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Transcatheter aortic valve implantation and its impact on mitral valve geometry and function

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Abstract

Background: The aim of this study was to evaluate the impact of transcatheter aortic valve implantation (TAVI) on mitral valve geometry and function.

Methods: Eighty-four patients underwent TAVI. Forty-four (52%) patients received a balloon-expandable valve and 40 (48%) were implanted with a self-expandable valve. All patients underwent three-dimensional-volumetric transesophageal echocardiography of the mitral valve before and immediately after TAVI. A dedicated software was used for assisted semiautomatic measurement of mitral annular geometry.

Results: During systole, the anterior to posterior (AP) diameter was significantly reduced after the procedure (3.4 ± 0.5 cm vs 3.2 ± 0.5 cm; $P < .05$). The mitral annular area (10.8 ± 2.8cm^2 vs 9.9 ± 2.6cm^2; $P < .05$) as well as the tenting area (1.6 ± 0.7 cm^2 vs 1.2 ± 0.6 cm^2; $P < .001$) measured at mid-systole were reduced after TAVI. Diastolic measures were similar. Patients treated with balloon-expandable valves showed a significantly larger reduction in the AP diameter compared to self-expandable valves (−0.25 cm vs −0.11 cm; $P < .05$). The reduction of the annular area was higher in the balloon-expandable group (−1.2 ± 1.59 vs −0.22 ± 1.41; $P < .05$). Grade of mitral regurgitation did improve or remained stable after TAVI.

Conclusion: TAVI significantly impacts the mitral valve and mitral annular geometry and morphology. The choice of the prosthesis (balloon- vs self-expandable) may be relevant for those changes.

KEYWORDS

3D echocardiography, aortic valve replacement, mitral annular geometry, mitral regurgitation, transcatheter aortic valve implantation (TAVI)

Abbreviations: ALPM diameter, anterolateral to posteromedial diameter of the mitral valve annulus; AP diameter, anterior to posterior diameter of the mitral valve annulus; MR, mitral regurgitation; TA, transapical; TAVI, transcatheter aortic valve implantation; TOE, transesophageal echocardiography.

Alexander Meyer and Dustin Greve contributed equally to the study.
Jörg Kempfert and Simon H Sündermann are senior authors.

1 | INTRODUCTION

A relevant number of patients with severe aortic stenosis suffers from functional mitral regurgitation (MR).[1,2] Improvement in MR after aortic valve interventions has been described.[3,4] A common explanation for this phenomenon is the reduced end-systolic load and pressure immediately after aortic valve replacement in patients with aortic stenosis and the long-term positive effects of reverse remodeling.[5] Due to the proximity of the aortic and mitral valve annulus, mechanical interactions affecting the aortomitral curtain may also be relevant modifiers of this effect. Changes in mitral annular geometry are known to affect the coaptation area and thereby function of the valve.[6] Changes in the degree of MR may also depend on the changes in mitral annular geometry after transcatheter aortic valve implantation (TAVI).[5] While this has been consistently described for patients undergoing conventional open surgical aortic valve replacement (SAVR),[7,8] studies in TAVI populations have shown contradictory results in this regard.[9,10] The aim of this study was to identify changes of the mitral annular geometry after TAVI procedures and to describe their potential impact on functional changes of the mitral valve using a dedicated software (4D MV-ASSESSMENT; Tomtec Imaging Systems GmbH, Unterschleissheim, Germany) for advanced four-dimensional (4D)-image analysis of preinterventional and postinterventional transesophageal echocardiography (TOE) of the mitral valve.

2 | METHODS

2.1 | Study population

This study was approved by the local ethics committee of the Charité—Universitätsmedizin Berlin (EA4/095/18). From May 2015 to June 2017, a total of 404 patients underwent an elective TAVI procedure at the German Heart Center Berlin and were screened for this study. All patients were prospectively enrolled in the TAVI database of the German Heart Center Berlin. For the study, the database was screened for patients who had a three-dimensional (3D)-TOE before and after the intervention. Data extraction and image analysis were performed in a retrospective manner. All patients who had a TAVI procedure at the German Heart Center Berlin and had preinterventional and post-interventional 3D-TOE of the mitral valve with sufficient imaging quality and quantity were eligible for the study. Exclusion criteria were: previous surgery on the aortic valve and interventions on the mitral valve, such as ring annuloplasty and mitral valve replacement. Fourteen patients were excluded due to previous procedures affecting the aortic valve or the MV apparatus. In addition, 240 patients were not eligible due to lack of complete preoperative or postoperative 3D-TOE data or lack of sufficient image quality. Additionally, 66 patients who underwent analgosedation with local anesthesia were excluded due to consecutive missing TOE examination. Hence, 84 patients were eligible for this study (Figure 1).

Around half of the patients had implantation of a balloon-expandable valve (Edwards SAPIEN 3; n = 44; 52%). All other patients had implantation of a self-expandable prosthesis, (Symetis ACURATE Neo; n = 12; 14%), Boston Scientific LOTUS (n = 6; 7%), St Jude Medical Portico (n = 8; 10%), Corevalve Evolut R (n = 11; 13%), Biotronik BIOVALVE (n = 2; 2%), and Direct Flow Medical, Inc (n = 1; 1%). Other comorbidities and baseline characteristics are shown in Table 1.

