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Mitral-Tricuspid Regurgitation Change After Transcatheter Aortic Valve Implantation and Its Effect on Mortality and Hospitalization

Transkateter Aort Kapağı İmplantasyonu Sonrası Mitral-Triküspit Yetersizliği Değişimi ve Bunun Mortalite ve Hospitalizasyona Etkisi

ABSTRACT

Objective: Moderate to severe mitral regurgitation (MR) and tricuspid regurgitation (TR) are present in approximately 20-60% of patients undergoing transcatheter aortic valve implantation (TAVI). This study aims to evaluate the impact of TAVI on MR and TR, pulmonary hypertension, and reverse cardiac remodeling in these patients.

Methods: Out of 240 patients who underwent TAVI, 79 who met the inclusion and exclusion criteria were analyzed.

Results: In our study, 46.8% (n = 37) of the patients were male. Nineteen (24.1%) patients died within two years. Before TAVI, 34 (43%) patients had moderate-to-severe MR, which decreased to 18 (22.7%) after the procedure ($P < 0.05$). Similarly, the number of patients with moderate-to-severe TR decreased from 26 (32.9%) before TAVI to 12 (15%) after the procedure ($P < 0.05$). Of the patients, 50.6% (n = 40) did not require hospitalization after the procedure, while 25 were hospitalized once, 12 twice, and 2 three times. The mean systolic pulmonary artery pressure (sPAP) values of the patients decreased from 44.30 ± 14.42 mmHg before the procedure to 39.09 ± 11.77 mmHg after the procedure (Z=-3.506, $P < 0.001$). No correlation was found between changes in MR and TR grades after TAVI and mortality or hospitalization during follow-up. Furthermore, there was no statistically significant difference in tricuspid annular plane systolic excursion (TAPSE), free wall annular S' velocity, left atrial volume (LAV), or LAV index (LAVI) before and after TAVI.

Conclusion: There was a significant decrease in moderate-to-severe MR and TR after TAVI; however, this did not impact hospitalization or mortality rates. Additionally, no significant differences were observed in right ventricular systolic function or in LAV and LAVI before and after TAVI.

Keywords: Aortic valve stenosis, transcatheter aortic valve replacement, mitral valve, tricuspid valve

ÖZET

Amaç: Transkateter aort kapağı implantasyonu (TAVİ) uygulanan hastaların yaklaşık %20-60'ında orta-ciddi mitral yetersizliği (MY) ve triküspit yetersizliği (TY) eşlik eder. Bu çalışmada, TAVİ uygulanan hastalarda TAVİ'nin MY ve TY, pulmoner hipertansiyon ve ters kardiyak yeniden şekillenme üzerindeki etkisini değerlendirmeyi amaçladık.

Yöntem: TAVİ uygulanan 240 hastadan dahil etme ve hariç tutma kriterlerini karşılayan 79 hasta analiz edildi.

Bulgular: Çalışmamızda hastaların %46,8'i (n = 37) erkekti. Hastaların 19'u (%24,1) iki yıl içinde öldü. TAVİ öncesi orta-ciddi MY'si olan 34 (%43) hasta varken işlem sonrası bu sayı 18'e (%22,7) düştü ($P < 0,05$). TAVİ öncesi 26 hastada (%32,9) orta-ciddi TY mevcuttu, işlem sonrası bu oran 12'ye (%15) düştü ($P < 0,05$). Hastaların %50,6'sı (n = 40) işlem sonrası hiç hastaneye başvurmazken, 25'i 1, 12'si 2, 2'si 3 kez hastaneye yatırıldı. Hastaların işlem öncesi ve sonrası ortalama sistolik pulmoner arter basıncı (sPAB) değerleri sırasıyla 44,30 ±14,42 mmHg ve 39,09±11,77 mmHg idi (Z=-3,506, $P <0,001$). TAVİ sonrası MY ve TY derece değişiklikleri ile takip sırasında mortalite ve hastaneye yatış ihtiyacı arasında korelasyon yoktu. TAVİ öncesi ve sonrası triküspit anüler plane sistolik ekskürsiyon (TAPSE), serbest duvar anüler S' hızı ve sol atrial volüm (LAV) ve indeksi (LAVİ) arasında da istatistiksel olarak anlamlı bir fark yoktu.

Sonuç: TAVİ sonrası orta-ciddi MY ve TY hastalarında anlamlı bir azalma oldu, ancak bu, hastaneye yatış ve mortaliteyi etkilemedi. TAVİ öncesi ve sonrası sağ ventrikül sistolik fonksiyonları ve LAV ve LAVİ'de anlamlı fark yoktu.

