjection to conventional surgery by a multidisciplinary heart team consisting of cardiologists and cardiothoracic surgeons. Study patients were included only if they underwent both pre-procedural MDCT and post-procedural transthoracic echocardiography (TTE). The exclusion criteria included patients who presented with a previous history of PPM and the presence of a bicuspid aortic valve. Clinical data, operative outcomes, and 1-year follow-up data according to the valve academic research consortium (VARC) 2 recommendations,[9] were retrospectively obtained from our institutional database. Baseline, immediate post-op, and pre-discharge electrocardiograms (ECGs) were retrospectively analyzed by an investigator, blinded to the clinical data for the presence of CD according to the American College of Cardiology guidelines.[10] Implant-related new or worsened CD cases were determined as new-onset LBBB along with high-degree atrioventricular (AV) block (defined as third-degree AV block or Mobitz type II second-degree AV block), and the need for PPM within 30 days after TAVI was assessed. The ethics committee of our institute approved the protocols of this study. Ethics committee approval was received for this study from the University of Health Sciences İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital (Approval Date: November 26, 2019; Approval Number: #2019-76). The study protocol conformed to the ethical guidelines of the Declaration of Helsinki.

Abbreviations:

AKI	*Acute kidney injury*
AS	*Aortic stenosis*
AV	*Atrioventricular*
CD	*Conduction disturbances*
CI	*Confidence interval*
ECGs	*Electrocardiograms*
LVOT	*Left ventricular outflow tract*
MDCT	*Multidetector computed tomography*
MI	*Myocardial infarction*
OR	*Odds ratio*
PAR	*Paravalvular aortic regurgitation*
PPM	*Permanent pacemaker*
STS	*Society of Thoracic Surgery*
TAVI	*Transcatheter aortic valve implantation*
THV	*Transcatheter heart valves*
TTE	*Transthoracic echocardiography*
VARC	*Valve academic research consortium*

MDCT image analysis

All patients were subjected to scanning using a second-generation 320-row MDCT scanner (Aquilion ONE Vision Edition, Toshiba Medical Systems, Otawara, Japan). All MDCT examinations were re-

viewed by 2 experienced cardiac MDCT readers. The aortic annulus was defined as the virtual plane containing the basal attachment of the 3 aortic valve leaflets on a double-oblique transverse view. Planimetry yielded luminal area, perimeter, maximum and minimum diameters. Other parameters including measurements of left ventricular outflow tract (LVOT), distance from annulus to coronary ostia, the sinus of Valsalva, and ascending aorta diameter were assessed. A semi-quantitative model was performed to analyze the calcification of the annulus as per previously described methods.[11] The eccentricity index was calculated based on MDCT annulus measurements as 1-(minimum diameter/maximum diameter).[12] The 23-, 25-, 27-, and 29-mm Portico transcatheter heart valves (THV) have nominal areas of 415.2, 490.6, 572.2, and 660.1 mm^2 and perimeters of 72.2, 78.5, 84.7, and 91.0 mm, respectively. The percentage of oversizing was calculated as: (THV nominal perimeter/MDCT annulus perimeter-1)×100.[13]

TAVI procedure and valve selection

All TAVI procedures were conducted via a transfemoral approach and under conscious sedation in a fully equipped operating room. In all patients, TAVI implantation technique for the Portico valve was performed as per previously described methods.[14] Initially, balloon valvuloplasty was performed in all patients for preparation of the valve landing zone and deployment of the THV without rapid pacing. Post-dilatation under rapid pacing was considered if remaining moderate or severe PAR and/or THV was observed under expansion. A final control was performed by aortography. The percutaneous closure system (Perclose ProGlide; Abbott laboratories, Abbott Park, Illinois) was used to close the vascular access site. Implantation depth was determined fluoroscopically as per previously described protocols.[12] The appropriate valve size was selected from the 4 available sizes (23, 25, 27, and 29 mm) covering an aortic annulus diameter between 19 and 27 mm based on MDCT according to the manufacturer's instructions.[14]