2.2 | TAVI procedure and echocardiographic assessment

TOE was routinely performed in cases with TAVI under general anesthesia. Besides the assessment of the aortic valve, evaluation of the mitral valve was performed during the standard TOE protocol. Imaging of the mitral valve was done preoperatively and postoperatively. The images were prospectively stored followed by image analysis at a later stage.

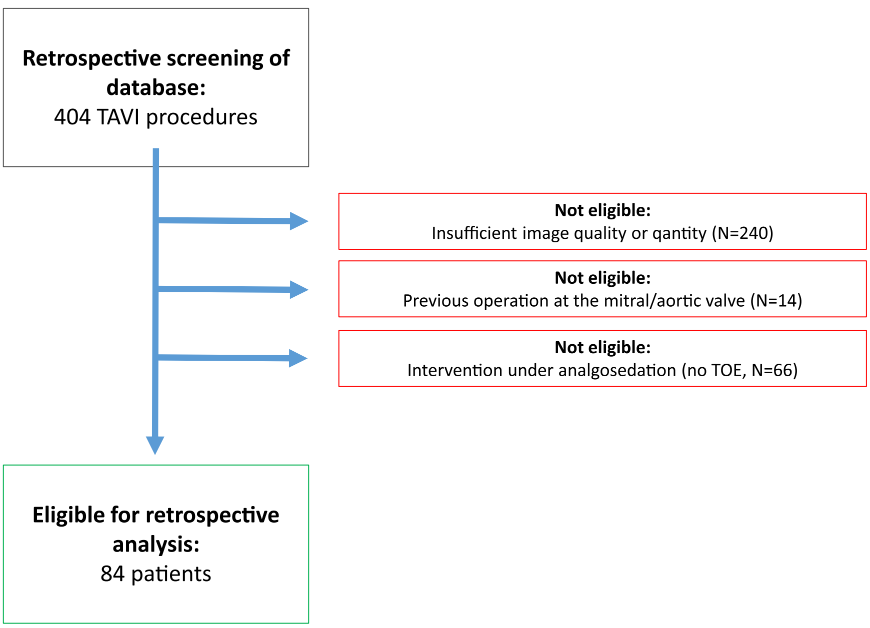


FIGURE 1 Screening process. TAVI, transcatheter aortic valve implantation; TOE, transesophageal echocardiography

TABLE 1 Characteristics of the study population

N	84
Female, n (%)	30 (35.7)
Age, mean (SD)	79.00 (7.32)
BMI, mean (SD)	28.16 (6.13)
Procedure, n (%)	
TAVI TA	20 (23.8)
TAVI TF	62 (73.8)
TAVI transaortic	1 (1.2)
TAVI transaxillary	1 (1.2)
Prosthesis, n (%)	
Self-expanding	40 (48)
Biovalve	2 (2)
Direct flow	1 (1)
EvolutR	11 (13)
Lotus	6 (7)
Portico	8 (10)
Symetis	12 (14)
Balloon-expanding	44 (52)
Sapien 3	44 (52)
Comorbidities, n (%)	
Peripheral artery disease	24 (29)
COPD	20 (24)
Diabetes	21 (25)
Coronary artery disease	34 (40)
NYHA	
I	0
II	10 (12)
III	48 (57)
IV	7 (8)
N.N	19 (23)
Atrial fibrillation	23 (27)
Echo characteristics	
LVEF, mean (SD)	49.24 (14.39)
LVEDD, mean (SD)	47.41 (8.08)
MR ≥ 2, n (%)	16 (19)
Risk scores	
EuroSCORE I, mean (SD)	10.78 (3.73)
Logistic EuroSCORE, mean (SD)	18.08 (12.15)
EuroSCORE II, mean (SD)	8.23 (8.61)
STS Score mortality, mean (SD)	6.85 (7.12)

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; N.N, no information available; NYHA, New York Heart Association Functional Classification; TA, transapical; TAVI, transcatheter aortic valve implantation; TF, transfemoral.

Four to six cardiac cycles were captured to generate high-resolution images with an average of 19 frames per cardiac cycle, which were then used to reconstruct and measure the mitral annulus. Preoperative recordings were assessed after induction of anesthesia right at the beginning of the procedure before any manipulation of the heart. Postoperative TOE was performed after the confirmation of the final valve position and with the patient experiencing stable hemodynamics. All 3D-TOE examinations were carried out by a senior anesthesiologist with high expertise in TOE using either a Phillips EPIQ 7 (Philips Health System, Bothell, WA) or a GE Vivid E9 (GE Healthcare, Wauwatosa, WI) ultrasound system equipped with 3D-capable ultrasound probes. To evaluate the preprocedural and postprocedural degree of MR intraprocedural TOE recordings, as well as TTE recordings assessed during the hospitalization before discharge were reviewed and classified as none, mild, moderate, or severe (0-3). The grading was performed by a single investigator (DG) and reviewed by another investigator (SHS), who retrospectively assessed all the available preoperative and postoperative echocardiographic images. Grading was done according to the current guideline definitions.[11,12]

2.3 | Postprocessing and measurement of annular geometry

The TOMTEC ImageArena (TomTec Imaging Systems GmbH, Unterschleißheim, Germany) software provides a "4D MV-Assessment" tool, which was used for the reconstruction of the mitral valve annulus. The software allows for semiautomatic measurement of a variety of static and dynamic parameters of the mitral annulus. Required landmarks were determined under the following conditions and order: (1) long-axis view showing a mid-systolic frame, (2) determination of the first four annular landmarks—setting up the anterior, posterior, anterolateral, and posteromedial boundaries of the annulus, (3) alignment to the aortic valve, and (4) determination of the coaptation point, and (5) a reference point on the aortic root.

