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Evaluation of the Transcatheter Aortic Valve Replacement Results in Patients with Borderline Aortic Annulus and the Impact of Under- or Oversizing the Valve

ABSTRACT

Background: Optimal valve sizing provides improved results in transcatheter aortic valve replacement. Operators hesitate about the valve size when the annulus measurements fall into borderline area. Our purpose was to compare the results of borderline versus non-borderline annulus and to understand the impact of valve type and under or oversizing.

Methods: Data from 338 consecutive transcatheter aortic valve replacement procedures were analyzed. The study population was divided into 2 groups as "borderline annulus" and "non-borderline annulus." Balloon expandable valves already have a grey zone definition. Similar to balloon expandable valves, annulus sizes that are within 15% above or below the upper or lower limit of a particular self-expandable valve size are defined as the "borderline annulus" for self-expandable valves. The borderline annulus group was also divided into 2 subgroups according to the smaller or larger valve selection as "undersizing" and "oversizing." Comparisons were made regarding the paravalvular leakage and residual transvalvular gradient.

Results: Of these 338 patients, 102 (30.1%) had a borderline and 226 (69.9%) had a non-borderline annulus. Both the transvalvular gradient (17.81 ± 7.15 vs. 14.44 ± 6.27) and the frequency of paravalvular leakage (for mild, mild to moderate, and moderate, 40.2%, 11.8%, and 2.9% vs., 18.8%, 6.7%, and 0.4%, respectively) were significantly higher in the borderline annulus than the non-borderline annulus group ($P < .001$). There were no significant differences between the groups balloon expandable versus self-expandable valves and oversizing versus undersizing regarding the transvalvular gradient and paravalvular leakage in patients with borderline annulus ($P > .05$).

Conclusion: Regardless of the valve type and oversizing or undersizing, borderline annulus is related to significantly higher transvalvular gradient and paravalvular leakage when compared to the non-borderline annulus in transcatheter aortic valve replacement.

Keywords: Borderline aortic annulus, grey zone annulus, transcatheter aortic valve replacement

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has emerged as a revolutionary treatment in patients with severe aortic stenosis (AS) who are deemed surgically inoperable or intermediate to high risk and recommendations will potentially expand to patients with lower surgical risk categories.[1-3] Preprocedural imaging and subsequent optimal transcatheter heart valve (THV) sizing, which is primarily based on computed tomography angiography (CTA), provides improved long-term results and outcomes by reducing paravalvular leakage (PVL) and residual transvalvular gradient (TVG).[4,5] Moreover, inappropriate sizing may lead not only to PVL or TVG but also to severe complications such as annular rupture, obstruction of coronary ostia, atrioventricular block, or valve embolization.[6,7]

The aortic annulus has a complex anatomy with an oval, crown-like shape and an oblique plane orientation relative to the body axis, and its diameter is dynamically dependent on the cardiac cycle.[8] Therefore, proper sizing is a challenging issue.

ORIGINAL INVESTIGATION

Erkan Yıldırım
Uygar Çağdaş Yüksel
Murat Çelik
Barış Buğan
Serdar Fırtına
Yalçın Gökoğlan
Salim Yaşar
Suat Görmel
Serkan Asil
Ender Murat
Serkan Yener
Hatice Tolunay
Ayşe Saatçi Yaşar
Hasan Kutsi Kabul
Cem Barçın

Department of Cardiology, Gülhane Training and Research Hospital, Ankara, Turkey

Corresponding author:
Erkan Yıldırım
✉ dr_erkanyildirim@yahoo.com.tr

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Furthermore, the technique of measurement is a very complex process and depends on the operator, and few data are available regarding intra- and inter-observer variability of this technique.

For balloon-expandable (BE) valves, there is an overlap between 2 different prosthesis sizes, and some patients' annulus area falls within areas of "grey zones" between 2 THV sizes. However, there is no grey zone definition for self-expandable (SE) valves according to the company's recommendations. Nevertheless, in daily practice, due to the difficulties in measurement technique and possible intra- and inter-observer variability, operators are hesitating about the size of the valve when the annulus diameter falls very close to the borderline numbers for SE valves. For patients with grey zone or borderline annulus size, THV size selection is made by the physician based on uncertain parameters such as the degree of calcification, risk of annular rupture, anticipation of the degree of PVL, and sinotubular junction dimensions.[9,10]

The purpose of this study was to compare the results of the TAVR procedure in patients with borderline versus non-borderline annulus and BE versus SE aortic valves in patients with the borderline annulus and to understand the impact of under or oversizing THV within this group of patients.

