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The Impact of Transcatheter Aortic Valve Replacement on Mitral Regurgitation and Pulmonary Hypertension

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ABSTRACT

Background: The presence of concomitant Mitral Regurgitation (MR) and Pulmonary Hypertension (PH) is a common issue in patients undergoing Transcatheter Aortic Valve Replacement (TAVR). Transthoracic echocardiography plays a role in detecting MR severity and PH before and after TAVR.

Objectives: This study aimed to investigate the impact of TAVR on MR severity and PH and to detect the predictors of their improvement.

Methods: Totally, 111 patients underwent TAVR at Rajaee Heart Center, Tehran, Iran from December 2012 to January 2021. In this retrospective study, these patients were evaluated for MR and PH improvement after TAVR. The final analysis was performed separately on 32 patients who had moderate or more severe baseline MR and 56 patients with any grade of PH at baseline. Group comparisons based on the MR severity, PH severity, and improvement of MR and PH were analyzed using student t-test for continuous variables and chi-square or Fisher's exact test for categorical ones. Finally, the percentage of the patients with improved MR or PH as well as the factors associated with the improvements were determined.

Results: Moderate or more severe baseline MR improved by at least one grade one year post-TAVR in 56.2% of the cases, and TAVR with a balloon-expandable valve was associated with a higher probability of MR improvement. Baseline left ventricular ejection fraction was significantly lower in patients with a higher degree of PH than in those with lower degrees (43% vs. 30%, $P < 0.001$). In addition, right ventricular dysfunction was more prevalent in patients with a higher degree of PH. Post-TAVR reduction in systolic pulmonary pressure (at least 10 mmHg) was observed in 77% of the patients after one year.

Conclusions: TAVR positively affected MR and PH and reduced their severity in most patients. Tricuspid native aortic valve (in comparison with bicuspid), normal sinus rhythm (in comparison with atrial fibrillation), left ventricular ejection fraction improvement, and absence of left atrial enlargement were associated with a greater MR improvement after TAVR. Left ventricular ejection fraction improvement and TAVR with a balloon-expandable valve were also significantly associated with PH improvement post TAVR.

1. Introduction

The incidence of both Aortic Stenosis (AS) and Mitral Regurgitation (MR) increases as age advances, and the concomitant AS and MR is a common clinical problem (1). In the setting of Transcatheter Aortic Valve Replacement (TAVR), concomitant moderate or more severe MR continues to be a challenging clinical issue. Clinical guidelines recommend double valve intervention if both valves are severely diseased. Nevertheless, there is no absolute evidence supporting this strategy (2). Despite this

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obvious importance, only a few studies have addressed this particular issue, partially resulting in oppositional conclusions. The transmission of increased left ventricular diastolic and left atrial pressure led to secondary Pulmonary Hypertension (PH) (3). PH is also a common finding in patients with AS, especially those with post-capillary PH due to left heart disease (4-11). Moreover, previous studies showed increased mortality after aortic valve replacement in patients with PH, with PH being a marker of poor prognosis. Furthermore, controversial results have been obtained regarding the outcomes of residual PH (5, 8, 12-14).

2. Objectives

Considering the heterogeneities in the few existing studies, there still exists a lack of information concerning TAVR patients with concomitant MR and PH. Thus, the present study aims to recognize the potential impact of TAVR on the concomitant moderate or more severe MR and any grade of PH (14-18).

3. Methods

3.1. Study Population

Totally, 111 patients underwent TAVR at Rajaee Heart Center, Tehran, Iran from December 2012 to January 2021. In this retrospective study, these patients were evaluated for MR and PH improvement after TAVR. The participants included 32 patients (29%) presented with moderate or more severe baseline MR and 56 patients (50%) presented with mild or more severe baseline PH. The final analysis was performed separately on 32 patients who had moderate or more severe MR and 56 patients with any grade of PH. The patients were divided into normal, mild, moderate, and severe categories using echocardiography based on the American Society of Echocardiography (ASE) guideline 2016 for cardiac chamber quantification. This study was approved by the local Ethics Committee. Eligibility for TAVR was determined by the local heart team consisting of cardiologists and cardiac surgeons, taking into account the patient's age, operative risk, anatomical considerations, life expectancy, and the likelihood that TAVR would lead to a significant clinical improvement.