All examinations in ImageArena were performed by a single investigator (DG). Previous studies have shown that this method of image analysis needs to have high reliability regarding intraobserver and interobserver, reproducibility.[13] The tool was adapted by the user to track the parameters during systole and diastole. Diastolic values of parameters that were rendered unusable were discarded (ie, tenting parameters).

The examined parameters were: anterior to posterior diameter (AP), anterolateral to posteromedial (ALPM) diameter, sphericity index (AP diameter/ALPM diameter), nonplanar angle, circumference, the annular area in 2D and 3D, annular height, tenting volume (during systole), commissural diameter, posterior leaflet angle, tenting height (during systole), tenting area (during systole), the angle from the mitral annulus to the aortic annulus, annular displacement, and displacement velocity. As an example, the assessment of AP diameter, pre- and post-TAVI, is shown in Figure 2 and in the online Supporting Information.

2.4 | Statistical analysis

Raw data from the ImageArena was exported and processed to allow comparability of the measurements. To deal with varying frame

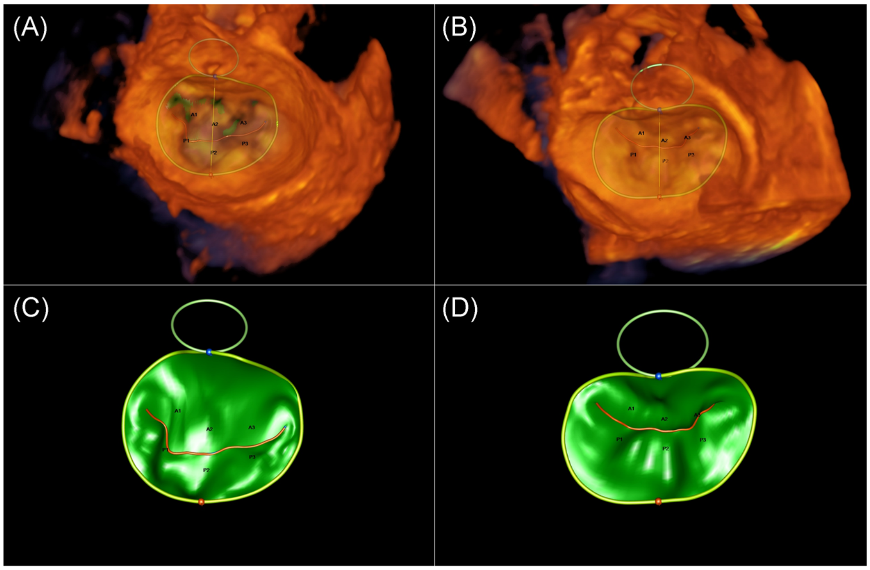


FIGURE 2 Images from the mitral annular assessment with the TomTec 4D Mitral Valve assessment tool. A,B, Three-dimensional visualization of the mitral valve with the measurement of the AP diameter pretranscatheter aortic valve implantation (TAVI; A) and after TAVI implantation (B). A1 to A3 and P1 to P3 are the parts of the anterior and posterior mitral leaflets. C,D, Automatic assessment of the area of the mitral annulus (C) pre- and (D) post-TAVI implantation. A1 to A3 and P1 to P3 are the parts of the anterior and posterior mitral leaflet

numbers per cycle, the data were transformed as briefly described: The raw echocardiographic data consists of two variables per measured parameter, where *x* designates the time of measurement in milliseconds from the start of the heart cycle and *y* designates the actual measured value. Time *x* was scaled to a decimal range of zero to one (Figure 3), so that the start of the systole corresponds to $x = 0$ and the end to $x = 1$. The same scaling was applied to diastolic measurements. The start times of the cycles were defined by an electrocardiography trigger-point. The time standardized measurements were interpolated via cubic spline at 80 equally spaced points per cycle spanning the range 0 to 1 (Figure 3).

This approach results in 214 240 interpolated and comparable values at any point of time in the heart cycle. Baseline data was gathered from the institutional TAVI database and by reviewing surgery reports. The analysis was performed for systole and diastole, as well as for the entire cardiac cycle. Subgroups were formed for the implanted prosthesis to compare changes of annular geometry in 44 balloon-expanded vs 40 self-expanding valves. Data were presented as means with standard deviation for continuous variables. The Student *t* test was used to compare means of continuous variables for paired groups. At a *P* value of less than .05, results were rated significant. Statistical analyses were performed using R 3.4.2 (R Development Core Team. R: A Language and Environment for Statistical Computing11); data preparation, processing, and plotting were supported by tidyverse packages.[14]