Anahtar Kelimeler: Aort kapak stenozu, transkateter aort kapak replasmanı, mitral kapak, triküspit kapak

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

Samir Adıgözelzade[1]
Serkan Asil[2]
Ömer Faruk Keskin[2]
Sıddık Erdoğan[3]
Suat Görmel[2]
Salim Yaşar[2]
Serdar Fırtına[2]
Erkan Yıldırım[2]
Barış Buğan[2]
Murat Çelik[2]
Cem Barçın[2]
Uygar Çağdaş Yüksel[2]

[1]*Central Military Hospital of Ministry Defence of Azerbaijan, Bakü, Azerbaijan*
[2]*Department of Cardiology, Gülhane Training and Research Hospital, Ankara, Türkiye*
[3]*Department of Cardiology, İstanbul Şile City Hospital, İstanbul, Türkiye*

Corresponding author:
Serkan Asil
✉ dr_serkanasil@hotmail.com

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Aortic Stenosis (AS) is the most common valve disease necessitating valve replacement globally.[1] It can be treated using transcatheter aortic valve implantation (TAVI) as an alternative to surgery in patients at high surgical risk. AS leads to increased pressure on the left ventricle (LV), resulting in LV hypertrophy. Prolonged exposure to this pathophysiological mechanism may give rise to secondary LV dilatation and functional mitral regurgitation (MR).[2] Furthermore, pulmonary hypertension (PH) and tricuspid regurgitation (TR) may develop due to increased LV diastolic and left atrial (LA) pressure in AS patients. Consequently, functional moderate to severe mitral and tricuspid regurgitation is observed in approximately 20-60% of TAVI patients.[2] This study seeks to evaluate the impact of TAVI on MR and TR, PH, right ventricular function, and LA volume. Additionally, it examines the association between reductions in MR and TR grade and both mortality and hospital admission.

Materials and Methods

Patient Population and Data Collection

In this single-center, retrospective observational study, 79 patients, who fulfilled the inclusion and exclusion criteria from a pool of 240 TAVI patients between 2016 and 2019, were analyzed. Exclusion criteria included patients whose records were inaccessible or lacked sufficient data, as well as those with primary mitral and tricuspid regurgitation. The study data were extracted from our hospital's electronic health database and patient archive files. Additionally, the survival data of the patients were retrieved through the Ministry of Health's current death notification system using their identification numbers. In this context, we collected general demographic data on the patients, as well as information on comorbidities, pre- and post-procedural transthoracic echocardiograms, 2-year mortality status, and the number of hospitalizations. Ethics Committee of The University of Health Sciences Gülhane Training and Research Hospital approved the study (Approval Number: 2021/08, Date: 14.01.2021). This study was conducted in accordance with the Helsinki Declaration.

Echocardiographic Assessment

The patients underwent evaluation using the Vivid S70N (Vingmed-General Electric, Norway) echocardiography machine.

ABBREVIATIONS

AS	Aortic stenosis
AVR	Aortic valve replacement
EROA	Effective regurgitant orifice area
IVC	Inferior vena cava
LA	Left atrial
LAV	Left atrial volume
LAVI	Left atrial volume index
LV	Left ventricle
LVEF	Left ventricular ejection fraction
MR	Mitral regurgitation
PARTNER	Placement of aortic transcatheter valves trial
PH	Pulmonary hypertension
Pro-BNP	Pro-brain natriuretic peptide
sPAP	Systolic pulmonary artery pressure
TAPSE	Tricuspid annular plane systolic excursion
TAVI	Transcatheter Aortic Valve Implantation
TRV	Tricuspid regurgitation velocity
VC	Vena contracta
TR	Tricuspid regurgitation

We recorded echocardiographic parameters using a 2.5 MHz phased-array transthoracic echo probe, basing our findings on three consecutive measurements. The patients had a post-procedural control transthoracic echocardiogram approximately one month after TAVI. All echocardiographic assessments were performed according to the recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging guidelines.[3-5] We obtained left ventricular dimensions using M-Mode imaging from the parasternal long axis. The report on left ventricular ejection fraction (LVEF) was based on the modified Simpson method. To determine the severity of AS, we measured mean and peak gradients through the aortic valve using the modified Bernoulli equation. The calculation of the aortic valve area was done by the continuity equation. Left atrial volumes (LAV) were calculated using the prolate ellipse method, with left atrial diameters obtained from parasternal long-axis and apical 4-chamber images. We calculated the left atrial volume index (LAVI) by finding the ratio of LAV to body surface area. Right ventricular dimensions were measured from the right ventricular free wall to the interventricular septum at the base on apical 4-chamber view. Free wall S' velocity was recorded on the tricuspid lateral annulus by pulsed-wave tissue Doppler at the apical 4-chamber view. To estimate systolic pulmonary artery pressure (sPAP), classic echocardiographic approach utilizes a derivation of right ventricular pressure from the tricuspid regurgitation velocity (TRV), supplemented by a qualitative assessment of right atrial pressure (RAP).[4] For simplicity in reporting, specific values of RAP, rather than ranges, were used to determine sPAP. An inferior vena cava (IVC) diameter < 2.1 cm that collapses > 50% with a sniff suggests a normal RA pressure of 3 mmHg (range, 0-5 mmHg), whereas an IVC diameter > 2.1 cm that collapses < 50% with a sniff suggests a high RA pressure of 15 mmHg (range, 10-20 mmHg). In scenarios where the IVC diameter and collapse do not fit this paradigm, an intermediate value of 8 mmHg (range, 5-10 mmHg) was used.[4] Tricuspid annular plane systolic excursion (TAPSE) was measured from the lateral tricuspid annulus using M-Mode at the apical 4-chamber view.