3.2. Imaging Evaluation and Procedure

Pre- and post-TAVR data (at baseline and after one year) like MR and PH improvement were retrospectively analyzed from the hospital database. Other parameters included end-diastolic left ventricular volume in the apical 4 chamber view, left ventricular ejection fraction, determination of the organic or functional origin of MR, mitral annular calcification, right ventricular function, and post-TAVR paravalvular leakage. PH was assessed by tricuspid regurgitation gradients and the estimated right atrial pressure on 2D transthoracic echocardiography. Finally, the percentage of the patients whose MR or PH had improved as well as the factors associated with their improvement were determined.

3.3. Statistical Analysis

The data have been expressed as absolute frequency and percentages for qualitative variables. Quantitative variables were described as mean ± Standard Deviation (SD), depending on their distribution. Group comparisons based on the MR severity, PH severity, and improvement of MR and PH were analyzed using student t-test for continuous variables and chi-square or Fisher's exact test for categorical ones. To determine the predictors of MR or PH improvement, multivariate logistic regression was used. Moreover, Kaplan-Meier estimation was employed to determine the survival rate and Log rank test was applied to evaluate the association between echocardiographic indices and time to death. $P < 0.05$ was considered statistically significant.

4. Results

4.1. Baseline Characteristics of the Study Population

Out of the 111 patients who underwent TAVR since 26 December 2012 until 18 January 2021, seven patients (6%) died during the primary hospital stay, 32 (29%) presented with moderate or more severe baseline MR, and 56 (50%) presented with mild or more severe baseline PH. Baseline characteristics of all the 111 patients have been summarized in Table 1. The mean age of the global TAVR population was 76 years and 56% were male. Besides, 32 patients (29%) presented with moderate or more severe MR at baseline evaluation by transthoracic echocardiography and 56 (55.9%) had pulmonary hypertension. Additionally, 41.4% and 58.6% of the patients underwent TAVR by using the Edwards SAPIEN (balloon-expandable valve) and the Corvalve evolute (self-expandable valve), respectively. Among the 111 patients, 73% had MR with a primary (organic) etiology. In addition, mitral annular calcification was present in 45 patients (40%) and left ventricular enlargement in 46 ones (41.4%). Left atrial enlargement was also present in 80 patients (72%). Finally, two patients had the history of mitral valve replacement.

4.2. Main Clinical and Echocardiographic Characteristics of the Global Population according to the Baseline Degree of Mitral Regurgitation and Pulmonary Hypertension

During the follow-up (mean duration of five years), a total of 33 patients died, leading to an overall mortality of 29.7%. As shown in Table 2, there was no significant difference between the patients with moderate or more severe baseline MR and those with lower degrees of MR in terms of body mass index and age. However, the patients with moderate or more severe MR mostly had a secondary etiology compared to those with MR of a lower degree (19.3% vs. 7.3%, $P < 0.001$). Left ventricular ejection fraction was also significantly lower in the patients with moderate or more severe MR (34% vs. 44%, $P = 0.001$). The mean of systolic pulmonary pressure was significantly higher in the patients with significant MR (52 mmHg vs. 38 mmHg, $P < 0.001$). Left atrial volume index was also significantly higher in the patients with significant MR compared to those with a lower degree of MR (52 mL/m2 vs. 37 mL/m2, $P < 0.001$). Additionally, the right ventricular midcavitary diameter was higher in the patients with significant MR than in those with a lower degree of MR (3.16 cm vs. 3.38 cm, $P = 0.02$).