3 | RESULTS

3.1 | Changes of the mitral valve geometry before and after TAVI

At mid-systole, AP diameter was significantly reduced after the procedure (3.42 ± 0.50 cm vs 3.24 ± 0.52 cm; $P = .02$), while the anterolateral-posteromedial (ALPM) diameter (3.77 ± 0.48 cm vs 3.66 ± 0.46 cm; $P = .123$) was not. Area of the mitral annulus at mid-systole was significantly smaller after TAVI (10.8 ± 2.83 cm^2 vs 9.94 ± 2.64 cm^2; $P = .044$) and the angle between aortic and mitral annulus was significantly less steep after the procedures ($128.8 \pm 14.09°$ vs $137.18 \pm 14.45°$; $P < .001$). The sphericity index reduced significantly (0.91 ± 0.07 vs 0.88 ± 0.07; $P = .032$), as well as the annular height (0.79 ± 0.24 cm vs 0.64 ± 0.19 cm; $P < .001$). Annular displacement and displacement velocity did not differ significantly before and after implantation of the prosthesis during systole. Analysis at mid-diastole revealed similar observations (Table 2 and Figure 4; a table in the online Supporting Information shows an overview of all measured parameters) indicating that mitral valve geometry undergoes substantial changes after TAVI procedures.

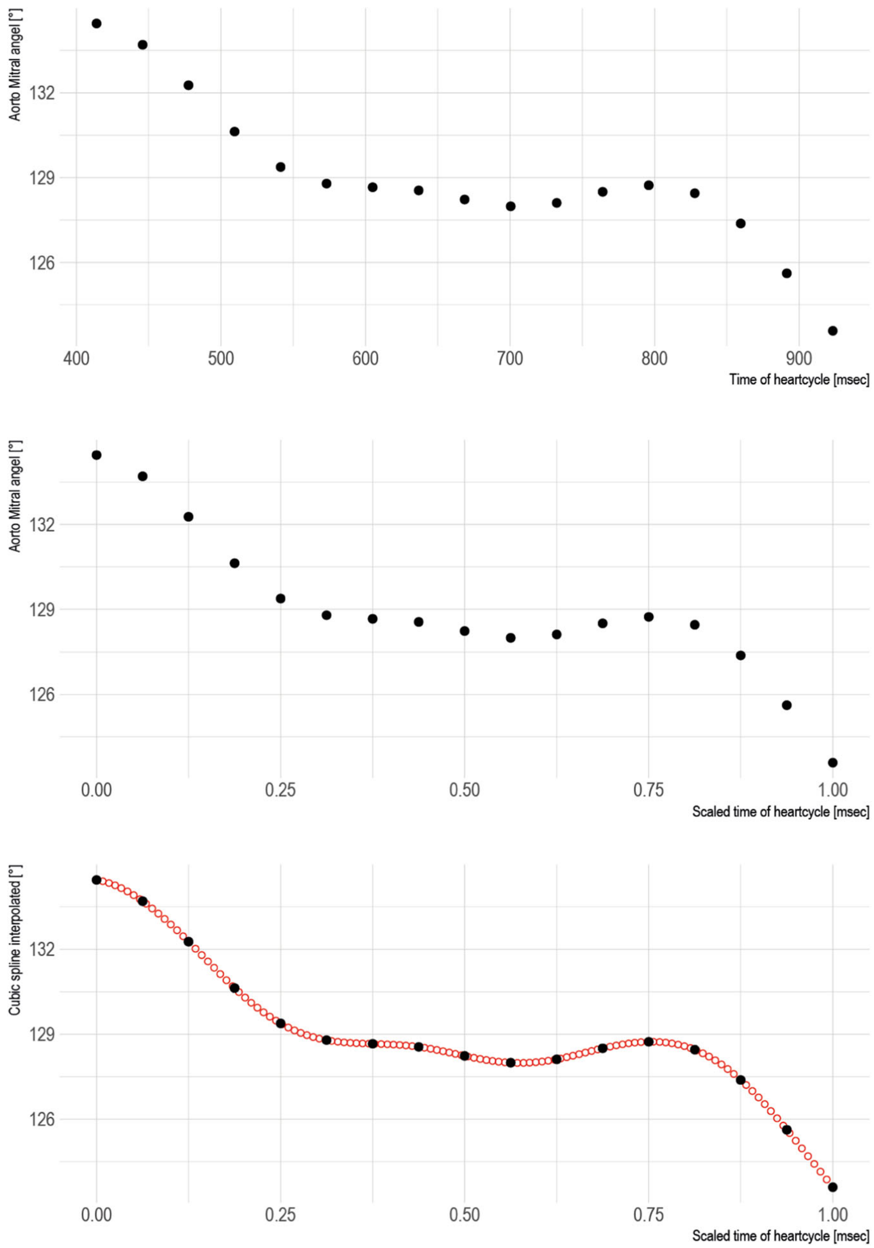
3.2 | Impact of balloon- vs self-expandable valves

A larger reduction in AP diameter was seen in patients who underwent TAVI with a balloon-expandable valve compared to those implanted with a self-expandable valve (−0.25 cm vs −0.11 cm; $P < .05$). This observation was, however, only evident in mid-systole while it was not present in mid-diastole. The reduction of the annular area was significantly higher in the balloon-expandable group (-1.2 ± 1.59 cm^2 vs -0.22 ± 1.41 cm^2; $P < .05$). A similar reduction was found during diastole (-1.23 ± 1.57 cm^2 vs -0.39 ± 1.46 cm^2; $P < .05$) (Table 3 and Figure 5).