Study endpoints

The intraoperative and postoperative outcomes and clinical endpoints were defined according to the standardized criteria proposed by VARC-2. The following major intraoperative outcomes were recorded: procedural mortality, conversion to surgery, coronary obstruction, malposition of the Portico device, second THV implantation, annular rupture, cardiac tamponade, and perioperative infarction. Clinical outcomes assessed at the end of 1 year included all-cause death, cardiovascular mortality, myocardial infarction (MI), acute kidney injury (AKI), cerebrovascular events, the occurrence of CD, and new PPM. Post-TAVI bioprosthetic functions, including device success and PAR were assessed in all patients at the 30-day follow-up visit. For the assessment of PAR, TTE examinations were performed by an experienced cardiologist with echocardiography training who was blinded to clinical and procedural parameters. PAR was graded in line with the guidelines prescribed by VARC-2 in all patients.[9]

Statistical analysis

Statistical analysis of the study was performed using the Statistical Package for Social Sciences version 24.0 program (IBM Corp.; Armonk, NY, USA). Variables showing normal distribution were evaluated using graphical (histograms, probability curves) and numerical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). Continuous variables were expressed as mean (SD) or as median (interquartile range) if not exhibiting normal distribution. Categorical variables were presented as frequency and percentage. The patients were categorized into 2 groups depending on the degree of perimeter-derived oversizing percentage determined by receiver operating characteristic curve (ROC) analysis in the following groups: below 13.9% and above 13.9%. For comparison of continuous variables, the Student's t-test or Mann-Whitney U test was used as appropriate. Categorical variables were analyzed using the chi-squared or Fisher's exact tests. The ROC curve analysis and Youden index (max [sensitivity+selectivity-1]) were used to determine the cutoff value of oversizing percentage for predicting CD and mild or moderate PAR. Univariate logistic regression analyses were performed primarily to determine the independent variables that could be used to predict patients with PAR and CD. Variables with a p-value <0.1 in univariate analysis were evaluated via multivariate analysis. The 95% confidence interval (CI) was used to estimate the precision of the odds ratio (OR) in each model. Statistical significance was considered at a p-value <0.05.

RESULTS

Study population

The study included 63 patients with severe AS treated using a Portico valve. The mean age of the study cohort was 80.2±6.7 years, 38.1% were men, and the median STS score was 8.4 (6.5-10.3). Except for basal creatinine levels, there was no significant difference in clinical or demographic baseline characteristics. The baseline demographic, clinical, and echocardiographic characteristics of the study population are presented in Table 1.

Multidetector computed tomography findings

MDCT-derived measurements stratified by the extent of oversizing have been shown in Table 2. The degree of oversizing differed significantly between groups I and II and was 10.2% (7.2-12.6) and 15.71% (14.83-17.79), p<0.001, respectively. The mean eccentricity ratio was 0.22 (0.19-0.25) and did not vary between the groups. There were no differences in the severity of annular calcification between the groups, which was evaluated semi-quantitatively. No relevant differences were observed for the other MDCT parameters.

Procedural data and outcomes

The TAVI procedures were usually performed under conscious sedation by utilizing the transfemoral approach. Post dilatation was performed in 47.6% of the patients. No differences in TAVI approach, conscious sedation, and balloon post dilatation were observed between both the groups. Device success, defined by the guidelines prescribed by VARC-2, was achieved in 93.7% with comparable outcomes in both the groups (91.2 vs. 96.6, p=0.383). Detailed procedural data and clinical outcome data according to the VARC-2 criteria are summarized in Table 3. A single