Table 1. Baseline Characteristics of the Study Population (n = 111)

Index		N (%)
Sex	Male	63 (56.8)
	Female	48 (43.2)
Native valve	Unknown*	12 (10.8)
	Bicuspid	20 (18.0)
	Tricuspid	79 (71.2)
TAVR valve type	Balloon expandable	46 (41.4)
	Self-expandable	65 (58.6)
Mitral regurgitation	< moderate MR	79 (71)
	≥ moderate MR	32 (29)
Pulmonary hypertension	No	49 (44.1)
	Mild	28 (25.2)
	Moderate	10 (9)
	Severe	24 (21.6)
Left ventricular ejection fraction	Normal	36 (32)
	Mild dysfunction	24 (21)
	Moderate dysfunction	19 (17)
	Severe dysfunction	32 (28)
Pre-TAVR MR mechanism**	Primary	80 (73)
	Secondary	29 (27)
Presence of mitral annular calcification	No	66 (59.5)
	Yes	45 (40.5)
Left ventricular end-diastolic volume	Normal	65 (58.6)
	Mild enlargement	18 (16.2)
	Moderate enlargement	11 (9.9)
	Severe enlargement	17 (15.3)
Left atrial volume index	Normal	31 (27.9)
	Mild	49 (44.1)
	Moderate	8 (7.2)
	Severe	23 (20.7)
Pre-TAVR diastolic function***	Normal	2 (1.8)
	Mild	37 (59.6)
	Moderate	15 (24.1)
	Severe	9 (14.5)
Pre-TAVR LVH severity	Normal	15 (13.5)
	Mild	63 (56.8)
	Moderate	30 (27.0)
	Severe	3 (2.7)
History of mitral valve replacement		2(1)

*Unknown because of severe calcification; ** if MR was moderate or more severe, the mechanism of MR was assessed; ***if MR was moderate or more severe, diastolic function was not interrogated.
Abbreviations: TAVR, transcatheter aortic valve replacement; MR, mitral regurgitation; LVH, left ventricular hypertrophy.

Finally, 18 patients (56.2%) out of the 32 who had moderate or more severe baseline MR demonstrated an improvement of MR (by at least one degree) one year post-TAVR.

As shown in Table 3, body mass index was significantly lower in the patients without PH than in those with moderate PH (25 kg/m^2 vs. 30kg/m^2, P = 0.015). However, there was no significant difference between the patients with and without PH regarding the history of hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, and Coronary Artery Bypass Graft (CABG) surgery. Left ventricular ejection fraction was significantly lower in the patients with considerable PH compared to those without PH (30% vs. 47%, P < 0.001). Additionally, right ventricular dysfunction was significantly detected in the patients with PH in comparison to those without PH (7 patients vs. 1 patient, P = 0.001).

4.3. Clinical and Imaging Predictors of MR Improvement in Patients with Moderate or More Severe Mitral Regurgitation at Baseline

The associated factors with MR improvement have been presented in Table 4. After a one-year follow-up, MR improvement occurred in 18 patients (56.2%) who had moderate or more severe baseline MR. In comparison with bicuspid, tricuspid native aortic valve was associated with higher MR improvement after TAVR (43.7% vs. 25.8%, P = 0.005). Normal sinus rhythm was also significantly associated with MR improvement compared to atrial fibrillation (51% vs. 3.5%, P = 0.05). Improvement of left ventricular ejection fraction was also associated with MR improvement (33.3% vs. 22.2%, P = 0.02). If the baseline left ventricular ejection fraction was normal, the probability of MR improvement exceeded (75% vs. 25%, P = 0.05). The absence of left atrial enlargement was also associated with MR improvement (22.4% vs. 20.6%, P = 0.005). However, mitral annular calcification was not significantly associated with MR improvement after

Table 2. The Main Clinical and Imaging Characteristics of the Global Population according to the Degree of Mitral Regurgitation at Baseline