METHODS

Study Design and Population

Data from 338 consecutive patients with intermediate to high surgical risk who underwent the TAVR procedure between September 2016 and June 2022 were analyzed retrospectively. Patients' baseline demographic variables, medical histories, and clinical features, as well as in-hospital major adverse events, were obtained from the hospital's electronic records. Types of the used valves were Edwards Sapien-XT (ESXT), SAPIEN-3 (ES3), (Edwards Lifesciences Inc., Irvine, Calif, USA), Medtronic CoreValve Evolut R (Medtronic, Minneapolis, Minn, USA), Portico valve (Abbott Vascular, Santa Clara, Calif, USA), ACURATE neo (Boston Scientific, Marlborough, Mass, USA), and Myval (Meril Life Sciences, Gujarat, India). Annulus area (mm^2) and annulus perimeter (mm) derived from pre-procedural CTA imaging were used respectively for BE and SE valve sizing as recommended by manufacturers. Initially, the study population was divided into 2 groups as "borderline annulus" and "non-borderline annulus" according to their aortic annulus area or perimeter measured from the CTA records. Based on manufacturer recommendations while BE valves (ESXT, ES3, and Myval) have already grey zones, there is no grey zone or borderline annulus definition regarding annular sizing for SE valves. Similar to the grey zone definition in BE valve sizing, the native annulus sizes that are within 15% above or below the upper or lower limit of a particular SE prosthetic valve size are defined as the "borderline annulus" for SE valves.[11] Annular measurements, which are smaller than the manufacturers' recommended diameter for the smallest valve and larger measurements than the recommended diameter for the largest valve of each valve type were accepted as borderline annulus as well. Table 1 shows the accepted borderline annular areas and perimeters for each valve. For borderline cases, valve size selection was left to the implanter's choice based on individual decision-making. Unlike the Edwards Sapien valves, Myval (Meril Life Sciences, Gujarat, India) platform has intermediate-sized valves such as sizes of 21.5 mm, 24.5 mm, and 27.5 mm. Those patients with grey zone annulus and treated with intermediate-sized Myval THV were accepted as the non-borderline annulus group.

After determining the patients with borderline annulus, the study population was divided into 2 groups as "self-expandable valves" and "balloon-expandable valves." Afterward, borderline annulus group was also divided into 2 subgroups according to the smaller or larger THV selection as "undersized valve" and "oversized valve." Follow-up visits were recommended at 1 and 3 months, 6 and 12 months postoperatively, and on a yearly basis thereafter in our center. Echocardiographic examinations were done by Vivid S70 (General Electric Healthcare, Chicago, Ill, USA) and results of the third follow-up visit were obtained from the local hospital data system and analyzed for PVL and residual transvalvular gradients.

Comparisons between the groups "borderline annulus" versus "non-borderline annulus," "Self-expandable valves" versus "Balloon expandable valves" in the borderline annulus patient group, and "undersized valve" versus "oversized valve" in patients with borderline annulus were made. The decision for TAVR was made by a multidisciplinary heart team (composed of cardiac surgeons, interventional cardiologists, and a cardiac anesthesiologist) according to current recommendations and the procedures were performed according to standard techniques.[12,13] The Local Ethics Committee approved the study protocol.

Statistical Analysis

Data have been processed by means of the Statistical Package for Social Sciences 20.0 statistical package (SPSS Inc, Chicago, Ill, USA). To test the normal distribution of the variables Kolmogorov–Smirnov test was used. Continuous variables with normal distribution are expressed as mean ± standard deviation (SD) and compared by Student's *t*-test. Non-normally distributed data are presented as median and interquartile range (25%-75%) and compared by the

HIGHLIGHTS

- The hemodynamic results of the patients with borderline annulus were worse than non-borderline annulus patients regarding the paravalvular leakage and post-procedural transvalvular pressure gradient in the transcatheter aortic valve replacement procedure.
- Both the balloon expandable valves and self-expandable valves have similar results when annular measurements fall into borderline zones.
- Oversizing or undersizing the valve does not make any difference if again the annulus size is within the borderline zone.
- The impact of these results on clinical outcome should be evaluated with further studies.

