Effect of Aortic Angulation on Outcomes in Transcatheter Aortic Valve Implantation with the Self-Expanding Portico Valve

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ABSTRACT

Introduction: Aortic angulation (AA), defined as the angle between the aortic annulus plane and the horizontal plane, may result in failed prosthesis positioning. The effect of AA on the procedural and short-term outcomes with the portico valves for transcatheter aortic valve implantation (TAVI) has not been fully investigated. The present study aimed to evaluate the impact of AA on device success and early outcomes of TAVI using a self-expanding portico valve.

Patients and Methods: Preoperative computed tomography scans of 121 consecutive patients treated with the portico valve were analyzed. TAVI device success and outcomes were determined according to VARC-3 definitions. Patients were divided into two groups based on mean AA.

Results: The mean AA was 48.7 ± 8.9°. There were no differences in technical success (92.2 vs 89.5%, p= 0.604), device success (81.2% vs 77.2%, p= 0.582), and early safety endpoints (68.8% vs 61.4%, p= 0.397) between the AA≤ 48° and AA> 48° groups. The frequency and severity of paravalvular aortic regurgitation (PAR) was statistically higher in patients with AA> 48° (p= 0.028). Moreover, an increased AA was also associated with valve malposition (12.3% vs. 1.6%, p= 0.018), prolonged procedure time (85 ± 26 vs. 75 ± 20 minutes, p= 0.028), and greater Δimplantation depth (2.2 ± 0.5 vs. 0.8 ± 0.1 mm; p< 0.001).

Conclusion: Despite comparable device success and early outcomes rates, increased AA is associated with higher rates of PAR and valve malposition, with the self-expanding portico valve.

Key Words: Aortic angulation; computed tomography; self-expanding valve; transcatheter aortic valve implantation

Kendiliğinden Genişleyen Portico Kapak ile Transkateter Aort Kapak İmplantasyonunda Aort Açılanmasının Sonuçlara Etkisi

ÖZET

Giriş: Aort anulus düzlemi ile yatay düzlem arasındaki açı olarak tanımlanan aort angülasyonu (AA), protezin başarılı bir şekilde konumlandırılamamasına neden olabilir. AA'nın transkateter aort kapak implantasyonu (TAVI) için portico kapakları ile prosedürel ve kısa vadeli sonuçlar üzerindeki etkisi tam olarak araştırılmamıştır. Bu çalışma, kendiliğinden genişleyen portico kapağın kullanıldığı TAVI'de AA'nın cihaz başarısı ve erken sonuçlar üzerindeki etkisini değerlendirmeyi amaçladı.

Hastalar ve Yöntem: Portico kapakla tedavi edilen ardışık 121 hastanın ameliyat öncesi bilgisayarlı tomografi görüntüleri analiz edildi. TAVI cihaz başarısı ve sonuçları VARC-3 tanımlarına göre belirlendi. Hastalar ortalama AA'ya göre iki gruba ayrıldı.

Bulgular: Ortalama AA 48.7 ± 8.9° idi. ≤48° AA ve AA> 48° grupları arasında teknik başarı (%92.2'ye karşı %89.5, p= 0.604), cihaz başarısı (%81.2'ye karşı %77.2, p= 0.582) ve erken güvenlik sonlanım noktalarında (%68.8'e karşı %61.4, p= 0.397) bir fark yoktu. AA> 48° olan hastalarda paravalvüler aort yetersizliğinin (PAR) sıklığı ve şiddeti istatistiksel olarak daha yüksekti (p= 0.028). Ayrıca, artmış AA, kapak malpozisyonu (%12.3'e karşı %1.6, p= 0.018), uzamış işlem süresi (85 ± 26'ya karşı 75 ± 20 dakika, p= 0.028) ve daha büyük Δimplantasyon derinliği (2.2 ± 0.5 vs. 0.8 ± 0.1 mm; p< 0.001) ile ilişkilendirilmiştir.

Sonuç: Karşılaştırılabilir cihaz başarısı ve erken sonuç oranlarına rağmen, artmış AA kendiliğinden genişleyen portiko kapak için daha yüksek PAR oranları ve kapak malpozisyonuyla ilişkilidir.