Clinical Variables		**Total (n = 109)* (100%)**	**MR < Moderate (n = 73) (67.0%)**	**MR ≥ Moderate (n = 36) (33.0%)**	**P-value**
Age (yrs.)		76.74 ± 7.11	76 ± 5.8	76 ± 9.2	0.985
BMI (kg/m²)		26.32 ± 5.21	26 ± 4.6	26 ± 6.5	0.948
Sex (male)		63 (57.8%)	44 (69.8%)	19 (30.2%)	0.456
History of hypertension		57 (52.3%)	35 (61.4%)	22 (38.6%)	0.196
History of diabetes mellitus		30 (27.5%)	20 (66.7%)	10 (33.3%)	0.967
History of dyslipidemia		30 (27.5%)	18 (60.0%)	12 (40.0%)	0.340
History of chronic kidney disease		8 (7.3%)	6 (75.0%)	2 (25.0%)	0.616
History of CABG		22 (20.2%)	16 (72.7%)	6 (27.3%)	0.521
History of stroke		2 (1.8%)	2 (100.0%)	0 (0.0%)	1.000
Previous atrial fibrillation		17 (15.6%)	9 (52.9%)	8 (47.1%)	0.1
MR mechanism	Primary	80 (73.4%)	65 (59.6%)	15 (13.8%)	< 0.001
	Secondary	29 (26.6%)	8 (7.3%)	21 (19.3%)	
Transthoracic echocardiography data before TAVR					
Left ventricular ejection fraction (%)		41.28 ± 13.82 [10-65]**	44 ± 12.34 [15-65]	34 ± 14.64 [10-55]	0.001
Systolic pulmonary arterial pressure (mmHg)		43.09 ± 15.33 [20-82]	38.08 ± 12.31 [20-77]	52.97 ± 14.35 [26-82]	< 0.001
Left ventricular end-diastolic volume index (mL/m2)		70 ± 21.85	69.5 ± 22.80	74.1 ± 21.06	0.3
Left atrial volume index (mL/m2)		42. 0± 15.53	37.19 ± 13.37	52.35 ± 15.06	< 0.001
Right ventricular midcavitary diameter (cm)		3.2 ± 0.46	3.16 ± 0.44	3.38 ± 0.46	0.02

*Two patients had a history of mitral valve replacement and MR was not interrogated in them; ** the values in parentheses represent the minimum and maximum of indices.

Abbreviations: MR, mitral regurgitation; TAVR, transcatheter aortic valve replacement; BMI, body mass index; CABG, coronary arteries bypass graft.

Table 3. The Main Clinical and Imaging Characteristics of the Global Population according to the Degree of Pulmonary Hypertension at Baseline

Clinical variables		**Total (n = 111) (100%)**	**No PH (n = 50) (44.5%)**	**Mild PH (n = 28) (25.5%)**	**Moderate PH (n = 10) (9.1%)**	**Severe PH (n = 23) (20.9%)**	**P-value**
Age (yrs.)		76 ± 7.25	77 ± 5.75	75 ± 8.20	74 ± 8.78	75 ± 8.37	0.347
BMI (kg/m²)		26 ± 5.21	25 ± 4.54	26 ± 4.42	30 ± 7.98	27 ± 5.31	0.015
Sex (male)		62 (56.4%)	31 (50.0%)	15 (24.2%)	5 (8.1%)	11 (17.7%)	0.597
History of hypertension		58 (52.7%)	25 (43.1%)	14 (24.1%)	8 (13.8%)	11 (19.0%)	0.341
History of diabetes mellitus		29 (26.4%)	12 (41.4%)	6 (20.7%)	6 (20.7%)	5 (17.2%)	0.1
History of dyslipidemia		30 (27.3%)	11 (36.7%)	11 (36.7%)	4 (13.3%)	4 (13.3%)	0.207
History of chronic kidney disease		10 (9.1%)	3 (30.0%)	3 (30.0%)	1 (10.0%)	3 (30.0%)	0.863
History of coronary artery bypass graft		22 (20.0%)	12 (54.5%)	6 (27.3%)	1 (4.5%)	3 (13.6%)	0.578
Previous atrial fibrillation		17 (15.5%)	4 (23.5%)	7 (41.2%)	1 (5.9%)	5 (29.4%)	0.301
History of stroke		2 (1.8%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	1.000
Transthoracic echocardiography							
Left ventricular ejection fraction		41.64 ± 13.82 [10-65]*	47.86 ± 9.94 [20-65]	43.75 ± 12.66 [15-55]	30.50 ± 14.80 [10-50]	30.65 ± 12.46 [10-50]	< 0.001
Right ventricular dysfunction	No	109 (88.4%)	48 (43.2%)	27 (24.3%)	9 (8.1%)	19 (17%)	0.001
	Yes	8 (11.6%)	1 (0.9%)	2 (1.8%)	1 (0.9%)	4 (3.4%)	

*The values in parentheses represent the minimum and maximum of indices.