Table 1. Borderline and Non-borderline Annular Areas and Perimeters for Each Valve

	Sapien-XT Annulus Area (mm^2)	SAPIEN-3 Annulus Area (mm^2)	Myval Annulus Area (mm^2)	Evolut R Annulus Perimeter (mm)	Portico Valve Annulus Perimeter (mm)	ACURATE Neo Annulus Perimeter (mm)
Non-borderline intervals	301-379 (23) 416-489 (26) 531-619 (29)	281-319 (20) 341-419 (23) 441-529 (26) 551-679 (29)	271-329 (20) 361-439 (23) 461-559 (26) 571-699 (29) 721-820 (32)	57.6-61.7 (23) 64.3-70.8 (26) 73.8-80.2 (29) 83.6-92.3 (34)	61.1-64.9 (23) 67.1-70.9 (25) 73.1-77.9 (27) 80.1-83.9 (29)	67.1-70.9 (S) 73.1-77.9 (M) 80.1-83.9 (L)
Borderline intervals	270-300 380-415 490-530 620-650	260-280 320-340 420-440 530-550 680-710	250-270 330-360 440-460 560-570 700-720	54.5-57.5 61.8-64.2 70.9-73.7 80.3-83.5 92.4-96.0	59-61 65-67 71-73 78-80 84-86	65-67 71-73 78-80 84-86

Mann–Whitney *U* test. Categorical data are presented as frequencies and percentages and compared using the chi-square test. A *P*-value <.05 was considered significant. All authors have read and agreed to the manuscript as written.

RESULTS

Baseline and Periprocedural Characteristics

The study population consisted of 338 patients with severe aortic stenosis who underwent the TAVR procedure. Of these 338 patients, 157 (46.4%) were male and 181 (53.6%) were female. The mean age of the study population was 77.98 ± 7.97 years and the mean preprocedural mean transvalvular pressure gradient (PG) was 48.51 ± 11.60 mm Hg. According to pre-interventional CTA imaging, 102 (30.1%) patients had a borderline annulus size and the remaining 226 (69.9%) patients had non-borderline annulus size. Baseline demographical characteristics are presented in Table 2. There were no significant differences in baseline characteristics between the groups borderline annulus and non-borderline annulus. Procedural and postprocedural characteristics of the study population and the 2 groups are shown in Table 3. The number of the valves implanted for ESXT, ES3, Evolute R, Portico Valve, ACURATE neo, and Myval were 108 (32.0%), 24 (7.1%), 137 (40.5%), 22 (6.5%), 9 (2.79%), and 38 (11.2%), respectively. The distribution of the implanted valves among the study population is shown in Figure 1. Procedural complications are also shown in Table 3 and there were no significant differences between the groups.

Postprocedural Echocardiographic Results

Regarding postprocedural echocardiographic evaluation, the maximum transvalvular pressure gradient was significantly higher in the borderline annulus group than in the non-borderline annulus group (17.81 ± 7.15 vs. 14.44 ± 6.27, *P* < .001). The echocardiographic assessment of postprocedural PVL also revealed a higher frequency of PVL in the borderline annulus group than in the non-borderline annulus group (Table 4). The frequency of more than minimal PVL was higher in the borderline annulus group than non-borderline annulus group (for mild, mild to moderate, and moderate, 40.2%, 11.8%, and 2.9% vs. 18.8%, 6.7%, and 0.4%, respectively) and the frequency of less than mild PVL (absent and minimal, 40.6% and 33.5% vs. 21.6% and 23.5%, respectively) was higher in the non-borderline annulus group than borderline annulus