Anahtar Kelimeler: Aort angülasyonu; bilgisayarlı tomografi; kendiliğinden genişleyen kapak; transkateter aort kapak implantasyonu

Cite this article as: *Aslan S, Türkvatan A, Güner A, Kahraman S, Bulut Ü, Demirci G, et al. Effect of aortic angulation on outcomes in transcatheter aortic valve implantation with the self-expanding portico valve. Koşuyolu Heart J 2022;25(2):132-140.*

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Submitted: 08.02.2022
Accepted: 20.05.2022
Available Online Date: 20.08.2022

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) has developed rapidly in the last two decades as an alternative treatment option for patients with severe aortic stenosis who are at intermediate-to-high or prohibitive risk for surgery, and it is expected to expand in the future to the treatment lower-risk patients[1-4]. Despite the role of advances in implantation techniques and/or prosthesis design in reducing TAVI complications and the promising results of clinical trials, particular anatomical circumstances may pose challenges for the proper positioning and consequent functioning of self-expandable TAVI valves[5,6].

Aortic angulation (AA), quantified by computed tomography angiography (CTA) and defined as the angle between the aortic annulus plane and the horizontal plane (Figure 1), can make successful positioning and optimal placement of the self-expanding prosthesis more challenging, especially in cases of the excessively angled aortic root[7,8]. Several studies using different valve designs have produced contradictory results regarding the effect of increased AA on TAVI outcomes[9-11]. Nevertheless, data on predictors of device success of the Portico transcatheter heart valve (THV) system (Abbott Vascular, Santa Clara, CA, USA) after TAVI is scarce; particularly, the effect of increased AA on the acute procedural and early outcomes has not been fully investigated.

The present study aimed to evaluate the impact of AA on device success, and procedural and short-term outcomes in patients who underwent TAVI with a self-expanding portico valve.

PATIENTS and METHODS

Study Population and Design

We conducted a retrospective review of 128 consecutive patients who underwent a TAVI with a self-expanding Portico TAVI system at our hospital from March 2017 to October 2021. A total of seven patients were excluded from the analysis for the following reasons: Bicuspid valve (n= 5), previously implanted surgical bioprosthetic valves (n= 1), and inability to access all medical records (n= 1). The remaining 121 patients repre-

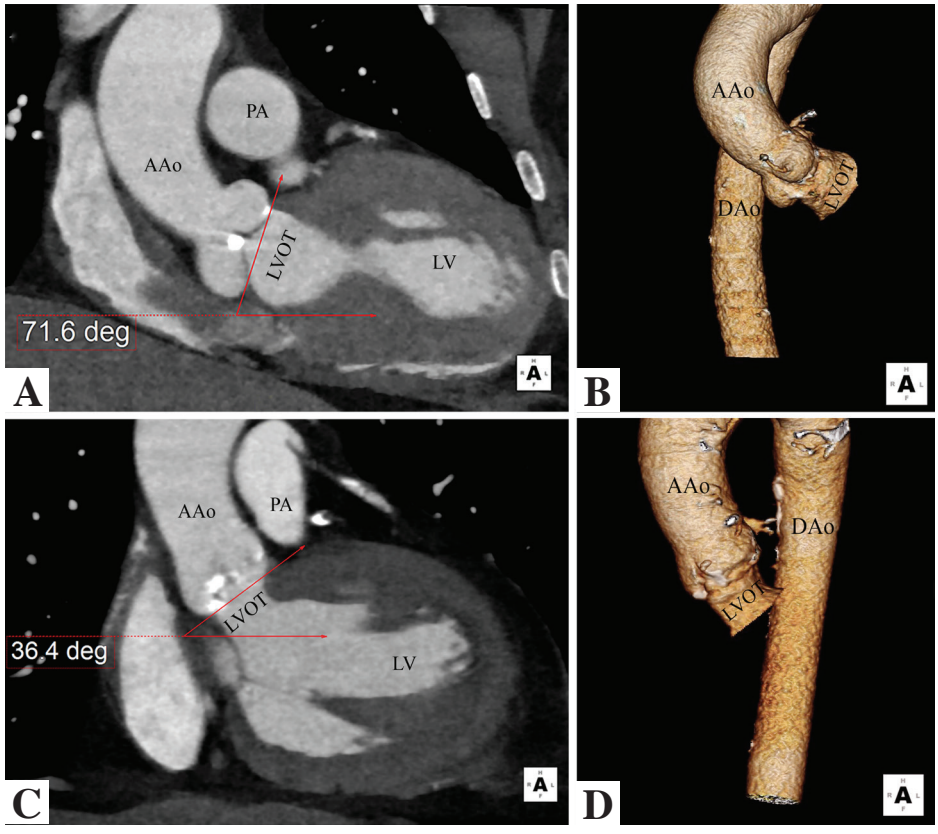

Figure 1. Measurement of the aortic angulation is performed on a coronal multiplanar reformatted image of CT angiography. Aortic angulation is defined as the angle between the plane of the aortic annulus and the horizontal plane. Coronal multiplanar reformatted and volume rendering images of two TAVI candidates of high (71.6°) aortic angulation **(A and B)** and low (36.4°) aortic angulation **(C and D)** are presented (AAo: Ascending aorta; DAo: Descending aorta; LV: Left ventricle; LVOT: Left ventricular outflow tract; PA: Pulmonary artery).