Table 1. Major baseline and clinical parameters

Group		I	II	
Perimeter-based oversizing	All N=63	<13.9 N=34	≥13.9 N=29	*p*
Age (years)	80.2±6.7	81.2±6.8	79.5±6.5	0.210
Sex (male)	24 (38.1)	15 (44.1)	9 (31.0)	0.287
STS risk score	8.4 (6.5-10.3)	8.7 (6.5-11.8)	8.3 (5.7-10.0)	0.444
Coronary artery disease	46 (73.0)	26 (76.5)	20 (69.0)	0.504
COPD	25 (39.7)	12 (35.3)	13 (44.8)	0.441
Diabetes mellitus	24 (38.1)	11 (32.4)	13 (44.8)	0.310
Renal failure	19 (30.2)	13 (38.2)	6 (20.7)	0.130
Hypertension	39 (61.9)	19 (55.9)	20 (69.0)	0.287
Prior CABG	13 (20.6)	5 (14.7)	8 (27.6)	0.208
Pulmonary hypertension	23 (36.5)	14 (41.2)	9 (31.0)	0.405
Peripheral vascular disease	18 (28.6)	10 (29.4)	8 (27.6)	0.873
Atrial fibrillation	16 (25.4)	9 (26.5)	7 (24.1)	0.832
Creatinine	1.0 (0.8-1.3)	1.1 (0.9-1.3)	0.9 (0.7-1.2)	0.033
Echocardiographic data				
LVEF (%)	60 (50-60)	56 (47-60)	60 (57-65)	0.058
Aortic valve area (cm^2)	0.75±0.14	0.74±0.14	0.76±0.13	0.578
Maximum aortic transvalvular velocity (m/s)	4.34±0.42	4.34±0.38	4.35±0.47	0.926
Maximum aortic transvalvular gradient (mm Hg)	75.6±15.3	73.7±15.5	78.0±15.1	0.273
Mean aortic transvalvular gradient (mm Hg)	47.7±11.1	46.1±10.2	49.7±12.0	0.205

Values represent mean±SD, n (%) or median (interquartile range).
CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction, STS: the Society of Thoracic Surgeons, SD: standard deviation.

Table 2. MDCT dimensions for all patients and implanted valve size

Group		I	II	
Perimeter-based oversizing	All N=63	<13.9 N=34	≥13.9 N=29	*p*
Device-annular sizing ratio (%)	13.7 (9.7-15.7)	10.2 (7.2-12.6)	15.71 (14.83-17.79)	<0.001
Membranous septum length (mm)	7.61±0.99	7.64±0.97	7.58±1.04	0.826
Annulus perimeter (mm)	76.9±5.7	78.7±6.1	74.7±4.4	0.004
Virtual diameter (perimeter-derived) (mm)	24.5±1.8	25.1±1.9	23.8±1.4	0.004
Minimum annulus size (mm)	21.2±1.8	21.5±1.9	20.7±1.5	0.060
Maximum annulus size (mm)	27.3±1.9	28.0±1.9	26.6±1.7	0.002
Mean annulus size (mm)	24.2±1.7	24.8±1.7	23.6±1.4	0.006
Eccentricity ratio	0.22 (0.19-0.25)	0.22 (0.19-0.26)	0.23 (0.18-0.25)	0.793
Annulus calcification				
0	27 (42.9)	14 (41.2)	13 (44.8)	0.365
1	22 (34.9)	10 (29.4)	12 (41.4)	
2	12 (19.0)	8 (23.5)	4 (13.8)	
3	2 (3.2)	2 (5.9)	0 (0.0)	
Height right coronary ostium (mm)	18.1±2.6	18.4±3.0	17.8±2.1	0.301
Height left coronary ostium (mm)	13.7±2.6	13.8±3.0	13.6±2.2	0.778
Mean diameter of the sinus of Valsalva (mm)	31.2±2.3	31.4±2.6	31.0±2.0	0.451
Mean height of the sinus of Valsalva (mm)	21.9 (3.0)	22.0 (3.1)	21.7 (2.8)	0.654
Ascending aorta (mm)	35.2±3.4	34.9±3.7	35.4±3.0	0.575
Bioprosthesis diameter (mm)	27.5±1.7	27.4±1.9	27.8±1.6	0.358
Bioprosthesis perimeter (mm)	86.4±5.4	85.8±5.9	87.1±4.9	0.358
Implantation depth (mm)	7.90±1.97	7.89±1.61	7.92±2.35	0.942

Values represent mean±SD, n (%) or median (interquartile range).
MDCT: multidetector computed tomography; SD: standard deviation.

procedure-related death occurred associated with the device migration requiring a second valve in group I. A total of 4 (6.3%) patients received more than 1 THV during the index procedure because of device migration (n=2) or owing to the existence of more than moderate PAR (n=2). In the remaining patients, the valve was observed to be in a proper position. There were 2 (5.9%) post-procedural deaths in group I and 1 (3.4%) death in group II. In group I, 1 of the 2 deaths was caused by heart failure which ended in hemodynamic instability and finally resulted in the death of the patient. Another death occurred owing to cardiac tamponade caused by right ventricular perforation related to temporary transvenous pacing wire 2 days after TAVI. In group II, the cause of death was sepsis-related complications. With the exception CD and PAR, no other differences were observed between the groups in terms of 1-year mortality or other major complications.