Table 2. Baseline Characteristics of the Study Population

	Study Population (n = 338)	Non-borderline Annulus (n = 226)	Borderline Annulus (n = 102)	*P*
Male gender	157 (46.4%)	107 (47.3%)	50 (49.0%)	.533
Age, years	77.98 ± 7.97	78.42 ± 7.69	76.95 ± 8.53	.118
LVEF, %	53.48 ± 14.66	54.21 ± 13.83	51.87 ± 16.32	.204
Preprocedural mean transvalvular PG, mm Hg	48.51 ± 11.60	48.50 ± 11.39	48.53 ± 12.11	.656
Aortic annulus area (mm^2)	471.50 ± 95.90	463.90 ± 87.66	488.78 ± 110.95	.290
Aortic annulus perimeter, mm	77.56 ± 33.55	77.74 ± 40.05	77.15 ± 9.20	.882
History of CAD, n (%)	156 (46.7)	112 (47.9)	44 (44.0)	.517
Diabetes mellitus, n (%)	105 (31.8)	76 (33.0)	29 (29.0)	.469
Hypertension, n (%)	171 (51.4)	118 (50.6)	53 (53.0)	.693
CRD, n (%)	25 (7.6)	12 (5.2)	13 (13.0)	.150
White blood cell (10^3/μL)	7.27 ± 2.08	7.26 ± 2.03	7.28 ± 2.20	.936
Hematocrit (%)	36.33 ± 5.02	36.45 ± 4.88	36.06 ± 5.34	.527
Platelet count (10^3 / μL)	219.82 ± 74.93	218.83 ± 71.66	222.04 ± 82.11	.722

Values are mean ± SD, n (%).
LVEF, left ventricular ejection fraction; CRD, chronic renal disease; CAD, coronary artery disease; SD, standard deviation.

Table 3. Procedural and Periprocedural Characteristics

	Study Population (n = 338)	Non-borderline Annulus (n = 226) (66.8%)	Borderline Annulus (n = 102) (30.1%)	*P*
Valve type, n (%)				
Sapien-XT	108 (32.0)	83 (36.7)	25 (24.5)	.056
SAPIEN-3	24 (7.1)	13 (5.7)	11 (10.7)	
Evolut R	137 (40.5)	96 (42.4)	41 (40.1)	
Portico valve	22 (6.5)	12 (5.3)	10 (9.8)	
ACURATE neo	9 (2.7)	4 (1.7)	5 (4.9)	
Myval	38 (11.2)	28 (12.3)	10 (9.8)	
Balloon dilation, n (%)				
No dilation	86 (25.4)	46 (20.3)	40 (39.2)	.001
Predilation	173 (51.1)	131 (57.9)	42 (41.1)	
Postdilation	27 (7.9)	17 (7.5)	10 (9.8)	
Pre+post-dilation	52 (15.3)	42 (18.5)	10 (9.8)	
Complications, n (%)				
Vascular complications (major)	5 (1.4)	3 (1.3)	2 (1.9)	.956
Vascular complications (minor)	24 (7.4)	17 (7.5)	7 (7.1)	.921
Stroke (disabling)	5 (1.5)	3 (1.3)	2 (1.9)	.640
Pacemaker implantation	22 (6.5)	17 (7.5)	5 (4.9)	.566
Acute Kidney Injury	14 (4.2)	9 (3.9)	5 (4.9)	.767
Valve pop-out	5 (1.4)	3 (1.3)	2 (1.9)	.640
Device embolization	2 (0.5)	1 (0.4)	1 (0.9)	.302
Cardiac rupture	1 (0.2)	1 (0.4)	0 (0)	1.000
Postprocedural maximum transvalvular PG, mm Hg	15.49 ± 6.73	14.44 ± 6.27	17.81 ± 7.15	<.001

group (*P* < .001). Severe PVL did not occur in any of our study patients.

For the borderline annulus group, comparisons between the BE valves versus SE valves and oversizing the valve versus undersizing the valve were also done. Regarding the both maximum TVG and PVL, there were no significant differences between the group BE valves and SE valves (*P* values were .429 and .240, respectively) (Table 5). When comparing the oversizing versus undersizing, there were again no differences between the 2 groups regarding the maximum TVG and PVL (*P* values were .878 and .317, respectively) (*P* > .05 for both) (Table 6). Hemodynamic data of each valve across the oversizing and undersizing categories in borderline annulus patients were also given in supplement (Supplementary Table 1), and no significant differences were found between these 2 groups among the different types of valves.