sented the final study population. Consistent with the previously published research, the study population was divided into two groups based on the mean AA to evaluate whether AA affected clinical outcomes in patients undergoing TAVI. All baseline demographic and clinical information, echocardiography and CTA imaging data, procedural details, and 30-day outcomes were obtained from the institutional TAVI database and compared between the two groups. This study was approved by the institutional review board and complied with the Declaration of Helsinki.

TAVI Procedure

All patients were discussed in our institutional Heart Team meetings and were considered at high risk for valve surgery. All TAVI procedures were performed in a hybrid catheterization laboratory under local anesthesia with conscious sedation and were performed by experienced, formally trained physicians. A pre-shaped extra stiff Safari Guidewire (Boston Scientific, Marlborough, Massachusetts, USA) was used in all patients. The portico valve was implanted under fluoroscopic guidance via transfemoral access as previously described[12]. Post-dilatation under rapid pacing was considered in the case of incomplete frame expansion or remaining moderate or severe paravalvular aortic regurgitation (PAR). A final control was performed by aortography. Implantation depth was assessed in the implantation projection by fluoroscopy as the length of the stent frame from the aortic annular plane to the left ventricular outflow tract (LVOT), measured at the level of the noncoronary cusp (NCC) and left coronary cusp (LCC). ΔImplantation depth was calculated as the length of the LCC implantation depth minus the NCC implantation depth.

CTA Data Acquisition and Image Analysis

CTA acquisitions of all patients were performed using a 320-row CTA scanner (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan). All CTA examinations were evaluated using a dedicated workstation (Vitrea version 6.4, Vital Images, USA) to allow for multiplanar reconstruction analysis. Since aortic root dimensions are typically larger in systole, a double oblique transverse view (en face view of the aortic valve) was created during the systolic phase (20-40%) of the cardiac cycle to measure the aortic root dimensions. The aortic annulus was defined as the virtual basal ring aligned with the most basal attachments (basal hinge points) of the three aortic valve cusps on a double-oblique transverse view. First, the minimum and maximum diameters of the annulus were obtained. The annular perimeter was manually drawn using a planimetry tool, after which the area and circumference of the annulus were derived by a workstation software. The percentage of oversizing was calculated with the following equation: (prosthesis/annulus perimeter - 1)*100[13]. The eccentricity index was calculated with the following formula: 1 - (minimum diameter/maximum diameter)[14]. The degree of aortic valve commissural calcification was visually graded from 0 to 3 (0= no calcification, 1= single lesions< 5 mm, 2= calcium lesions> 5 mm or affecting 2 or more leaflets, 3= severe calcification affecting all 3 leaflets) by a semi-quantitative model as described in the previous publication[15]. AA was measured from the implantation projection derived from the reconstruction of CTA and was defined as the angle between the plane of the aortic annulus and the horizontal plane.

Echocardiographic Study

The experienced physicians who were blinded to the patients' clinical characteristics performed all the echocardiographic measurements at baseline and within 30 days. The severity of aortic stenosis, left ventricular ejection fraction, or PAR were evaluated according to the guidelines[16]. The five-class grading scheme (mild, mild-moderate, moderate, moderate-severe, and severe) recommended by Valve Academic Research Consortium (VARC)-3 was used to define residual PAR[17]. For the purposes of this paper, trivial jets were classified as having no PAR, whereas moderate and severe PAR were grouped together.

Definition of Endpoints of the Study

TAVI device success, the intra-, and postoperative data, and 30-day clinical outcomes were defined according to the standardized criteria proposed by VARC-3[17]. The primary endpoint of the present study was device success, which was defined as the combined endpoint of technical success, freedom from all-cause mortality (within 30 days), absence of surgery or intervention related to the procedural complications, and intended valve performance (mean gradient< 20 mmHg, and less than moderate PAR). The secondary endpoints of the study included clinical outcomes of all-cause mortality, stroke, acute kidney injury, myocardial infarction, major vascular complications, life-threatening bleeding, moderate or severe PAR, and new pacemaker implantation within 30-days or during the index hospitalization stay.