3.3 | Relevance for mitral valve function

Before TAVI, of the 84 patients, 2 had an MR of grade 3, 4 had an MR of grade 2 to 3, 11 had an MR of grade 2, 3 had an MR of grade

FIGURE 3 Transformation of raw measurements (here, aortomitral angle) with varying frame numbers into a standardized timeline and interpolated by a cubic spline. Upper row: raw data of one exemplary variable with standard time frame from the echo machine; middle line: same data set after time-scaling into an *x*-axis from 0 to 1; bottom row: interpolation via cubic spline at 80 equally spaced points per cycle spanning the range 0 to 1 (in this example for presentation purposes, we used 120 equally spaced points)



1 to 2, 49 had an MR of grade 1, 4 had an MR of grade 0 to 1, and 11 had no MR.

After the procedure, 2 of the 84 patients had an MR of a grade more than 2 to 3, 5 had an MR of grade 2, 1 had an MR of grade 1 to 2, 52 had an MR of grade 1, 7 patients had an MR of grade 0 to 1, and 17 had no MR. The degree of MR decreased in 21 (25%) patients and did not change in the remaining 63 cases. Worsening or newly occurring MR was not observed (Figure 6).

4 | DISCUSSION

In this study, we could show that TAVI is associated with substantial changes in mitral annular geometry as assessed by 4D-echocardiography and measured with a semiautomated software tool. In contrast to the previous studies, which only examined systolic changes,[7-10] the observed effects were observed throughout the entire cardiac cycle; however, most of them did not differ significantly when compared to systole and diastole.

We found different changes at the mitral valve geometry, depending on the type of prosthesis implanted (balloon- vs self-expandable). Changes were more relevant in the patients who had implantation of a balloon-expandable valve.

Previous studies investigating the effects on surgical SAVR also found significant changes in mitral valve geometry and function after surgical implantation of aortic valve prostheses. Mahmood et al[7,8] report in a single-center cohort study with 35 patients a significant reduction of mitral annular area, circumference, AP diameter, and

TABLE 2 Measurements of mitral geometry pre- and post-TAVI compared for mid-systole and -diastole

	Systole			Diastole		
Parameter	Pre	Post	*P* value	Pre	Post	*P* value
AP diameter, cm	3.42 (0.50)	3.24 (0.52)	.20	3.43 (0.48)	3.22 (0.50)	.005
ALPM diameter, cm	3.77 (0.48)	3.66 (0.46)	.123	3.77 (0.47)	3.65 (0.45)	.082
Annulus area, cm^2	10.80 (2.83)	9.94 (2.64)	.044	10.79 (2.78)	9.85 (2.54)	.024
Sphericity index	0.91 (0.07)	0.88 (0.07)	.032	0.91 (0.07)	0.88 (0.08)	.009
Aortomitral angle, °	128.80 (14.09)	137.18 (14.45)	<.001	129.34 (13.63)	134.57 (14.56)	.017
Annular height, cm	0.79 (0.24)	0.64 (0.19)	<.001	0.73 (0.23)	0.61 (0.18)	<.001
Annular displacement, mm	2.71 (1.69)	3.15 (1.87)	.110	2.11 (1.54)	1.95 (1.43)	.479
Displacement velocity, mm/s	17.53 (10.83)	17.27 (9.32)	.867	−4.87 (7.33)	−5.42 (13.09)	.734

Note: Values are given as means and standard deviation.
Abbreviations: ALPM, antrolateral-posteromedial; AP, anteriorposterior.

anterolateral-posteromedial diameter after implantation of mainly tissue prostheses. The anterior annulus length was more reduced indicating the mechanical pressure on the annulus. While the ALPM diameter did not change in our observations, the effect was comparable with regard to AP diameter, annular area, and circumference. As the vertical annular displacement did not show any significant alteration in our study, the dynamic motion of the annulus seemed to be not restricted after TAVI. In line with the study of