Abbreviations: PH, pulmonary hypertension; BMI, body mass index.

TAVR. Additionally, post-TAVR significant paravalvular leakage was not significantly associated with MR grade change (P = 0.7). Nonetheless, it should be noted that the subjective evaluation of MR as being primary or functional by transthoracic echocardiography failed to predict MR change. Furthermore, the use of different types of valve did not affect MR evolution post TAVR.

4.4. Clinical and Imaging Predictors of Pulmonary Hypertension Improvement in Patients with Pulmonary Hypertension at Baseline

The clinical and imaging factors of PH improvement after TAVR have been depicted in Table 5. After a one-year follow-up, systolic pulmonary pressure decreased by at least 10 mmHg in 45 patients (77.5%). Age, rhythm, and body mass index were not significantly associated with PH improvement. However, left ventricular ejection fraction improvement was significantly associated with PH improvement (47.2% vs. 30.2%, P = 0.02). Additionally, TAVR with a balloon expandable valve was associated with PH improvement compared to using a self-expandable valve (40% vs. 37%, P = 0.04). Moreover, PH improvement after the TAVR procedure was significantly associated with MR improvement (53.3% vs. 20%, P = 0.003). It is noteworthy that right ventricular function improvement and pre-TAVR right ventricular function could not predict PH improvement (P = 0.2).

Table 4. The Associated Factors with Mitral Regurgitation Improvement after Transcatheter Aortic Valve Replacement

		MR Improvement at Least One Grade		
		Yes n = 18	No n = 14	P-value
MR mechanism	Primary	9 (28.1%)	5 (15.6%)	0.41
	Secondary	9 (28.1%)	9 (28.1%)	
LV ejection fraction improvement after one year	Yes	9 (33.3%)	2 (7%)	0.02
	No	6 (22.2%)	10 (37%)	
Rhythm	Normal sinus	14 (51%)	7 (26%)	0.05
	Atrial fibrillation	1 (3.5%)	5 (18.5%)	
Left ventricular enlargement before TAVR	Yes	7 (21%)	8 (25%)	0.3
	No	11 (34.5%)	6 (18.5%)	
Native valve	Bicuspid	0	5 (15.6%)	0.005
	Tricuspid	3 (9.3%)	1 (3.1%)	
	Unknown*	14 (43.7%)	8 (25.8%)	
Valve type	Balloon-expandable	9 (29%)	6 (19.3%)	0.7
	Self-expandable	8 (25.8%)	8 (25.8%)	
Post-TAVR significant paravalvular leakage	Yes	1 (3%)	3 (10.5%)	0.7
	No	16 (55.5%)	9 (31%)	
Pre-TAVR significant left ventricular hypertrophy	Yes	7 (21.8%)	2 (6%)	0.1
	No	11 (34.3%)	12 (37.5%)	
Mitral annular calcification	Yes	7 (21.9%)	2 (6.3%)	0.1
	No	11 (34.4%)	12 (37.5%)	
Left atrial enlargement	Yes	7 (20.6%)	8 (23.5%)	0.005
	No	11 (22.4%)	6 (13.8%)	

*Because of severe calcification.

Abbreviations: MR, mitral regurgitation; LV, left ventricular; TAVR, transcatheter aortic valve replacement.

Table 5. Probability of Pulmonary Hypertension Improvement after Transcatheter Aortic Valve Replacement

		Improvement of Pulmonary Hypertension		P-value
		Yes n = 45	No n = 11	
Age	-	77.83±6.9	77.86±8.18	0.99
BMI	-	28±7.35	24.7±5.6	0.27
LV ejection fraction improvement	Yes	25 (47.2%)	3 (5.7%)	0.02
	No	16(30.2%)	9(17%)	
Rhythm				0.56
	NSR	33 (63%)	9 (17%)	
	AF	7 (13%)	3 (6%)	
Valve type				0.04
	Balloon expandable	23 (40%)	3 (5%)	
	Self-expandable	21 (37%)	10 (18%)	
Native valve type				0.23
	Bicuspid	10 (18%)	1 (2%)	
	Tricuspid	29 (52%)	9 (16%)	
	Unknown*	4 (7%)	3 (5%)	
Leakage				0.85
	No	38 (70%)	11 (20%)	
	Yes	4 (7%)	1 (2%)	
MR improvement	Yes	16 (53.3%)	1 (3.3%)	0.003
	No	6 (20%)	7 (23.3%)	
RV function improvement	Yes	23 (44.2%)	6 (11.5%)	0.2
	No	15 (28.8%)	8 (15.4%)	
Pre-TAVR RV dysfunction	Yes	16 (27.6%)	6 (10.3%)	0.4
	No	29 (50%)	7(12.1%)	

*Because of severe calcification.