Mitral and tricuspid regurgitation were assessed based on qualitative, semi-quantitative, and quantitative parameters.[5] MR was evaluated by qualitative methods according to color-Doppler flow with a 50 cm/sec Nyquist limit as grade 1-4. Grade 2 and more severe MR were further evaluated with semi-quantitative and quantitative methods using the vena contracta (VC) and flow convergence method (proximal isovelocity surface area [PISA] method). An effective regurgitant orifice area (EROA) of 0.2-0.4 cm^2 and VC of 3-7 mm were assessed as moderate MR, whereas an EROA ≥ 0.4 cm^2 and VC ≥ 7 mm were evaluated as severe MR.[5] Patients with an EROA ≥ 0.2 cm^2 and a VC ≥ 3 mm were included in the moderate-severe MR group.[5] TR severity was determined similarly to MR, using qualitative, semi-quantitative, and quantitative methods.[5]

Statistical Analysis

All statistical analyses were performed using the IBM Statistical Package for the Social Sciences (SPSS) Version 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as percentages, and continuous variables were expressed as arithmetic means ± standard deviations. The

Kolmogorov-Smirnov test was used to assess the normality of data distribution. To compare pre- and post-TAVI variables in paired groups, the T-test, Wilcoxon Signed Rank Test, and Marginal Homogeneity test were used, taking into account data characteristics and normal distribution. The Mann-Whitney U test, t-test, and Chi-square (χ^2) tests were utilized for independent group comparisons. A P value of less than 0.05 was considered statistically significant.

Results

A total of 79 patients were included in our study. Baseline characteristics of the patients are presented in Table 1. Pre- and post-TAVI echocardiographic parameters of the patients are shown in Table 2. sPAP and TRV values were significantly different between pre-and post-TAVI assessment (44.30 ± 14.42 mmHg and 39.09 ± 11.77 mmHg, respectively $P < 0,001$; 2.91 ± 0.58 m/sec and 2.88 ± 3.34 m/sec, $P = 0.01$).

The severity and alteration of mitral and tricuspid regurgitation after TAVI are shown in Table 3. MR was not detected in 14 patients; Grade 1 MR was present in 31 patients (39.2%), Grade

Table 1. Baseline Characteristics of the Patients

Variables	Total (n = 79)	
	n	%
Mean Age (years)	77.67 ± 7.50	
Sex		
Female	42	53.2
Male	37	46.8
Comorbidities		
Hypertension	54	73
Coronary Artery Disease	44	59.5
Diabetes Mellitus	28	37.8
Atrial Fibrillation	19	25.7
Coronary Artery Bypass Graft	17	23
Chronic Obstructive Pulmonary Disease	17	23
Congestive Heart Failure	10	13.5
Chronic Kidney Disease	5	6.8
Peripheral Arterial Disease	2	2.7

Table 2. Echocardiographic Parameters of the Patients Pre- and Post-TAVI

Variables	Number of Patients	Pre-TAVI	Post-TAVI	*P*
Aortic valve max gradient (mmHg)	79	74.94 ± 20.43	29.66 ± 19.94	**<0.001**
Aortic valve mean gradient (mmHg)	79	47.06 ± 11.47	16.23 ± 10.02	**<0.001**
sPAP (mmHg)	79	44.30 ± 14.42	39.09 ± 11.77	**<0.001**
TRV (m/sec)	79	2.91 ± 0.58	2.88 ± 3.34	**0.001**
TAPSE (mm)	79	19.35 ± 2.95	19.48 ± 2.58	0.446
Free wall S' (cm/sec)	79	11.08 ± 1.83	11.13 ± 1.69	0.500
LAV (mL)	79	72.32 ± 37.18	71.5 ± 37.53	0.138
LAVI (mL/m^2)	79	39.44 ± 19.55	39.03 ± 19.56	0.251
LVEF %	79	54.15 ± 13.78	56.49 ± 12.88	0.321

Free wall S', longitudinal velocity of the tricuspid annulus by tissue Doppler; LAV, left atrial volume; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TRV, tricuspid regurgitation velocity.

Table 3. Pre- and Post-TAVI Evaluation of MR and TR Grade Change

		Pre-TAVI		Post-TAVI	
Mitral Regurgitation Grade		**n**	**%**	**n**	**%**
	None	14	17.7	14	17.7
	1	31	39.2	47	59.4
	2	29	36.7	16	20.2
	3	5	6.3	2	2.6
	4	0	-	0	
Tricuspid Regurgitation Grade					
	None	12	15.1	18	22.7
	1	41	51.8	41	51.8
	2	22	27.8	18	22.7
	3	3	3.7	2	2.5
	4	1	1.2	0	-

For **Mitral Regurgitation**: Std. Marginal Homogeneity Statistic: 4.912, ***P* < 0.001;**
For **Tricuspid Regurgitation**: Std. Marginal Homogeneity Statistic: 1.693, ***P*** = 0.090.