Statistical Analysis

The normality of the sample data distribution was tested visually (with histograms and probability curves) or statistically (with Kolmogorov-Smirnov and Shapiro-Wilk tests). Continuous variables were summarized using mean ± standard deviation or median [interquartile range (IQR)] and were compared by using the Student's t-test or Mann-Whitney U test, where appropriate. Categorical and dichotomous variables are presented as frequencies and percentages and were compared by using Pearson Chi-square or Fisher exact test, as appropriate.

Receiver operating characteristic (ROC) analyses were performed to determine the cut-off value of AA that provided the best combination of sensitivity and specificity for device success. All statistical analyses were two-tailed tests with p< 0.05 considered statistically significant. The statistical analyses were conducted with the SPSS software, version 24.0 (SPSS Inc., Chicago, Illinois, United States).

RESULTS

The baseline clinical patient characteristics, echocardiographic, and pre-procedural CTA imaging details of the study population are displayed in Table 1. The mean age of the study population was 80.2 ± 6.2 years; 36.4% were male and had a median STS score of 6.2 (4.0-8.9). Coronary artery disease (71.1%) was the most common comorbidity in TAVI patients, followed by hypertension (64.5%) and diabetes (42.1%). The mean AA was 48.7 ± 8.9°. This value was used as a cut-off to identify the two study groups (AA≤ 48°: 64 and AA> 48°: 57 patients). Baseline patient and pre-TAVI imaging characteristics were comparable between both groups. The analysis is detailed in Table 1.

Procedural details and acute perioperative outcomes are displayed in Table 2. Δimplantation depth was found to be statistically higher in patients with AA> 48° compared with those with AA≤ 48° (2.2 ± 0.5 mm vs 0.8 ± 0.1 mm; p< 0.001). The procedure time was significantly (10 min) longer in the higher AA group (85 ± 26 minutes in its favor when compared to the lower AA group 75 ± 20 minutes, p= 0.028). The prolonged procedure time in the higher AA group was due to the extra time required to implant the second valve in the event of valve malposition or moderate-to-severe PAR. In eight of 121 (6.6%) patients, the implant was initially unsuccessful. Malposition of the prosthesis was significantly higher among patients with increased AA (>48°: seven of 57 patients, 12.3% vs. ≤48°: one of 64 patients, 1.6%, p= 0.018). In four of these cases in the higher AA group, the valve prosthesis moved up upward, within the aortic annulus following initial correct positioning. In the other three patients, the valve prosthesis moved upward into the ascending aorta after complete deployment and could not be retrieved. The valves were withdrawn using a snare technique and were fixed within the ascending aorta, without affecting the coronaries. Only one patient in the ≤48° group developed valve migration requiring a second valve. The need for the second valve was numerically higher in patients with AA> 48° compared with those with AA≤ 48° (seven of 57 patients, 12.3% vs. three of 64 patients, 4.7%, p= 0.188), but did not reach significance due to case numbers. In summary, technical success was achieved in 90.9% of patients and was comparable between the two groups (AA> 48°: 89.5% vs. AA≤ 48°: 92.2%, p= 0.604) (Table 3). In the overall cohort, device success at day 30 was 79.3%. No significant difference was found between groups for the device success, the primary endpoint of the study (AA> 48°: 77.2% vs. AA≤ 48°: 81.2%, p= 0.582). As shown in Figure 2, the AUC of 0.514 for AA of >50° to predict device success failed to distinguish between those with and without device success (AUC= 0.514; 95% CI= 0.385-0.642, p= 0.835). There was no significant difference in early safety endpoints between AA groups (AA> 48°: 61.4% vs. AA≤ 48°: 68.8%, p= 0.397). Further details are provided in Table 3.

One of the primary findings of this study was that the frequency and severity of PAR, as measured by the VARC-3, were statistically higher in the higher AA group (p= 0.028). Figure 3 illustrates the frequency and severity of PAR. Of the 118 patients with interpretable echocardiography studies within 30 days, PAR grading was determined in 76 patients (64.4%), with no subject presenting with severe PAR. In the higher AA group, PAR was none/trace in 22.2%, mild in 44.4%, mild-moderate in 25.9%, and moderate in 7.4%. In the lower AA group, PAR was none/trace in 46.9%, mild in 32.8%, and mild-moderate in 18.8%. Only one (1.6%) patient had moderate PAR. These findings suggest that there is a relationship between the severity of PAR and AA.

DISCUSSION

The principal findings of this investigation are as follows:

1) There is no statistically significant relationship between increased AA and TAVI device success rates or short-term outcomes,

2) Increased AA is associated with more frequency and severity of PAR, higher rates of valve malposition, and prolonged procedure time,

3) There is a statistically significant relationship between AA and Δimplantation depth. To the best of our knowledge, this is the first study focusing on the Portico valve system performance based on AA, with a cut-off value of >48° consistent with previous reports.