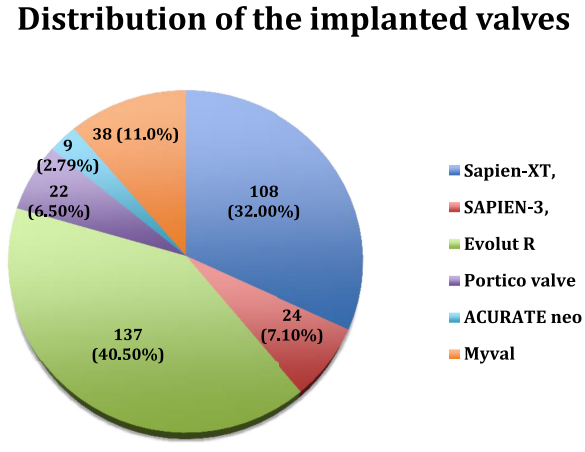

Figure 1. Distribution of the implanted valves among the study population.

DISCUSSION

The present study is the first to demonstrate 3 main findings. First, the results of the patients with borderline annulus were worse than non-borderline annulus patients regarding the PVL and postprocedural transvalvular pressure gradient in the TAVR procedure. Second, both the BE valves and SE valves have similar results when annular measurements fall into borderline zones. And third, oversizing or undersizing the valve does not make any difference if again the annulus size is within the borderline zone.

After obtaining promising results in the intermediate and even in the low-risk population, progressive expansion of TAVR indications toward younger and lower-risk patients seems to be inevitable and long-term durability of the valves becomes an increasingly important issue.[3,14,15] Despite these promising results, several advantages, and rapidly increasing popularity, concerns are also raised about the durability of THVs due to the relatively short-term follow-up of these patients. The durability of a THV depends on

Table 4. Comparison of Echocardiographic Results of the Non-borderline Annulus Versus Borderline Annulus

	Non-borderline Annulus (n = 226)	Borderline Annulus (n = 102)	*P*
Paravalvular leakage, n (%)			
Absent	91 (40.6)	22 (21.6)	<.001
Minimal	75 (33.5)	24 (23.5)	
Mild	42 (18.8)	41 (40.2)	
Mild to moderate	15 (6.7)	12 (11.8)	
Moderate	1 (0.4)	3 (2.9)	
Moderate to severe	0 (0)	0 (0)	
Postprocedural maximum transvalvular PG, mm Hg	14.44 ± 6.27	17.81 ± 7.15	<.001

Table 5. Comparison of Echocardiographic Results of BE and SE Valves in Patients with Borderline Annulus

	BE Valve (n = 46)	SE Valve (n = 56)	*P*
Paravalvular leakage, n (%)			
Absent	14 (30.4)	8 (14.3)	.240
Minimal	11 (23.9)	13 (23.2)	
Mild	15 (32.6)	26 (46.4)	
Mild to moderate	4 (8.7)	8 (14.3)	
Moderate	2 (4.3)	1 (1.8)	
Moderate to severe	0 (0)	0 (0)	
Postprocedural maximum transvalvular PG, mm Hg	18.43 ± 7.61	17.30 ± 6.77	.429

BE, balloon-expandable; SE, self-expandable.

several factors such as aortic calcification, valve geometry and morphology and type of expansion, and patient-prosthesis mismatch.[16]

Several previous reports revealed that THVs are related to higher frequencies of valve deterioration when compared to surgical valves, mainly because of the higher PVL which is one of the major drawbacks of this procedure.[17,18] As a result, preprocedural imaging and optimal THV sizing became an essential step providing improved long-term results and outcomes.[19] Appropriate sizing with pre-procedural imaging plays a crucial role in the determination of accurate valve sizing, and it is not only related with the long-term results but also it is related to the prevention of severe complications such as annular rupture, obstruction of coronary ostia, atrioventricular block, or valve embolization.[20,21]

In daily practice, patient annulus areas or perimeters can commonly fall into the grey zone between 2 THV sizes for BE or very close to borderline numbers for SE THVs. Furthermore, intra- and inter-observer variability regarding the annulus measurements may sometimes lead to such uncertain situations. In such circumstances, clinical decision-making may be very challenging and is often left to the operator's discretion based on parameters such as calcification, risk of annular rupture, the anticipation of the degree of PVL, and sinus valsalva dimensions.[9,10] The degree of under- or over-sizing impacts the deployed THV shape and leaflet coaptation and both oversized and undersized valves can lead to undesirable long-term results and periprocedural complications.