Table 4. Pre- and Post-TAVI Evaluation of MR and TR Grade Change in Patients with Moderate-Severe MR and TR

		Pre-TAVI		Post-TAVI	
Mitral Regurgitation Grade		**n**	**%**	**n**	**%**
	None				
	1	-	-	19	55.88
	2	29	85.3	13	38.23
	3	5	14.7	2	5.88
	4	0	-	0	
Std. Marginal Homogeneity Statistic: 4.355, ***P* < 0.001**					
Tricuspid Regurgitation Grade					
	None			8	30.8
	1	-	-	6	23.1
	2	22	84.6	11	42.3
	3	3	11.5	1	3.8
	4	1	3.8	0	
Std. Marginal Homogeneity Statistic: 3.297, ***P* = 0.001**					

Table 5. Evaluation of Pre- and Post-TAVI Echocardiographic Parameters in Patients with Moderate-Severe MR and TR

	Variables	n	Pre-TAVI	Post-TAVI	t/Z	*P*
Moderate-Severe Mitral Regurgitation Patients	VC (mm)	34	3.86 ± 0.67	2.46 ± 1.14	-4.650[z]	**<0.001**
	EROA (cm^2)	34	0.25 ± 0.04	0.21 ± 0.24	-4.177[z]	**<0.001**
	sPAP (mmHg)	34	48.70 ± 16.1	40.06 ± 12.52	-3.225[z]	**0.001**
	TRV (m/sec)	30	3.44 ± 5.13	3.11 ± 0.51	-2.651[z]	**0.008**
	TAPSE (mm)	34	18.59 ± 3.23	18.65 ± 2.84	-0.255[t]	0.801
	RV free wall annular S' (cm/sec)	34	10.59 ± 2.06	10.62 ± 1.92	-0.211[z]	0.833
	LAV (mL)	34	79.56 ± 32.71	77.47 ± 32.38	1.878[t]	0.069
	LAVI (mL/m^2)	34	43.59 ± 17.91	42.38 ± 17.48	2.021[t]	0.051
Moderate-Severe Tricuspid Regurgitation Patients	sPAP(mmHg)	26	56.23 ± 15.20	46.65 ± 14.62	-2.877[z]	**0.004**
	TRV (m/sec)	22	3.40 ± 0.50	3.13 ± 0.50	-2.166[z]	**0.030**
	TAPSE (mm)	26	18.54 ± 3.25	18.54 ± 2.73	0.000[t]	1.000
	RV free wall annular S' (cm/sec)	26	10.62 ± 2.02	10.70 ± 1.71	-0.615[z]	0.539

t: Paired Groups t-Test, Z: Wilcoxon Signed Rank Test. EROA, effective regurgitant orifice area; LAV, left atrial volume; LAVI, left atrial volume index; RV free wall annular S', right ventricular longitudinal velocity of the tricuspid annulus by tissue Doppler; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TRV, tricuspid regurgitation velocity; VC, vena contracta.

2 MR was present in 29 (36.7%), and Grade 3 MR was present in 5 patients (6.3%). TR was not detected in 12 patients; Grade 1, 2, 3, and 4 TR were present in 41 (51.8%), 22 (27.8%), 3 (3.7%), and 1 patient (1.2%), respectively. Table 4 shows the pre- and post-TAVI evaluation of MR and TR grades, as well as changes in moderate-severe MR and TR. Evaluation of pre- and post- TAVI echocardiographic parameters in patients with moderate-severe MR and TR is presented in Table 5. The mean VC of moderate-severe MR patients was 3.86 ± 0.67 mm pre-TAVI and 2.46 ± 1.14 mm post-TAVI (Z=-4.650, $P < 0.001$). Similarly, the mean EROA of moderate-severe MR patients was 0.25 ± 0.04 cm^2 pre-TAVI and 0.21 ± 0.24 cm^2 post-TAVI (Z=-4.177, $P < 0.001$). Two-year mortality status of the patients and

Table 6. 2-Year Mortality Status of the Patients and Number of Hospitalizations

		n	%
2-year Mortality	Exitus	19	24.1
	Survival	60	75.9
Number of Hospital Admissions	None	40	50.6
	1 Time	25	31.6
	2 Times	12	15.2
	3 Times	2	2.5
	Total	79	100.0

Table 7. Evaluation of Pre- and Post-TAVI VC and EROA Measurement Differences in Terms of 2-Year Mortality and Number of Hospital Admissions

		Alive (n = 25)	Dead (n = 9)	U	*P*
	n	Mean	Mean		
VC (mm) (Difference)*	34	1.52 ± 0.90	1.11 ± 1.21	88.00	0.330
EROA (cm2) (Difference)*	34	0.03 ± 0.26	0.08 ± 0.07	112.00	0.984
		Number of Hospital Admissions			
VC (mm) (Difference)*	**r**	-0.287	*P* = 0.118		
EROA (cm2) (Difference)*	**r**	-0.122	*P* = 0.512		

***Pre-TAVI Measurement - Post-TAVI Measurement. EROA, effective regurgitant orifice area; VC, vena contracta; U, Mann-Whitney U Test; r, Spearman Correlation Coefficient.