Increased AA causes the valve to be subjected to a higher degree of bending, which can make it difficult to position the valve properly. Asymmetric positioning of the valve may affect the success of the acute procedure adversely. The fact that the self-expanding valves have a longer stent frame and the delivery systems lack active flexion and extension makes it more difficult to optimize the co-axial alignment of these prostheses than balloon-expandable valves. It has been clarified that the high-angle aorta negatively affects TAVI results with old-generation self-expanding prostheses[7,8,18]. Previously, Abramowitz et al. reported in their study evaluating the effect of increased AA on TAVI outcomes that increased AA adversely affected acute procedural success after the self-expandable valve, nevertheless, it did not affect TAVI results after affixing the balloon-expandable valve[7].

Table 1. Baseline characteristics of the study population according to the aortic angulation

		Aortic Angulation		
Parameters	**Total (n= 121)**	**≤48° (n= 64)**	**>48° (n= 57)**	**p**
Demographic and clinical characteristics				
Age (years)	80.2 ± 6.2	80.4 ± 6.2	80.0 ± 6.1	0.759
Gender (male)	44 (36.4)	19 (29.7)	25 (43.9)	0.106
Systemic hypertension	78 (64.5)	39 (60.9)	39 (68.4)	0.391
Diabetes mellitus	51 (42.1)	27 (42.2)	24 (42.1)	0.993
Coronary artery disease	86 (71.1)	49 (76.6)	37 (64.9)	0.158
Coronary bypass	27 (22.3)	11 (17.2)	16 (28.1)	0.151
Stroke/TIA	5 (4.1)	1 (1.6)	4 (7.0)	0.187
Heart failure	26 (21.5)	13 (20.3)	13 (22.8)	0.739
Chronic kidney disease	34 (28.1)	21 (32.8)	13 (22.8)	0.222
Peripheral artery disease	28 (23.1)	14 (21.9)	14 (24.6)	0.727
Pulmonary disease	37 (30.6)	21 (32.8)	16 (28.1)	0.572
Pacemaker	5 (4.1)	4 (6.2)	1 (1.8)	0.369
Atrial fibrillation	33 (27.3)	14 (21.9)	19 (33.3)	0.158
STS score	6.2 (4.0-8.9)	6.7 (4.8-9.0)	5.0 (3.0-8.3)	0.106
Echocardiographic characteristics				
LVEF (%)	54.2 ± 9.5	54.8 ± 8.3	53.5 ± 10.6	0.444
Aortic valve area (cm^2)	0.72 ± 0.13	0.71 ± 0.15	0.73 ± 0.10	0.247
Aortic mean pressure gradient (mmHg)	48.2 ± 11.7	48.8 ± 12.9	47.5 ± 10.4	0.554
Aortic peak pressure gradient (mmHg)	77.2 ± 16.9	78.7 ± 18.5	75.5 ± 15.0	0.304
Aortic peak systolic velocity (m/s)	4.4 ± 0.4	4.4 ± 0.4	4.3 ± 0.4	0.355
Computed tomography characteristics				
Left main height (mm)	14.7 ± 3.0	14.3 ± 2.8	15.0 ± 3.1	0.201
Right coronary artery height (mm)	17.2 ± 3.2	17.2 ± 3.1	17.3 ± 3.3	0.894
Annulus perimeter (mm)	76.1 ± 5.8	76.2 ± 6.1	76.1 ± 5.5	0.925
Annulus, perimeter derived diameter (mm)	24.2 ± 1.8	24.2 ± 1.9	24.2 ± 1.7	0.936
Annulus area (mm^2)	446.7 ± 69.0	447.1 ± 72.9	446.2 ± 65.1	0.941
Annulus min diameter (mm)	20.8 ± 1.8	20.8 ± 2.0	20.8 ± 1.6	0.963
Annulus max diameter (mm)	27.2 ± 2.1	27.2 ± 2.1	27.1 ± 2.0	0.693
Annulus mean diameter (mm)	24.0 ± 1.8	24.0 ± 1.8	23.9 ± 1.7	0.837
Index of eccentricity	0.23 ± 0.05	0.23 ± 0.05	0.23 ± 0.04	0.613
Mean sinus of valsalva diameter (mm)	30.8 ± 2.6	30.7 ± 2.6	30.9 ± 2.7	0.640
Ascending aorta diameter (mm)	34.6 ± 3.2	34.3 ± 3.3	35.0 ± 3.1	0.211
Aortic angulation (°)	48.7 ± 8.9	41.9 ± 4.6	56.3 ± 6.0	<0.001
Oversizing (%)	12.5 ± 4.8	12.7 ± 5.0	12.3 ± 4.6	0.705
Commissural calcification score	2.23 ± 0.86	2.19 ± 0.80	2.28 ± 0.94	0.636

Values represent mean ± SD, n (%) or median (interquartile range).
LVEF: Left ventricular ejection fraction, LVOT: Left ventricular outflow tract, STS: Society of thoracic surgeons, TIA: Transient ischemic attack.