An undersized THV increases the risk of both paravalvular regurgitation and residual transvalvular pressure gradient due to patient-prosthesis mismatch. It can also lead to migration of the valve through the ventricle or aorta.[22] From a hemodynamics standpoint, it is expected that larger THVs decrease the risk of residual transvalvular gradient

Table 6. Comparison of Over-sizing Versus Under-sizing in Patients with Borderline Annulus

	Oversizing (n = 56)	Undersizing (n = 46)	*P*
Paravalvular leakage, n (%)			
Absent	10 (17.9)	12 (26.1)	.317
Minimal	13 (23.2)	11 (23.9)	
Mild	25 (44.6)	16 (34.8)	
Mild to moderate	5 (8.9)	7 (15.2)	
Moderate	3 (5.4)	0 (0)	
Moderate to severe	0 (0)	0 (0)	
Postprocedural maximum transvalvular PG, mm Hg	17.74 ± 8.21	17.93 ± 5.80	.878

and PVL and maximizes effective orifice area to decrease patient–prosthesis mismatch. However, choosing the larger valve which may seem to be the "safe" solution may also increase the risk of PVL and residual transvalvular pressure gradient when the optimal expansion of the valve cannot be achieved due to the relatively narrow annulus and heavy calcification.[23] Moreover, oversized valves may be related to mechanical complications such as coronary occlusion or rupture of the annulus area, which is usually accompanied by increased mortality and increased rate of permanent pacemaker implantation due to the compression of the conduction system.[19,24]

These challenges may be even more prominent in patients with borderline annulus, and the aim of the present study was to determine whether borderline annulus has an impact on results in clinical practice. There are very limited data regarding the patients with grey zone or borderline annulus. Patsalis et al[11] reported the data of 246 TAVR procedures with the BE bioprosthesis in grey zone annulus (ES3). They compared the procedural techniques of conventional sizing and nominal filling versus undersizing but overfilling in patients with grey zone aortic annulus. According to the results of this study, undersizing but overfilling was related to decreased PVL and mean postprocedural transvalvular pressure gradient and reduced incidence of annular rupture. Conversely, Xuan et al[25] evaluated the impact of THV size on leaflet stress in patients with grey zone annulus and implanted ESXT valves. Leaflet stress is considered to be related to accelerated valve degeneration and shorter durability according to the previous reports.[26,27] They concluded the study that for "grey zone" sizes, undersizing the larger THV resulted in lower leaflet stresses than oversizing the smaller THV.

Available data for grey zone annulus patients are limited to these 2 studies with balloon-expandable valves and our study is the first to define the borderline annulus term in SE valves. According to our results, the borderline annulus is not only a trouble for BE valves but also for SE valves which yields similar sub-optimal results in borderline annulus patients. Regardless of the type of valve used, either BE or SE, and under or oversizing the valves, the results of the borderline annulus patients were worse than non-borderline annulus patients.

According to our study result regarding the TVG, slight difference between the groups borderline and nonborderline annulus was statistically significant. This discrepancy may possibly stem from the inappropriate valve selection due to the challenging sizing in borderline annulus patients. Although it may indicate a better hemodynamic profile in the non-borderline annulus group, its impact on long-term clinical outcome is not clear. The cut-off point for an unacceptable postprocedural gradient is controversial in TAVR patients. In most previous studies evaluating this issue, ≥20 mmHg of mean TVG is accepted as a threshold for diagnosis of both patient prosthesis mismatch or structural valve deterioration and such high TVG was found to be related to worse clinical outcomes.[28] However, none of the patients in our study population had such high TVGs. Moreover, similar to TVG, the borderline annulus group had worse outcomes compared to non-borderline annulus group regarding the frequency of PVL. But again, the degree of PVLs in both groups was not that high grade (mostly less than moderate). Therefore, it seems not possible to speculate about long-term clinical outcome with our results. When discussing the outcomes of TAVR procedure, it is inevitable to mention the importance of experience as in all cardiac and non-cardiac procedures. Improved procedural results with greater TAVR experience have been described in several reports before. Wassef et al[29] reported that at least 225 procedures are required to optimize mortality rates for TAVR and procedural complications continue to decrease beyond the 225 case volume. According to this study, annual institutional volume of <50 procedures per year was associated with worse clinical and procedural outcomes. A significant number of initial cases of our institution could not be included in our study population due to the lacking data. From this point of view, most of the procedures evaluated in this present study were performed during the time period when our center was relatively more experienced. Therefore, lack of patients with more severe TVGs and PVLs in our study population may be attributable to institutional experience.