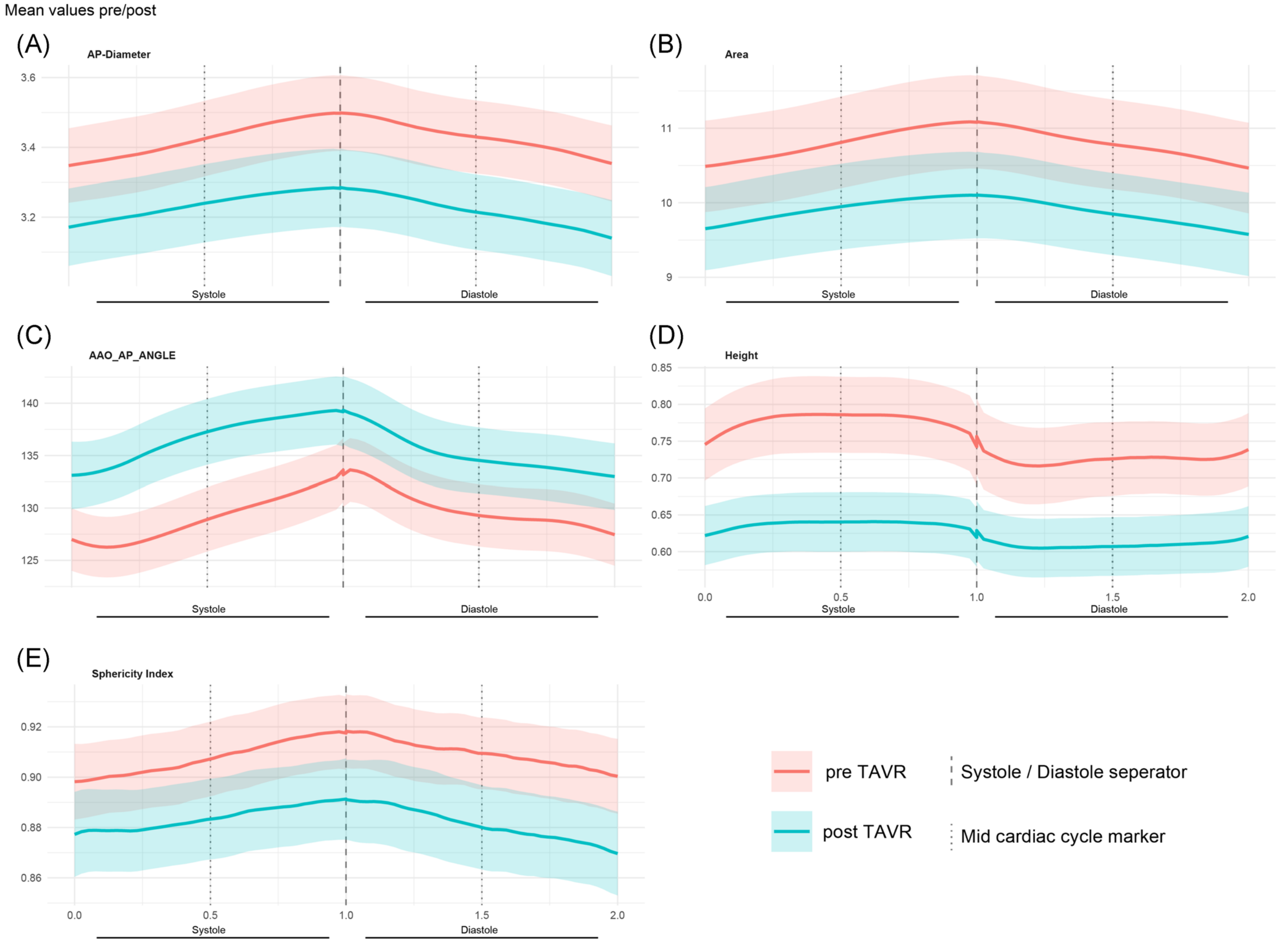


FIGURE 4 Changes of mitral valve geometry before and after transcatheter aortic valve implantation for all patients visualized over the whole heart cycle. A, Aortomitral angle (degree). B, AP diameter (cm); C, annulus area (cm^2). D, annular height (cm); E, sphericity index (cm/cm)

TABLE 3 Postprocedural differences in parameters (means [standard deviations]) of mitral geometry parameters compared for balloon- vs self-expandable valves

	Systole			Diastole		
Parameter	Balloon	Self	*P* value	Balloon	Self	*P* value
AP diameter, cm	−0.25 (0.32)	−0.11 (0.31)	.040	−0.27 (0.32)	−0.15 (0.34)	.108
ALPM diameter, cm	−0.20 (0.29)	−0.01 (0.28)	.003	−0.20 (0.28)	−0.03 (0.28)	.008
Annulus area, cm^2	−1.32 (1.68)	−0.33 (1.46)	.005	−1.33 (1.66)	−0.47 (1.52)	.016
Sphericity index	−0.02 (0.07)	−0.03 (0.07)	.573	−0.03 (0.07)	−0.03 (0.07)	.563
Aortomitral angle, °	9.94 (18.15)	6.53 (19.48)	.409	6.87 (18.32)	3.36 (19.57)	.398
Annular height, cm	−0.15 (0.22)	−0.14 (0.20)	.916	−0.12 (0.23)	−0.12 (0.20)	.962
Annular displacement, mm	0.50 (1.72)	0.37 (1.67)	.731	−0.11 (1.88)	−0.21 (1.10)	.767
Displacement velocity, mm/s	1.01 (12.15)	−2.31 (11.06)	.197	−1.52 (14.82)	0.55 (11.87)	.486

Abbreviations: ALPM, antrolateral-posteromedial; AP, anteriorposterior.

Mahmood et al[7] on SAVR, also in our study, a less-steep aortomitral angle was detected after TAVI.

A study comparing the effects of TAVI and AVR on mitral annulus geometry found significant effects for AVR, but noted no changes for TAVI and, therefore, suggested that TAVI was a more physiological approach.[10] Investigations by Shibayama et al[9] found that TAVI did not affect the mitral valve annular 3D parameters, but did improve mitral leaflet tethering. In contrast to both the reports, our study showed a significant impact of TAVI on mitral annular geometry.