Table 8. Evaluation of Pre- and Post-TAVI TR Measurement Differences in Terms of 2-Year Mortality and Number of Hospital Admissions

TR Measurement Difference*	Alive (n = 25)		Dead (n = 9)		Total		χ^2	*P*
	n	%	n	%	n	%		
0.50	1	100.0	0	0.0	1	100.0	8.126	0.322
0.00	8	80.0	2	20.0	10	100.0		
0.50	2	66.7	1	33.3	3	100.0		
1.00	3	75.0	1	25.0	4	100.0		
2.00	4	100.0	0	0.0	4	100.0		
2.50	0	0.0	1	100.0	1	100.0		
3.00	1	50.0	1	50.0	2	100.0		
3.50	0	0.0	1	100.0	1	100.0		
	Number of Hospital Admissions							
TR (Difference)*	**R**	0.283	*P* = 0.180					

***Pre-TAVI Measurement - Post-TAVI Measurement. χ^2, Chi-square test; r, Spearman Correlation Coefficient; TR, tricuspid regurgitation.

the number of hospitalizations are provided in Table 6. Nineteen patients (24.1%) died within two years. Differences in VC and EROA values for patients with moderate-severe MR pre- and post-TAVI did not show a statistically significant difference in terms of 2-year mortality status ($P > 0.05$). Similarly, no statistically significant difference was detected between the measurement differences of VC and EROA values for patients with moderate-severe MR pre- and post-TAVI, and the number of hospitalizations ($P > 0.05$) (Table 7). Changes in TR grade for patients with moderate-severe TR pre- and post-TAVI did not show a statistically significant difference in terms of 2-year mortality status ($P > 0.05$). Similarly, no statistically significant difference was detected between the changes in TR grade pre- and post-TAVI and the number of hospitalizations in patients with moderate-severe TR ($P > 0.05$) (Table 8).

Discussion

In our study, we observed that in patients with moderate-severe functional MR and TR, these regurgitations regressed after TAVI; however, this did not affect hospitalization and mortality rates.

Previous studies have reported the frequency of moderate-severe MR in patients with AS to be up to 15-70%.[6-8] Approximately 12-20% of patients who underwent TAVI were found to have moderate to severe MR.[9] In the Placement of Aortic Transcatheter Valves Trial (PARTNER) 1, the frequency of moderate-severe MR was 19.6% in the TAVI group and 21.2% in the surgery group.[10] Toggweiler et al.[11] found moderate-severe MR in 19.7% of patients in a Canadian-centered study. In our single-center study of 79 patients undergoing TAVI, 42.7% exhibited moderate-severe MR and 32.7% exhibited moderate-severe TR before the procedure. The rates of coronary artery disease and atrial fibrillation, which are the most common causes of functional MR, were similar in our study compared to other studies in the literature. The rate of coronary artery disease was 59.5% in our patients, and a history of atrial fibrillation was present in 25%. Based on these data, such a high incidence of moderate to severe MR was not explained by the rate of concomitant primary cardiac comorbidities. After TAVI, it is expected that the severity of functional MR would decrease. Decrease in afterload following valve replacement and increase in mitral valve coaptation due to the reduction in LV size are the mechanisms of MR reduction. In

the PARTNER study, MR severity decreased in 69.4% of patients with surgical aortic valve replacement (AVR) and 57.7% of patients with TAVI.[10] Toggweiler et al.[11] reported that 61% of patients with moderate-to-severe MR experienced a reduction in MR after TAVI. Hutter et al.[2] reported a decrease in MR grade after TAVI in 67% of patients with moderate-to-severe MR. The decrease in MR severity in our patients was also consistent with the main randomized controlled trials in the literature. In our study, no increase in MR grades was observed after TAVI. However, in the PARTNER study, MR severity increased in 2.8% of patients who underwent surgical AVR and 5.8% of those who underwent TAVI.[10] Most studies have evaluated MR severity using visual or semi-quantitative methods. Even the PARTNER study did not quantitatively evaluate MR severity. Our study is valuable in the literature because it quantitatively evaluated the severity of moderate-severe MR using both VC and EROA. We considered patients with VC ≥ 3 mm and EROA ≥ 0.2 cm^2 as having moderate to severe MR in our study.

Previous studies have reported conflicting results regarding the association between preprocedural moderate-severe MR and increased mortality after TAVI, with some studies finding an association and others not.[9,12-16] However, moderate-to-severe MR was not associated with long-term mortality in the TAVI group of the PARTNER trial.[10] In one study, MR was associated with early mortality but not with late mortality.[11] In our study, we hypothesized that a decrease in MR severity after TAVI may result in reduced mortality in patients with moderate to severe MR. However, our findings indicate that the quantitatively measured decrease in MR severity was not associated with a reduction in either 2-year mortality or hospitalizations.