Postprocedural PPM implantation was indicated in 19.0% of the patients with similar frequency in groups I and II. Third-degree AV block was the most frequent indication (n=7) for PPM implantation; other indications were second-degree AV block (n=1), bradycardia (<40 beats per minute) resulting in hemodynamic instability or requiring therapy (n=2), and first-degree AV block with LBBB (n=2). The most frequent CD after TAVI was determined to be new-onset LBBB (21/63, 33.3%). There were more patients with new-onset LBBB in group II (41.4%) than in group I (26.5%). The difference, however, was not significant, probably owing to the small sample size of the study population. The rate of CD was 47.6% in the total patient cohort. In group II, the rate

Table 3. Association with annular sizing ratio and procedural and clinical outcomes

Group Perimeter-based oversizing	All N=63	I <13.9 N=34	II ≥13.9 N=29	*p*
Procedural outcomes				
Conscious sedation	60 (95.2)	32 (94.1)	28 (96.6)	0.651
Balloon post-dilatation	30 (47.6)	19 (55.9)	11 (37.9)	0.155
Device success	59 (93.7)	31 (91.2)	28 (96.6)	0.383
Intra-procedural mortality	1 (1.6)	1 (2.9)	0 (0.0)	1.000
Valve migration	2 (3.2)	2 (5.9)	0 (0.0)	0.495
Coronary obstruction	0 (0.0)	0 (0.0)	0 (0.0)	-
TAV-in-TAV deployment	4 (6.3)	3 (8.8)	1 (3.4)	0.618
Conversion to open surgery	0 (0.0)	0 (0.0)	0 (0.0)	-
Cardiac tamponade	2 (3.2)	1 (2.9)	1 (3.4)	1.000
Annular rupture	0 (0.0)	0 (0.0)	0 (0.0)	-
Clinical outcomes				
All cause 30-day mortality	4 (6.3)	3 (8.8)	1 (3.4)	0.618
Stroke	2 (3.2)	1 (2.9)	1 (3.4)	1.000
Perioperative infarction	0 (0.0)	0 (0.0)	0 (0.0)	-
Conduction disturbances	30 (47.6)	12 (35.3)	18 (62.1)	0.034
New-onset LBBB	21 (33.3)	9 (26.5)	12 (41.4)	0.211
Permanent pacemaker	12 (19.0)	7 (20.6)	5 (17.2)	0.736
Frequency of PAR				0.009
None-trivial	27 (42.9)	8 (23.6)	19 (65.5)	
Mild	25 (39.6)	18 (52.9)	7 (24.2)	
Moderate	11 (17.5)	8 (23.5)	3 (10.3)	
Severe	0 (0.0)	0 (0.0)	0 (0.0)	

Values represent n (%).
LBBB: left bundle branch block; PAR: paravalvular aortic regurgitation; TAV: transcatheter aortic valve.

of CD was significantly more (62.1%) than that in group I (35.3%) (p=0.034).

PAR incidence and severity stratified by percentage perimeter oversizing

Frequency and severity of PAR categorized by degree of perimeter-based oversizing is listed in Table 3 and illustrated in Fig. 1. Briefly, PAR was graded none or trivial in 27 of the 63 patients (42.9%), mild in 25 of the 63 (39.6%) patients, and moderate in 11 of the 63 (17.5%) patients. No patient presented with severe PAR. Moreover, no patients in either groups I or II exhibited moderate or severe PAR when MDCT perimeter oversizing percentage exceeded 10%. When we compared the 2 groups in terms of PAR with post-procedural TTE, it also confirmed that PAR occurred significantly less frequently in group II (p=0.009). Mild and moderate PARs were observed in 52.9% (18 of 34) and 23.5% (8 of 34) of the patients in group I, respectively. Conversely, mild and moderate PARs were found in 24.2% (7 of 29) and 10.3% (3 of 29) of patients in group II, respectively. As the degree of oversizing increased, the frequency and severity of PAR decreased, indicating the existence of an inverse relationship between the severity of PAR and oversizing.