Most surprising finding of our study was the similar results regarding the PVL and TVG for both oversizing and undersizing groups in the borderline annulus patients. It is expected that while undersized valves increase the risk of both high PVL and TVG due to patient–prosthesis mismatch, larger valves decrease the risk of TVG and PVL and maximize effective orifice area. However, our results seem to be not consistent with this theory. We think that underlying mechanisms of similar results regarding the PVL and residual transvalvular gradient for both undersized and oversized valve groups were hypothetically, annulus–prosthesis mismatch for undersized valves and sub-optimal expansion of the valve due to the relatively narrow annulus and heavy calcification for oversized valves. It may also be due to experience in valve selection taking the patient and valve characteristics into consideration.

Another remarkable finding of the present study was that there was no significant difference between the group BE valves and SE valves in terms of both maximum transvalvular pressure gradient and PVL in patients with borderline annulus. Previous reports showed controversial results regarding a direct comparison of BE versus SE valves. The SOLVE TAVI trial showed non-inferiority between the 2 groups for mean transvalvular gradient and rates of PVL.[30] However, according to the data from PARTNER 3 and Evolut Low-Risk trials, more-than-mild PVL seems to be more frequent in SE than in BE devices (5.7% vs. 0.6%), and these findings were consistent with the recently published FRANCE-TAVI registry.[3,14,17,18]

While all these debates are going on for borderline annulus patients, among the BE valve family, Meril has announced the availability of intermediate sizes as a huge step in minimizing patient prosthetic mismatch.[31] Although this step hypothetically seems to be very promising among patients with the

borderline annulus, long-term data are needed to support this statement. Borderline annulus issue is not speculated yet among the SE valve family. However, we think that the results of our study may help arising the question of the need for intermediate sizes in SE THVs. We think that the aortic annulus or the aortic valve as one of the most extremely important anatomical structures for a human body deserves a much more careful and detailed evaluation. For instance, an atrial septal occluder device which is implanted in a relatively size-tolerant anatomy has sizes of 1 mm increments up to 20 mm and 2 mm increments over 20 mm.

Hereby, based on the results of our study and very limited previous data about borderline annulus patients, it does not seem possible to make certain recommendations regarding valve selection and procedural steps. For BE valves although the undersizing but overfilling strategy sounds like a reasonable strategy in most cases, the study by Xuan et al[25] has conflicting results to make such a recommendation. As a matter of fact, SE valves do not have such an option as underfilling or overfilling. Nevertheless, in patients with heavy calcification especially extending to the annulus, bicuspid valves and narrow sinus valsalva with low coronary ostial height, preferring an undersized valve seem to be a reasonable and safe approach. On the contrary, less amount of valvular calcification, larger sinus valsalva dimensions, and acceptable coronary heights should encourage the operator to choose an oversized valve. Although it may not be available in every country, Meril's Myval valve with intermediate-size valve dimensions may also be an option for these patients with borderline annulus. Perhaps, in the future, remaining companies' consideration of increasing the diversity of valve sizes may minimize the problems encountered in this patient group. As a result, with the available valve size options we have today, in patients with borderline annulus, it seems the most reasonable approach to make a decision based on the criteria which we still use and mostly based on our clinical experience.

Study Limitations

Our study has some important limitations. First and foremost, it has a retrospective, non-randomized and single-center design. Because of the non-randomized design, valve size selection for borderline annulus patients was left to the operator's discretion. Because of the missing data such as underfilling or overfilling for significant proportion of patients, these procedural details for BE valve implantations could not be given and discussed. This study did not take into account the long-term results. Impact of institutional experience on TAVR outcomes is unquestionable; therefore, these results may not be applicable to every center. Thus, the results of this study may not be extrapolated to long-term arguments. Because there is no standardized borderline annulus definition for SE valves, our method of determining the borderline annulus in this group is open to criticism. In borderline annulus, several factors such as degree of calcification, bicuspid valves, sinüs valsalva dimensions, and operator or institutional preference may affect the decision of valve selection. Moreover, a patient with borderline annulus for a specific valve type may not fall into borderline zone for a different valve type. These issues may be accepted as confounding points when evaluating the study results. Further clinical studies with the prospective and randomized design will be needed to support our findings. Despite these limitations, we believe that our results indicate a need for further studies.