Table 2. Procedural data

Parameters	Total (n= 121)	Aortic Angulation ≤48° (n= 64)	Aortic Angulation >48° (n= 57)	p
Implanted valve size, mm				
23	6 (5.0)	4 (6.2)	2 (3.5)	0.683
25	26 (21.5)	11 (17.2)	26.3	0.222
27	36 (29.8)	21 (32.8)	15 (26.3)	0.435
29	53 (43.8)	28 (43.8)	25 (43.9)	0.990
Conscious anesthesia	107 (93.0)	58 (96.7)	49 (89.1)	0.111
Operating room time (min)	125 ± 31	119 ± 29	132 ± 32	0.023
Procedure time* (min)	80 ± 23	75 ± 20	85 ± 26	0.028
Total contrast used, mL	150 (120-200)	140 (110-195)	157 (130-225)	0.110
Predilatation	109 (90.1)	59 (92.2)	50 (87.7)	0.412
Postdilatation	59 (48.8)	29 (45.3)	30 (52.6)	0.421
Aortic valve malpositioning	8 (6.6)	1 (1.6)	7 (12.3)	0.018
Valve migration	5 (4.1)	1 (1.6)	4 (7.0)	0.187
Valve embolization	3 (2.5)	0 (0.0)	3 (5.3)	0.201
Ectopic valve deployment	0 (0.0)	0 (0.0)	0 (0.0)	-
Implantation depth NCC (mm)	6.5 ± 2.5	7.0 ± 2.4	6.0 ± 2.3	0.035
Implantation depth LCC (mm)	8.0 ± 2.5	7.8 ± 2.5	8.2 ± 2.6	0.357
Implantation depth mean (mm)	7.2 ± 2.4	7.4 ± 2.5	7.1 ± 2.4	0.548
ΔImplantation depth	1.4 ± 0.7	0.8 ± 0.1	2.2 ± 0.5	<0.001
Need for second valve	10 (8.3)	3 (4.7)	7 (12.3)	0.188
Converted to surgical AVR	0 (0.0)	0 (0.0)	0 (0.0)	-
Coronary artery occlusion (%)	0 (0.0)	0 (0.0)	0 (0.0)	-
Cardiac tamponade	4 (3.3)	3 (4.7)	1 (1.8)	0.621

Values represent mean ± SD, n (%) or median (interquartile range).
AVR: Aortic valve replacement, LCC: Left coronary cusp, NCC: Non coronary cusp.
*Procedure time was defined as the time from arterial puncture, until vascular closure.

On the other hand, several studies conducted in collaboration with CoreValve reported conflicting results regarding the effect of AA on device success rates between higher and lower groups[9,10,19]. A subsequent study conducted by Popma et al. on self-expandable valves reported that there is no association between AA and procedural success or clinical outcomes. The authors attributed these findings to the use of the most up-to-date techniques in valve placement[19]. The differences in these results can probably be explained by the technical improvement in new-generation devices.

Only one study has examined the effect of aortic root opening on TAVI outcomes in patients who have been implanted with the portico valve. Gorla et al. evaluated this in a retrospective study of 392 patients who had undergone TAVI with Portico, Evolut-R, and Acurate-NEO[20]. Postoperative device success was specified based on the VARC-2 definition and was generally satisfactory for the Portico valve and was comparable in both the horizontal (95.0%) and non-horizontal (86.8%) groups. Similar to the previous study, primary device success in our study was not affected by AA and was comparable in both groups (AA≤ 48°: 81.2% vs. AA> 48°: 77.2%; p= 0.582). The results are relatively variable due to differences in the definition of device success in different studies. The reason why our device success proved to be lower than the other study is that we judged it according to the definition of device success criteria, which was updated in 2021 with the VARC-3 definitions. On the other hand, all other composite endpoints, including technical success and early safety were similar between both AA groups in our study.