ROC analyses for prediction of PAR and CD

In the ROC analysis, a cutoff value of 13.9% was identified as the best predictive value for mild or

Table 4. Predictors of paravalvular aortic regurgitation on univariate and multivariate analysis

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Implantation depth	1.14 (0.88-1.49)	0.307		
Eccentricity ratio	2.96 (0.0-42473)	0.824		
Annulus calcification	2.50 (0.89-6.987)	0.081	3.46 (1.08-11.09)	0.036
Oversizing (%) <13.9	6.17 (2.05-18.59)	0.001	6.38 (2.00-20.33)	0.002
Oversizing (%)	0.81 (0.70-0.93)	0.004		

CI: confidence interval; OR: odds ratio

Table 5. Predictors of conduction disturbances on univariate and multivariate analysis

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Implantation depth	2.129 (1.382-3.279)	0.001	1.997 (1.261-3.161)	0.003
Membranous septum	0.458 (0.254-0.826)	0.009	0.497 (0.247-0.999)	0.050
Eccentricity ratio	41.3 (0.00-620207)	0.448		
Annulus calcification	1.250 (0.459-3.403)	0.662		
Oversizing (%) >15.5	3.733 (1.125-12.39)	0.031	7.089 (1.220-41.18)	0.029
Oversizing (%)	1.118 (1.002-1.248)	0.046		

CI: confidence interval; OR: odds ratio

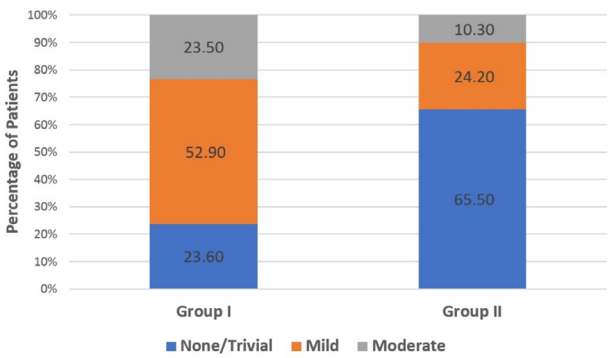

Figure 1. Assessment of paravalvular aortic regurgitation after TAVI.
TAVI: transcatheter aortic valve implantation; Group I: oversizing below 13.9%; Group II: oversizing above 13.9%.

moderate PAR, with 76.5% positive predictive value and 65.5% negative predictive value (area under the curve [AUC] 0.737, 95% CI 0.614-0.861, p=0.001) (Fig. 2A). As shown in Fig. 2B, for predicting CD, AUC of 0.658 for oversizing >15.5% mm indicated weak accuracy in discriminating CD from non-CD (p=0.032). In this study, we found that the optimal oversizing range which could significantly help reduce PAR risk, possibly without any additional risk, was between 10% and 15% based on perimeter measurements.

Predictors for PAR and CD

Table 4 represents the results of the univariate and multivariate analyses of predictors of PAR after TAVI. The univariate analysis showed that annulus calcification and oversizing were associated with the incidence of PAR ≥mild. According to the multivariate analysis, annulus calcification (OR: 3.46, 95% CI: 1.08-11.09, p=0.036) was found to be significant and independent predictors of mild or moderate PAR. Likewise, oversizing <13.9% significantly increased the odds of PAR (OR: 6.38, 95% CI: 2.00-20.33, p=0.002) and were the most powerful predictors of PAR. Univariate logistic regression analysis showed that implantation depth, membranous septum, and oversizing were associated with CD. The multivariate analysis revealed implantation depth and oversizing as powerful and independent predictors for postoperative CD (p=0.003 and p=0.029, respectively) and demonstrated borderline predictive character of membranous septum length (p=0.05) (Table 5).