Abbreviations: BMI, body mass index; LV, left ventricular; NSR, normal sinus rhythm; AF, atrial fibrillation; MR, mitral regurgitation; RV, right ventricular; TAVR, transcatheter aortic valve replacement.

Table 6. Mortality Rate and Improvement of Echocardiographic Indices after TAVR

		Death		P-value
		Yes	**No**	
TAVR valve type	Balloon-expandable	19 (17.1%)	27 (24.3%)	0.02
	Self-expandable	14 (12.6%)	51 (45.9%)	
MR improvement	Yes	4 (12.5%)	14 (43.8%	0.2
	No	6 (18.8%)	8 (25%)	
PH improvement	Yes	9 (15.5%)	36 (62.1%)	0.4
	No	4 (6.9%)	9 (15.5%)	
Left ventricular ejection fraction improvement	Yes	5 (7.1%)	29 (41.4%)	0.04
	No	12 (17.1%)	24 (34.4%)	
Right ventricular ejection fraction improvement	Yes	8 (13.3%)	27 (45%)	0.7
	No	5 (8.3%)	20 (33.3%)	

Abbreviations: MR, mitral regurgitation; PH, pulmonary hypertension; TAVR, transcatheter aortic valve replacement.

4.5. Predictors of Follow-up Mortality

As shown in Table 6, left ventricular ejection fraction improvement after TAVR was significantly associated with a reduced death rate (7.1% vs. 17.1%, P = 0.04). MR, PH, and right ventricular function improvement also had a positive effect on survival, but the difference was not statistically significant (P > 0.05).

5. Discussion

This study involving a centralized core laboratory analysis of transthoracic echocardiography demonstrated the presence of concomitant moderate or more severe baseline MR in 29% of the TAVR recipients and any degree of PH in 55.9% of the patients. The findings indicated that MR and PH were prevalent in patients undergoing TAVR and improved in a large proportion of them one year after TAVR. Additionally, left ventricular ejection fraction improvement after TAVR led to a lower mortality rate.

5.1. The Mechanism of Mitral Regurgitation Improvement

In patients who have AS, the MR severity increases as the Pressure Gradient (PG) rises along with AS progression. After aortic valve replacement, two processes result in MR regression: a) the reduction of left ventricular cavity pressure leading to a reduction in the ventricle-to-left atrium PG and b) the reduction of left ventricular diastolic volume and reverse remodeling of the left ventricle would recover its geometry, resulting in a decrease in mitral tethering (19, 20). Early after aortic valve replacement, the reduction in MR volume is greater than the decrease in the effective regurgitant orifice, denoting that hemodynamic rather than geometric changes are the basic determinant of MR improvement in this phase. Thereafter, left ventricular reverse remodeling is the main factor that leads to further MR improvement. This pattern of interactions suggested by the previous studies was further supported by the current study findings. Some studies showed that the MR mechanism (functional vs. organic) could not predict whether the regurgitant orifice was fixed or dynamic (21, 22). Therefore, even severe organic MR might significantly decrease in response to the changes in left ventricular hemodynamics. The current analysis confirmed this theory and it was not explored whether the mechanism of MR could influence the MR severity. It is also important to note that identifying the exact mechanism of MR in TAVR patients is challenging and a "mixed" etiology (e.g., left ventricular dysfunction, coronary disease, annular calcification, etc.) is common, especially in older populations.