Table 3. Composite endpoints

Parameters	Total (n= 121)	Aortic Angulation ≤48° (n= 64)	Aortic Angulation >48° (n= 57)	p
Technical success#	110 (90.9)	59 (92.2)	51 (89.5)	0.604
Absence of procedural mortality	118 (97.5)	63 (98.4)	55 (96.5)	0.492
Successful access, delivery, deployment, system retrieval	121 (100.0)	64 (100.0)	57 (100.0)	-
Correct positioning of one valve in proper location	111 (91.7)	61 (95.3)	50 (87.7)	0.188
Absence of surgery or intervention related to the procedural complications	118 (97.5)	63 (98.4)	55 (96.5)	0.492
Device success (at 30 days)	96 (79.3)	52 (81.2)	44 (77.2)	0.582
Technical success	110 (90.9)	59 (92.2)	51 (89.5)	0.604
Freedom from mortality	109 (90.1)	59 (92.2)	50 (87.7)	0.412
Absence of surgery or intervention related to the procedural complications	113 (93.4)	59 (92.2)	54 (94.7)	0.573
Intended valve performance*	114 (96.6)	63 (98.4)	51 (94.4)	0.331
Early safety (at 30 days)	79 (65.3)	44 (68.8)	35 (61.4)	0.397
All-cause mortality	12 (9.9)	5 (7.8)	7 (12.3)	0.412
All stroke	4 (3.3)	3 (4.7)	1 (1.8)	0.621
Myocardial infarction	0 (0.0)	0 (0.0)	0 (0.0)	-
Life-threatening bleeding	10 (8.3)	4 (6.2)	6 (10.5)	0.394
Major vascular complications	12 (9.9)	6 (9.4)	6 (10.5)	0.832
Acute kidney injury stage 3 or 4	5 (4.1)	3 (4.7)	2 (3.5)	1.0
Moderate or severe aortic regurgitation	4 (3.4)	1 (1.6)	3 (5.6)	0.331
New permanent pacemaker	27 (22.3)	13 (20.3)	14 (24.6)	0.575
Repeat procedure for valve dysfunction	0 (0.0)	0 (0.0)	0 (0.0)	-

#at exit from procedure room.
*Intended valve performance based on discharge echo included mean aortic valve gradient <20 mmHg, peak velocity <3 m/s, no moderate/severe prosthetic valve regurgitation.

The study conducted by Gorla et al. also examined the relationship between PAR and AA after TAVI[20]. It reported that in portico valves there is no association between AA and the incidence of moderate-to-severe PAR. However, the authors stated that these findings may have been affected by the low number of patients in the portico group (20 patients). Indeed, there were no patients who developed moderate to severe PAR after TAVI in the portico horizontal group in their study. The results of the study mentioned above regarding the relationship between AA angle and PAR were not confirmed by our findings. We identified a significant correlation between high AA and increased frequency and severity of PAR. In our study, we used the five-class grading scheme recommended by VARC-3, which can be easily narrowed down to the three-class scheme when needed in order to reduce variability between echocardiography laboratories[17,21]. The moderate PAR rate in our study was 4.2%, which is in line with previous reports[22-25]. With only five cases with moderate PAR after TAVI, no multivariate analysis regarding an AA and other variables as independent predictors for moderate to severe PAR could be offered. In our study, we hypothesize that asymmetrical positioning of the prosthetic stent frame within the implantation site and a consequent greater Δimplantation depth is also associated with the risk of PAR greater than mild in patients with TAVI. Briefly, the implantation depth was measured to be less on the non-coronary sinus side and more on the left coronary sinus side in patients with high AA. It was found to be statistically higher in patients with high implantation depth, which is an indication of asymmetrical localization (2.2 ± 0.5 mm vs. 0.8 ± 0.1 mm; p< 0.001).

Previously, Schultz et al. hypothesized that the apposition force exerted by the long prosthesis frame on the adjacent tissue of the annulus would be higher on the outer curve of the aorta or the right side of the annulus, and lower on the inner curve of the aorta or the left side of the annulus[26]. They supported their hypothesis by detecting a higher malposition rate at the implan-

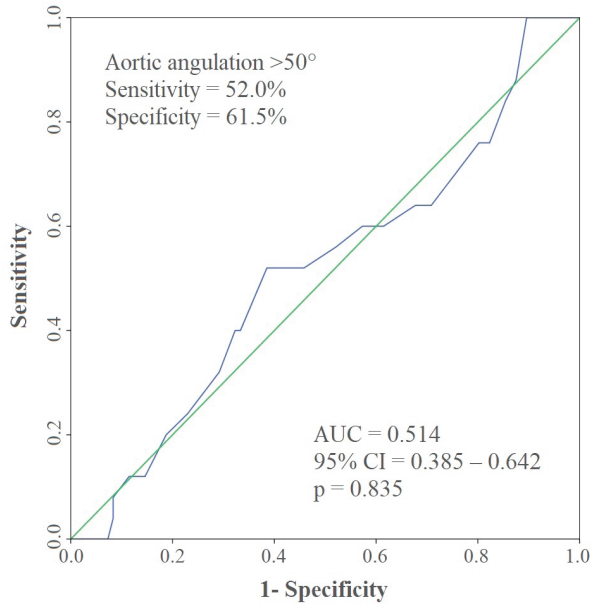

Figure 2. Receiver operating characteristic curves of aortic angulation as a predictor of device success. (AUC: Area under the curve, CI: Confidence interval).