Many of the observed parameters such as AP diameter, annular area, and tenting parameters are known to be increased in patients with MR.[15,16] Changes in those annular dimensions are likely to have

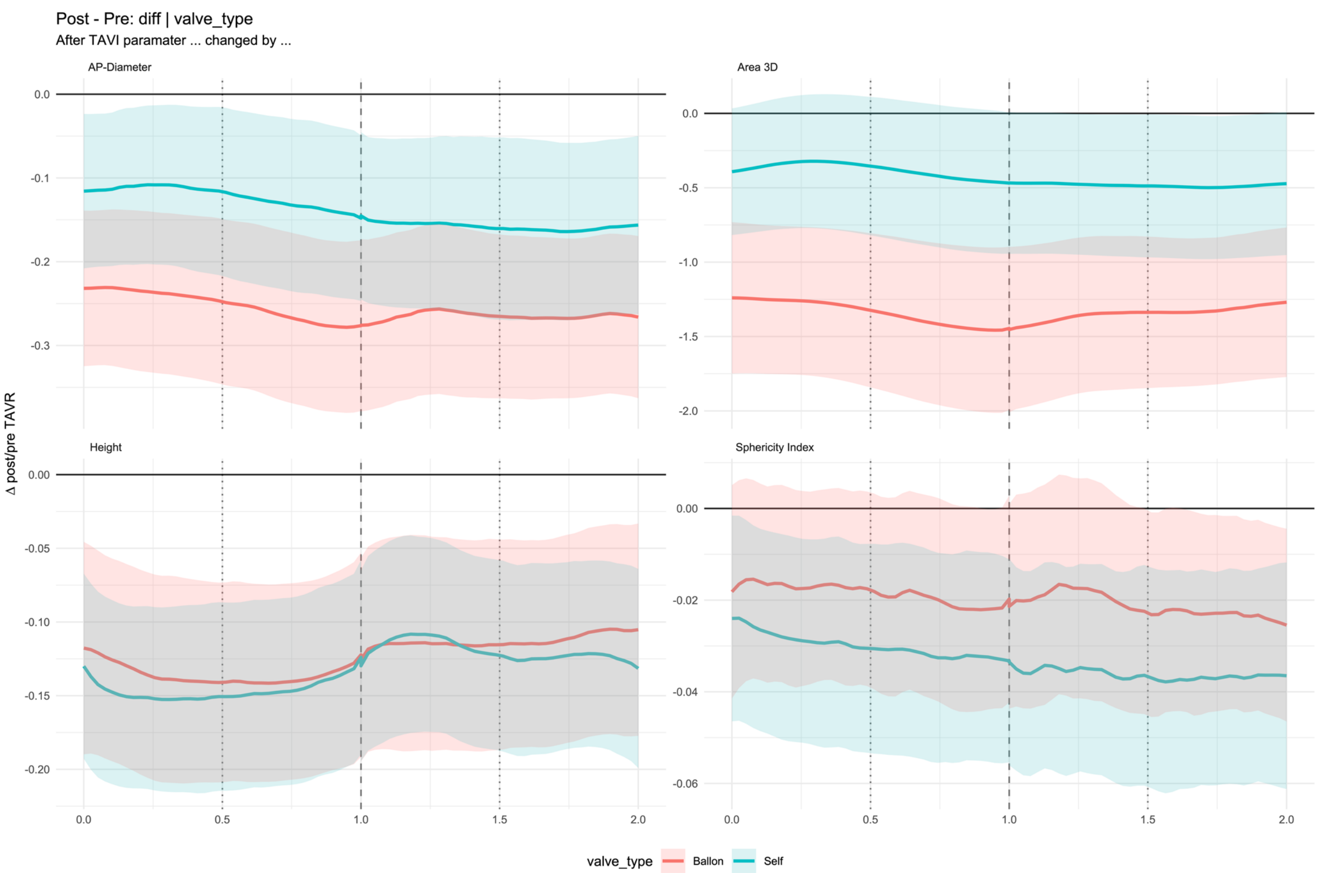


FIGURE 5 Changes of mitral geometry before and after transcatheter aortic valve implantation (TAVI) visualized over the whole heart cycle for balloon-expandable vs self-expandable valves. A, AP diameter (cm); B, annulus area (cm^2); C, annular height (cm); D, sphericity Index (cm/cm)