Also, many observational studies in the literature report a decrease in MR severity after surgical AVR or TAVI.[17-19] However, some observational trials have produced opposite results. In a study by Scisło et al.,[20] patients were divided into two groups: functional and primary mitral regurgitation. In conclusion, compared with baseline, no significant change in MR-EROA was observed after a 1-year follow-up, neither in the functional MR nor in the primary MR cohorts. In the literature, many studies have not differentiated between primary and functional MR. The examinations by Scisło et al.,[20] which classified MR types, are unique. However, contrary to expectations, no difference was observed. The most likely reason for this may be their small number of patients. In our study, we tried to exclude the possible confounding effect of primary MR by including only patients with functional MR.

Tricuspid regurgitation may occur functionally in AS patients due to both the left ventricular effect and right heart loading. In our study, the frequency of moderate-severe TR was 32.9%, which was slightly higher than in other studies in the literature. Hutter et al.[2] reported that the frequency of moderate-severe TR was 20.1%, Barbanti et al.[21] reported it was 15.2% in their study, and it was 26.6% in the PARTNER 2 study.[2,21,22] Although the history of comorbid diseases such as hypertension, chronic obstructive pulmonary disease, coronary artery bypass graft, atrial fibrillation, and heart failure was similar, the rate of patients with moderate to severe TR in our study was higher than in other studies. Higher rates of moderate-severe mitral regurgitation may have caused a higher rate of moderate-severe TR. In our study, there were 26 (32.9%) patients with moderate to severe TR, and this number decreased to 12 (15%) after TAVI. A reduction of at least one degree was observed in 53.8% of patients with moderate to severe TR. No increase was observed in TR grade. This result is generally consistent with the literature. Hutter et al.[2] reported that the severity of TR was reduced by at least one degree in 50% of patients with moderate to severe TR. This study was the first to demonstrate a reduction in TR in TAVI patients. In the PARTNER 2 study, one-third of the patients with moderate-to-severe TR showed a decrease of at least one degree.[22] Barbanti et al.[21] reported a decrease in TR grade in 15% of patients with moderate-severe TR, while 58% experienced no change, and 9% had worsening of their condition. They also noted that the mechanism behind this deterioration remained unclear.[21] In our study, we observed a decrease in TR severity consistent with the literature, but this did not correlate with a reduction in either 2-year mortality or hospitalizations.

Pulmonary hypertension is observed in 29-56% of patients with AS.[23] Increased sPAP and mean high left heart filling pressures are observed in AS, and previous studies have shown that PH is independently associated with adverse cardiac events and long-term mortality.[24-26] In our study, both sPAP and TRV were significantly reduced after TAVI, results that align with existing literature. Benfari et al.[23] found a relationship between PH and the mitral valve EROA in patients with AS, noting that every 0.1 cm^2 increase in mitral EROA doubles the risk of PH – a finding our study also supports. The mean sPAP in patients with moderate-severe MR was higher than that of the entire patient cohort. Additionally, subgroup analysis revealed significant changes in both sPAP and TR velocity in patients with moderate to severe MR.

Right ventricular dysfunction is present in 25-30% of patients with AS.[27] In our study, we utilized TAPSE and tricuspid lateral annular S' to assess right ventricular function. No significant differences were observed in TAPSE and RV annular S' measurements between pre- and post-TAVI evaluations. Similarly, when analyzing right ventricular function in patients with moderate to severe MR and TR, no statistically significant differences were found. These results may be attributed to the preservation of our patients' LVEF values both pre- and post- procedure, indicating that clinical right ventricular dysfunction had not yet begun. In the PARTNER 2 study, an association between increased mortality and the presence of moderate to severe TR and right ventricular dysfunction was found, whereas TR velocity and sPAP were not associated with increased mortality.[22] However, previous studies have demonstrated a relationship between mortality, sPAP, and TR velocity.[28,29] Lindman et al.[22] stated that numerous factors can cause an increase in sPAP, that right ventricular dysfunction might not be present in cases of increased sPAP, and that sPAP begins to decrease when right ventricular dysfunction occurs. In our study, we did not detect any significant changes in TAPSE and RV annular S' values; however, we did observe a significant difference in sPAP and TRV pre- and post-TAVI, aligning with these findings.

Several studies have investigated the prognostic impact of left atrial enlargement in AS, with most focusing solely on left atrial diameter.[30-32] Rusinaru et al.[33] demonstrated a correlation between LAVI and aortic valve area (AVA) in AS patients, noting that patients with higher LAVI values experienced higher 2-year

mortality and hospitalization rates for heart failure compared to those with lower LAVI.[33] In our study, we compared the LAV and LAVI in patients undergoing TAVI before and after the procedure but did not find a significant difference. To date, there are no studies in the literature evaluating changes in LAVI before and after surgical AVR or TAVI. Our study is valuable for this reason. In previous research, the size of the left atrium has been associated with regression of MR.[7] However, our study did not find a significant difference in LAV and LAVI, despite a decrease in the number of moderate-severe MR cases.