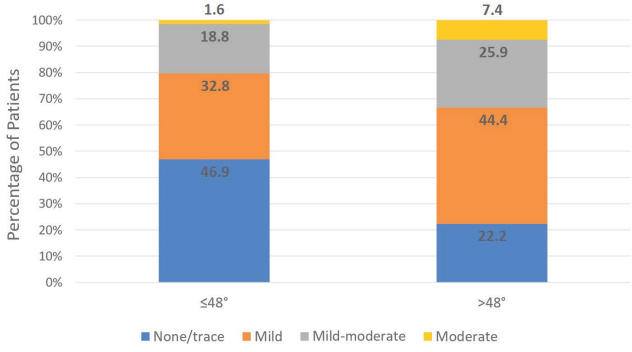

Figure 3. Assessment of paravalvular aortic regurgitation after TAVI according to the aortic angulation.

Percentage of patients with various degrees of paravalvular aortic regurgitation after TAVI. A significantly higher proportion of patients with higher aortic angulation had paravalvular aortic regurgitation (p= 0.028).

tation site within the curve. Increased AA may affect the radial strength of the prosthesis and its ability to completely seal the paravalvular space during TAVI. This increases the possibility of post-implantation complications such as paravalvular leakage, valve embolization, and THV-in-THV. Indeed, several procedural success criteria were found to be significantly different in the high AA group: Paravalvular leak, increased valve malposition rates, and prolonged procedure time. The results of our study confirmed the negative effect of increased AA after TAVI on prosthesis malposition, possibly resulting from the decrease in grip strength due to the insufficient apposition force of the frame and asymmetrical placement.

In fact, the design of the new generation of prostheses aims to simplify and standardize the TAVI procedure even in the most challenging anatomical scenarios. The self-expanding Portico THV system has recently undergone several improvements to the carrier unit (FlexNav, Abbott Cardiovascular) to support especially more precise valve placement and increase the procedural safety and accuracy of the platform. In a recent study by Fontana et al. Portico valve implantation with FlexNav was associated with an excellent safety profile and a technical device success of 96.7% within 30 days. Echocardiography revealed a moderate PAR of 4.1% on the 30th day[27]. However, 3.3% of subjects required a second valve to be implanted during the procedure. The overall success and all these added features in patients undergoing Portico transcatheter heart valve implantation with the new FlexNav delivery system now need to be tested in more specific and challenging anatomical scenarios such as in the presence of an angled aorta.

It is important to emphasize limitations pertinent to the methods of this study. First of all, this was a single-center retrospective study and included a relatively small patient population. However, it should be noted that it is currently the highest reported single-center study with the Portico valve in this field. Second, due to the limited number of patients with moderate/severe PAR, we were unable to perform a multivariate regression analysis on statistically significant univariate factors to determine whether AA is an independent predictor of PAR. Lastly, only the short-term follow-up data have been included. The present study focuses on device success and early composite endpoints. Future prospective, randomized studies with a larger number of patients and longer follow-up may clarify this subject.

In conclusion, the current study suggests that AA does not significantly affect device success or early clinical outcomes following TAVI with the self-expanding Portico THV system. Increased AA is associated with more frequency and severity of PAR, higher rates of valve malposition, and prolonged procedure time. Portico with the FlexNav delivery system, which facilitates control of valve delivery and predictable valve placement, may result in improved outcomes. Nevertheless, further large-scale studies are warranted to validate the findings of this study.

Ethics Committee Approval: The approval for this study was obtained from University of Health Sciences İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (Decision no: 2021-73, Date: 28.09.2021).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - SA, ME; Analysis/Interpretation - SA, AT, ÜB; Data Collection - SA, ÜB, GD, EA; Writing - SA, AT, AG; Critical Revision - AG, SK, ÖÇ; Final Approval - ME; Statistical Analysis - SA, SK; Overall Responsibility - SA.

Conflict of Interest: The authors declared that there was no conflict of interest during the preparation and publication of this article.

Financial Disclosure: The authors declared that this study has received no financial support.

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