5.2. Predictors of Mitral Regurgitation Improvement

The present study results revealed no significant reduction in MR until discharge (46.5%), but a significant reduction in MR after one year (57%). The patients who had atrial fibrillation presented a lower rate of MR improvement. This phenomenon might have been influenced by several factors. More advanced fibrous skeleton degeneration coupled with larger dimensions of the mitral apparatus and left atrium might have contributed to more frequent conduction system disturbances, resulting in a lower likelihood of MR improvement. However, left ventricular ejection fraction improvement contributed to a significant MR improvement. Because MR in low left ventricular ejection fraction was secondary to annular enlargement or leaflet tethering, an improvement of left ventricular ejection fraction would recover the leaflet tethering and lead to the normal shape of the mitral apparatus, thereby decreasing the MR severity. If the native valve was tricuspid rather than a bicuspid valve, the probability of MR improvement increased. This might be due to the underlying connective tissue disease in patients with a bicuspid aortic valve as a primary cause of MR.

5.3. The Prognostic Value of Mitral Regurgitation after Transcatheter Aortic Valve Replacement

Although improvement in MR (demonstrated in approximately 56.2% of the individuals) one year after TAVR translated into a reduction in all-cause mortality, it was not statistically significant (P = 0.2). This might be attributed to the small number of participants under investigation.

5.4. The Mechanism of Pulmonary Hypertension Improvement

It has been hypothesized that severe AS causes an increased rigidity of the left ventricle, progressive diastolic dysfunction, increased filling pressure, and high left atrial pressure reflected on the pulmonary vascular bed, which eventually leads to a secondary increase in pulmonary arteriolar tone and reactive PH (5, 23). After TAVR, that high left atrial pressure recovers, which decreases post-capillary pressure and diminishes PH secondary to high post-capillary pressure.

5.5. Predictors of Pulmonary Hypertension Improvement

This study indicated that left ventricular ejection fraction improvement resulted in a higher probability of PH improvement one year after TAVR. It seems that TAVR reduces valvular resistance and the global afterload on the left ventricle and relieves pulmonary resistances, leading to a reduction in pulmonary artery pressure. The present study findings showed a 55.5% reduction in PH (by at least 10 mmHg) until discharge and a 77.5% reduction after one year. Early reduction in Systolic Pulmonary Artery Pressure (SPAP) might be associated with the early hemodynamic changes, improvement of post-capillary pressure, and lowering of the left ventricular end-diastolic pressure. On the other hand, late reduction in SPAP might occur secondary to the reverse remodeling of left ventricular and mitral apparatus, leading to MR improvement and a decline in the PH grade. Patients who had MR improvement also tended to have right ventricular dysfunction improvement post TAVR (24). Decrease in systolic pulmonary artery pressure might result in a decline in right ventricular afterload, thereby recovering right ventricular function. If pulmonary vascular resistance remains high and PH is secondary to both post-capillary and pre-capillary hypertension, the probability of PH improvement decreases.

5.6. Prognostic Value of Pulmonary Hypertension after Transcatheter Aortic Valve Replacement

Several studies have demonstrated reduced outcomes in patients with AS and concomitant PH compared to those without PH (4, 7-9, 25). The present study findings revealed a higher five-year mortality in the patients who still had PH after TAVR (10% vs. 5.7%, P = 0.1), which might be attributed to a higher incidence of atrial fibrillation, severely impaired right ventricular function, and pulmonary artery hypertension.

5.7. Limitations

Study design was one of the limitations of this retrospective single-center study. Other limitations included small sample size, not using multislice computed tomography for accurate measurement of the mitral annular diameter, lack of MR standardized quantification, potential variations of information on MR etiology, and estimation of systolic pulmonary pressure by indirect indices on echocardiography. Nevertheless, the results were consistent with those of the prior studies. Hence, further prospective studies are required to identify a beneficial model of MR and PH improvement after TAVR.

5.8. Conclusion

TAVR could positively affect MR and PH and reduce their severity in most patients after one year.

5.9. Ethical Approval

IR.RHC.REC.1400.055

5.10. Informed Consent

This was a retrospective study and informed consent was optional based on the journal guideline.

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Authors' Contribution

Study concept and design: A.F.; analysis and interpretation of data: A.A., Z.R., and Z.H.; drafting of the manuscript: Z.R.; critical revision of the manuscript for important intellectual content: Z.R., K.R., and V.D.; statistical analysis: Y.K.

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