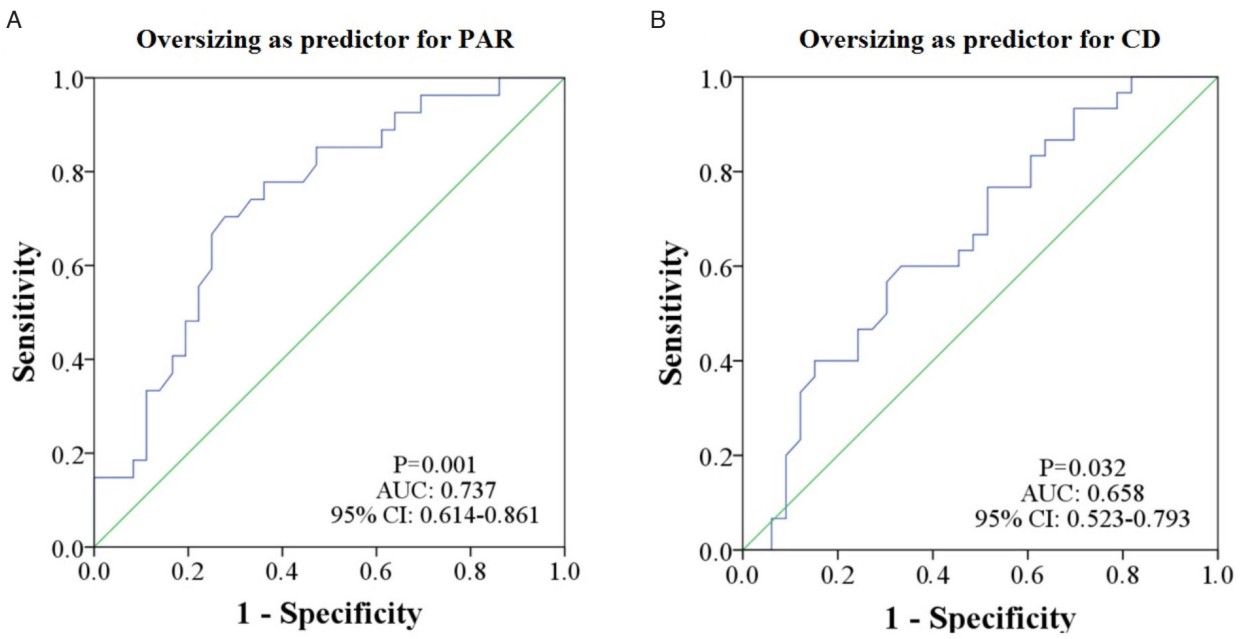

Figure 2. ROC analysis of the perimeter-based oversizing for prediction of **(A)** PAR and **(B)** CD.
AUC: area under the curve; CD: conduction disturbances; CI: confidence intervals; PAR: paravalvular aortic regurgitation.

DISCUSSION

To the best of our knowledge, this is the first study that demonstrates the impact of different degrees of oversizing on clinical and functional outcomes using a newer generation Portico device. Accordingly, the major findings of our study include the following:

PAR ≥mild was observed in 57.1% of the patients undergoing transfemoral TAVI using the Portico valve.

We identified an inverse relationship existing between oversizing and PAR.

Calcification in the aortic annulus and a low percentage of oversizing were independent determinants of PAR ≥mild.

An important relationship was revealed between the annular sizing by MDCT and the occurrence of CD.

No significant differences were observed between the groups in terms of procedural mortality, 1-year mortality, or other major complications, and these findings were similar to the findings reported by other Portico cohorts.[15, 16] Nevertheless, the two patients who exhibited valve migration despite optimal positioning had received a lower percentage of oversizing THV. In our opinion, the possible reasons that may account for this occurrence are the early learning curve and valve characteristics. The CoreValve frame has a tapering from the inflow to the constrained area of the valve.[17] In contrast, the Portico system was designed as a non-flared annulus section because of which lower oversizing might be more important for the Portico device than that for the CoreValve, and migration of the Portico valve from the implantation site in the presence of negative or smaller oversizing might be easier.[18] The previous studies have revealed that calcification of the aortic annulus plays a role in the incidence and severity of PAR.[19, 20] Concordant with preceding studies, we found that the severity of annular calcification was associated with mild or moderate PAR. Furthermore, no significant differences were observed between the groups.