Limitations

The most significant limitations of our study were the small number of patients, its single-center design, and its retrospective nature. Additionally, due to the study's retrospective format, we were unable to evaluate LV size, right ventricular size, sizes of mitral and tricuspid annuli, diastolic function, and more advanced assessments of right ventricular function, including strain imaging. We were also unable to analyze the Pro-Brain Natriuretic Peptide (Pro-BNP) value, a prognostic marker in valvular diseases and heart failure, as it was not available in the laboratory data. Furthermore, assessing echocardiographic variables and the severity of mitral and tricuspid regurgitation beyond one month could have provided additional insights.

Conclusion

TAVI has nearly become the standard treatment for high-risk AS patients. These patients usually present with moderate-severe MR and TR. Our study demonstrated a significant reduction in the incidence of moderate-severe MR and TR after TAVI. However, this reduction was not correlated with a decrease in 2-year mortality and hospitalization rates. Additionally, we observed no significant changes in right ventricular systolic function parameters or in LAV and LAVI before and after the procedure.

Ethics Committee Approval: Ethics committee approval was obtained from Ethics Committee of the University of Health Sciences Gülhane Training and Research Hospital approved the study (Approval Number: 2021/08, Date: 14.01.2021).

Informed Consent: Written informed consent was obtained from the patients.

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References

1. Vahanian A, Beyersdorf F, Praz F, et al.; ESC/EACTS Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2022;43(7):561-632. Erratum in: *Eur Heart J.* 2022. [CrossRef]
2. Hutter A, Bleiziffer S, Richter V, et al. Transcatheter aortic valve implantation in patients with concomitant mitral and tricuspid regurgitation. *Ann Thorac Surg.* 2013;95(1):77-84. [CrossRef]
3. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr.* 2015;28(1):1-39.e14. [CrossRef]
4. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr.* 2010;23(7):685-713;quiz 786-788.
5. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. American Society of Echocardiography: recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography: A report from the American Society of Echocardiography's Nomenclature and Standards Committee and The Task Force on Valvular Regurgitation, developed in conjunction with the American College of Cardiology Echocardiography Committee, The Cardiac Imaging Committee, Council on Clinical Cardiology, The American Heart Association, and the European Society of Cardiology Working Group on Echocardiography, represented by. *Eur J Echocardiogr.* 2003;4(4):237-261. [CrossRef]
6. Ruel M, Kapila V, Price J, Kulik A, Burwash IG, Mesana TG. Natural history and predictors of outcome in patients with concomitant functional mitral regurgitation at the time of aortic valve replacement. *Circulation.* 2006;114(1 Suppl):I541-6. [CrossRef]
7. Waisbren EC, Stevens LM, Avery EG, Picard MH, Vlahakes GJ, Agnihotri AK. Changes in mitral regurgitation after replacement of the stenotic aortic valve. *Ann Thorac Surg.* 2008;86(1):56-62. [CrossRef]
8. Barreiro CJ, Patel ND, Fitton TP, et al. Aortic valve replacement and concomitant mitral valve regurgitation in the elderly: impact on survival and functional outcome. *Circulation.* 2005;112(9 Suppl):I443- I447. [CrossRef]
9. Nombela-Franco L, Ribeiro HB, Urena M, et al. Significant mitral regurgitation left untreated at the time of aortic valve replacement: a comprehensive review of a frequent entity in the transcatheter aortic valve replacement era. *J Am Coll Cardiol.* 2014;63(24):2643-2658. [CrossRef]
10. Leon MB, Smith CR, Mack M, et al; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363(17):1597-1607. [CrossRef]
11. Toggweiler S, Boone RH, Rodés-Cabau J, et al. Transcatheter aortic valve replacement: outcomes of patients with moderate or severe mitral regurgitation. *J Am Coll Cardiol.* 2012;59(23):2068-2074. [CrossRef]
12. Sannino A, Grayburn PA. Mitral regurgitation in patients with severe aortic stenosis: diagnosis and management. *Heart.* 2018;104(1):16-22. [CrossRef]
13. Sannino A, Losi MA, Schiattarella GG, et al. Meta-analysis of mortality outcomes and mitral regurgitation evolution in 4,839 patients having transcatheter aortic valve implantation for severe aortic stenosis. *Am J Cardiol.* 2014;114(6):875-882. [CrossRef]
14. Vanden Eynden F, Bouchard D, El-Hamamsy I, et al. Effect of aortic valve replacement for aortic stenosis on severity of mitral regurgitation. *Ann Thorac Surg.* 2007;83(4):1279-1284. [CrossRef]
15. Zahn R, Gerckens U, Linke A, et al; German Transcatheter Aortic Valve Interventions-Registry Investigators. Predictors of one-year mortality after transcatheter aortic valve implantation for severe symptomatic aortic stenosis. *Am J Cardiol.* 2013;112(2):272-279. [CrossRef]
16. Bedogni F, Latib A, De Marco F, et al. Interplay between mitral regurgitation and transcatheter aortic valve replacement with the CoreValve Revalving System: a multicenter registry. *Circulation.* 2013;128(19):2145-2153. [CrossRef]