CONCLUSION

In conclusion, regardless of the valve type either BE or SE valve, and whether oversizing or undersizing the valve, the borderline annulus is related to significantly higher transvalvular pressure gradient and PVL when compared to non-borderline annulus sizes in TAVR procedure. Both of these 2 criteria are considered to be associated with long-term outcomes in TAVR. However, our findings need to be supported by further prospective and randomized studies including a large number of patients and a long-term follow-up period. We strongly believe that our results will inspire future studies evaluating this subject.

Ethics Committee Approval: University of Health Sciences Gülhane Training and Research Hospital Ethics (Committee date: April 05, 2022, decision no: 2022/14).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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Supplementary Table 1. Hemodynamic data of each valve across the oversizing and undersizing categories in borderline annulus patients

Valve type		Oversizing (n = 56)	Undersizing (n = 46)	*P*
Sapien-XT	***Paravalvular leakage, n (%)***			
	Absent	5 (31.2%)	2 (22.2%)	N/A
	Minimal	2 (12.5%)	3 (33.3%)	
	Mild	5 (31.2%)	2 (22.2%)	
	Mild to Moderate	2 (12.5%)	2 (22.2%)	
	Moderate	2 (12.5%)	0 (0%)	
	Postprocedural maximum transvalvular PG, mm Hg	15.68 ± 5.94	19.88 ± 8.16	0.151
SAPIEN-3	***Paravalvular leakage, n (%)***			
	Absent	1 (25.0%)	3 (42.9%)	N/A
	Minimal	1 (25.0%)	1 (14.3%)	
	Mild	2 (50.0%)	3 (42.9%)	
	Mild to Moderate	0 (0%)	0 (0%)	
	Moderate	0 (0%)	0 (0%)	
	Postprocedural maximum transvalvular PG, mm Hg	21.25 ± 11.87	18.28 ± 2.28	0.522
Evolut R	***Paravalvular leakage, n (%)***			
	Absent	2 (10.0%)	5 (23.8%)	N/A
	Minimal	3 (15.0%)	6 (28.6%)	
	Mild	13 (65.0%)	7 (33.3%)	
	Mild to Moderate	1 (5.0%)	3 (14.3%)	
	Moderate	1 (5.0%)	0 (0%)	
	Postprocedural maximum transvalvular PG, mm Hg	17.95 ± 8.94	17.14 ± 5.89	0.734
Portico valve	***Paravalvular leakage, n (%)***			
	Absent	0 (0%)	1 (33.3%)	N/A
	Minimal	2 (28.6%)	1 (33.3%)	
	Mild	3 (42.9%)	1 (33.3%)	
	Mild to Moderate	2 (28.6%)	0 (0%)	
	Moderate	0 (0%)	0 (0%)	
	Postprocedural maximum transvalvular PG, mm Hg	13.85 ± 3.97	18.66 ± 5.50	0.153
ACURATE neo	***Paravalvular leakage, n (%)***			
	Absent	1 (50.0%)	0 (0%)	N/A
	Minimal	1 (50.0%)	1 (33.3%)	
	Mild	0 (0%)	2 (66.7%)	
	Mild to Moderate	0 (0%)	0 (0%)	
	Moderate	0 (0 %)	0 (0%)	
	Postprocedural maximum transvalvular PG, mm Hg	17.50 ± 3.53	20.66 ± 2.30	0.300
Myval	***Paravalvular leakage, n (%)***			
	Absent	2 (28.6%)	1 (33.3%)	N/A
	Minimal	4 (57.1%)	0 (0%)	
	Mild	1 (14.3%)	2 (66.7%)	
	Mild to Moderate	0 (0%)	0 (0%)	
	Moderate	0 (0%)	0 (0%)	
	Postprocedural maximum transvalvular PG, mm Hg	23.57 ± 10.08	13.33 ± 5.03	0.141

N/A, not applicable