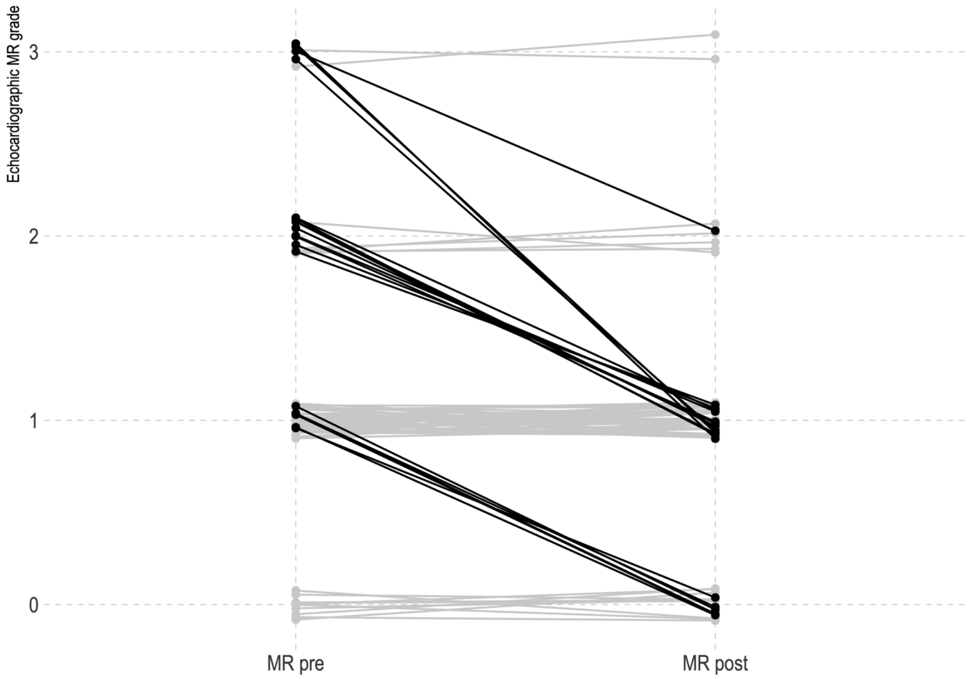


FIGURE 6 Echocardiographic grade of mitral regurgitation (MR) before (left side) and after (right side) individually visualized transcatheter aortic valve implantation for each patient

an impact on the coaptation of the mitral leaflets. Vergnat et al[10] demonstrated the severity of MR to have a significant impact on survival after TAVI and to decrease in grade after the procedure for a majority of patients. Our results are in line with these findings as a substantial part of our patients (25%) also showed a reduced grade of MR after TAVI. A meta-analysis by Nombela-Franco et al[17] observed a greater improvement of MR in patients treated with a balloon-expanded prosthesis. Although in our study, the geometric changes in the group of balloon-expanded valves were more pronounced, there was no evidence for the influence on improved MR in that group. While the ALPM diameter did not change significantly, the reduction of the AP diameter could be a surrogate for a mechanical component as an explanation for the observed changes, conceivable directly through the stent framework of the prosthesis pressing against the anterior mitral annulus. This hypothesis is further supported by the fact that significant differences were found between the groups of self-expanding vs balloon-expanded valves with a higher effect evident from balloon-expanded prostheses. However, hemodynamic changes due to the eliminated aortic stenosis such as afterload reduction may certainly also play a role.[18,19] Hence, we found possible causative factors for the observed changes, which still need to be validated in a larger patient cohort.

5 | LIMITATIONS

Our study was a single-center cohort study in which the collected data were retrospectively analyzed. Mitral calcification might affect the annular geometry but was not assessed in our study due to the assumption that calcifications affect the quality of imaging. Another aspect that most likely has an influence on mitral valve function and dynamics is the use of general anesthesia in all cases, but this might be less relevant because as a bias it equally affects all study patients. However, the exact influence of general anesthesia on mitral annular geometry is unknown. An approach through the apex for TAVI might impact the left ventricular geometry. The inclusion of transapical approaches, therefore, might bias the subgroup analysis for balloon-expandable valves because implantation of Edwards SAPIEN 3 prostheses is mandatory in those cases. The self-expandable group shows a certain heterogeneity with regard to the implant used. Due to different stent characteristics in various self-expandable prostheses, different effects on the mitral annulus would be possible. Heart rhythm during the (TOE) was not examined. A possible presence of post-implant pacing might cause an asynchrony and also affect the mitral dynamics. TOMTEC Imaging Systems provides its MV-ASSESSMENT tool only for systolic analysis of the mitral valve anatomy. We did also perform a diastolic analysis of annular dimensions, so that the validity of certain diastolic values may have potentially impacted the analysis to some extent. Therefore, diastolic parameters based on the mitral valve leaflets being closed (tenting area, tenting volume, and tenting height) were discarded. Since our measurements were only collected directly before and after the procedure, we cannot exclude that the results observed are short-term effects. Thus, subsequent long-term investigations, including a TOE follow-up examination, would be valuable but were beyond the scope of this study.

6 | CONCLUSIONS

This study demonstrates that mitral valve anatomy and geometry is significantly influenced by TAVI procedures. This is even more pronounced for balloon-expandable valves and, thus, may be relevant for planning procedures and prosthesis selection. Grade of MR improved or was unchanged, which may also be attributed to the relevant geometric changes of the annulus in addition to the established mechanism of afterload reduction. To further assess the clinical relevance of these findings, further investigation in larger cohorts including a long-term follow-up is warranted. The use of magnetic resonance imaging for assessing mitral annular geometry could also provide additional information.

AUTHOR CONTRIBUTIONS

AM: concept, design, data analysis/interpretation, statistics, and critical revision of the article; DG: concept, design, data collection, article drafting, and data analysis/interpretation; AU: data interpretation and critical revision of the article; MK and MYE: concept/design, data interpretation, and critical revision of the article; ChK: data collection, critical revision of the article; JaK: data collection and critical revision of the article; VF: concept, design, data interpretation, critical revision of article, and funding organization; JK: concept, design, data analysis/interpretation, critical revision of the article, funding organization, and approval of article; SHS: concept, design, data analysis/interpretation, article drafting, and approval of the article.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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