17. Voisine E, Beaupré F, O'Connor K, et al. Prognosis of functional mitral regurgitation after aortic valve replacement for pure severe aortic stenosis. *J Card Surg.* 2021;36(9):3100-3111. [CrossRef]
18. Miura M, Yamaji K, Shirai S, et al.; of the OCEAN-TAVI Investigators. Clinical Impact of Preprocedural Moderate or Severe Mitral Regurgitation on Outcomes After Transcatheter Aortic Valve Replacement. *Can J Cardiol.* 2020;36(7):1112-1120. [CrossRef]
19. Shibayama K, Harada K, Berdejo J, et al. Effect of transcatheter aortic valve replacement on the mitral valve apparatus and mitral regurgitation: real-time three-dimensional transesophageal echocardiography study. *Circ Cardiovasc Imaging.* 2014;7(2):344-351. [CrossRef]
20. Scisło P, Grodecki K, Rymuza B, et al. Impact of transcatheter aortic valve implantation on coexistent mitral regurgitation parameters. *Kardiol Pol.* 2021;79(2):179-184. [CrossRef]
21. Barbanti M, Binder RK, Dvir D, et al. Prevalence and impact of preoperative moderate/severe tricuspid regurgitation on patients undergoing transcatheter aortic valve replacement. *Catheter Cardiovasc Interv.* 2015;85(4):677-684. [CrossRef]
22. Lindman BR, Maniar HS, Jaber WA, et al. Effect of tricuspid regurgitation and the right heart on survival after transcatheter aortic valve replacement: insights from the Placement of Aortic Transcatheter Valves II inoperable cohort. *Circ Cardiovasc Interv.* 2015;8(4): e002073. [CrossRef]
23. Benfari G, Nistri S, Faggiano P, et al. Mitral Effective Regurgitant Orifice Area Predicts Pulmonary Artery Pressure Level in Patients with Aortic Valve Stenosis. *J Am Soc Echocardiogr.* 2018;31(5):570-577.e1. [CrossRef]
24. Bishu K, Suri RM, Nkomo VT, et al. Prognostic impact of pulmonary artery systolic pressure in patients undergoing transcatheter aortic valve replacement for aortic stenosis. *Am J Cardiol.* 2014;114(10):1562-1567. [CrossRef]
25. Sinning JM, Hammerstingl C, Chin D, et al. Decrease of pulmonary hypertension impacts on prognosis after transcatheter aortic valve replacement. *EuroIntervention.* 2014;9(9):1042-1049. [CrossRef]
26. Luçon A, Oger E, Bedossa M, et al. Prognostic implications of pulmonary hypertension in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation: study from the FRANCE 2 Registry. *Circ Cardiovasc Interv.* 2014;7(2):240-247. [CrossRef]
27. Galli E, Guirette Y, Feneon D, et al. Prevalence and prognostic value of right ventricular dysfunction in severe aortic stenosis. *Eur Heart J Cardiovasc Imaging.* 2015;16(5):531-538. [CrossRef]
28. Malouf JF, Enriquez-Sarano M, Pellikka PA, et al. Severe pulmonary hypertension in patients with severe aortic valve stenosis: clinical profile and prognostic implications. *J Am Coll Cardiol.* 2002;40(4):789-795. [CrossRef]
29. Ben-Dor I, Goldstein SA, Pichard AD, et al. Clinical profile, prognostic implication, and response to treatment of pulmonary hypertension in patients with severe aortic stenosis. *Am J Cardiol.* 2011;107(7):1046-1051. [CrossRef]
30. Beach JM, Mihaljevic T, Rajeswaran J, et al. Ventricular hypertrophy and left atrial dilatation persist and are associated with reduced survival after valve replacement for aortic stenosis. *J Thorac Cardiovasc Surg.* 2014;147(1):362-369.e8. [CrossRef]
31. Rossi A, Tomaino M, Golia G, et al. Usefulness of left atrial size in predicting postoperative symptomatic improvement in patients with aortic stenosis. *Am J Cardiol.* 2000;86(5):567-570,A9-10. [CrossRef]
32. Dalsgaard M, Egstrup K, Wachtell K, et al. Left atrial volume in patients with asymptomatic aortic valve stenosis (the Simvastatin and Ezetimibe in Aortic Stenosis study). *Am J Cardiol.* 2008;101(7):1030-1034. [CrossRef]
33. Rusinaru D, Bohbot Y, Salaun E, et al. Determinants of left atrial volume index in patients with aortic stenosis: A multicentre pilot study. *Arch Cardiovasc Dis.* 2017;110(10):525-533. [CrossRef]