Impact of oversizing on PAR and CD

PAR is the most frequent complication following TAVI and has been highlighted as an independent risk factor for late mortality.[3, 4] Additionally, CD, including new-onset LBBB and CHB requiring PPM, is the most frequent complication following TAVI, which results in LV asynchrony, cardiovascular mortality, and re-hospitalization.[5, 21] Selection of the ap-

propriate prosthesis is vital for the conduction of a TAVI procedure to avoid the abovementioned complications. It has been previously demonstrated that a lower oversizing may lead to PAR, or conversely, a severe oversizing may increase the chances of CD requiring PPM implantation.[7, 13, 22] As described previously by Buzzatti et al.,[7] an insufficient oversizing under 11% significantly increased the incidence of PAR for the CoreValve. Similar conclusions have been reported by Chodór et al.[13] They found that in patients who received a high degree of oversizing CoreValve, the occurrence of a condition of more than mild PAR was significantly less frequent. Leber et al.[22] concluded that aggressive oversizing (>25%) resulted in decreasing significant PAR but induced CD. Other authors such as Détaint et al.[23] reported that no patient exhibited a condition with significantly more than mild PAR when the degree of oversizing was greater than 8% for the Edwards SAPIEN valve. Regarding PAR after SAPIEN 3 implantation, Yang et al.[8] determined that the optimal cutoff value of MDCT area oversizing for the prediction of mild or moderate PAR was 4.17%. Therefore, the sizing algorithms are device-specific, and the sizing process should be modified with improvement and different algorithms depending on the new valve designs. In this study, a cutoff value of 13.9% was identified as the best predictive value for mild or moderate PAR. We found an inverse relationship between the device annular ratio and the occurrence of moderate or severe PAR after Portico placement in our study. In group II, mild PAR was observed in 24.2% of the patients, with 10.3% experiencing moderate PAR, which was significantly lower than in group I. These findings showed us that, in patients who presented with borderline cases, the selection of a larger Portico THV might result in lower PAR rates without an increase in overall clinical events.

Our study on the impact of different degrees of oversizing showed that increasing oversizing ratios were related to lower rates of mild or moderate PAR but might cause CD in a considerable number of patients. Briefly, the incidences of 33.3% NP-LBBB and 19.0% PPM reported herein were similar to those reported previously.[16, 24] New-onset LBBB were more frequent in group II than in group I; however, statistical significance was not observed owing to the small sample size. There was no difference between the groups regarding PPM. This might be because of the high implantation depth within the groups. It is recommended that the frame's inflow edge be placed 3-4 mm below the aortic annulus for ideal depth of implantation of the Portico valve.[14] The mean implantation depth in our study was 7.9±1.9 mm. Thus, deep deployment of the valve in the LVOT may influence the frequency and extent of CD. Additionally, there was no difference between groups I and II in terms of implantation depth. Therefore, assessment of the degree of perimeter-based oversizing and selection of the correct size of THV are a crucial part of this procedure. The selection of a larger Portico THV, not exceeding 15% oversizing, may result in lower rates of PAR without an increase in overall clinical events, especially in patients who present with borderline cases.

Limitations

Our study had a few limitations. First, it was a retrospective analysis and the statistical power might not be remarkable because of the small sample size of the study. A statistical significance and demonstration of a true association between oversizing and PAR or CD will be hopefully achieved with an increased number of patients. Kaneko et al.[25] considered PAR ≥mild as the primary outcome as the incidence of PAR ≥moderate was low in their study with SAPIEN 3. Owing to the limited sample size, the number of patients with PAR ≥moderate was small in our study. Therefore, we also considered PAR ≥mild as a postoperative outcome. Another limitation was that the data from this cohort represented our initial and ongoing experience with the Portico device, and the average implantation depth was deeper than the depth considered best practice presently owing to the potential impact of the learning curve. Additionally, the distribution of calcification was analyzed using a semi-quantitative approach.

Conclusion

Our study showed an inverse relationship existing between oversizing based on perimeter by MDCT and the occurrence of mild or moderate PAR in patients undergoing Portico TAVI. We demonstrated that the optimal oversizing range was between 10% and 15% according to perimeter measurements. Preoperative assessment of oversizing may help guide physicians in determining the optimal valve size; furthermore, in patients with borderline cases, oversizing may en-

sure the application of a supplementary tool for the improvement of the planning of TAVI procedures to prevent the incidence of PAR and new PPM implantation.

Ethics Committee Approval: Ethics committee approval was received for this study from the University of Health Sciences İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital (Approval Date: November 26, 2019; Approval Number: #2019-76).

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