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Research Article

Prevalence and Predictive Factors of Early Degeneration of Bioprosthetic Mitral Valves: A Single-Center Cohort Study

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Background. Bioprosthetic mitral valves (MV) have limited durability. Dysfunction and degeneration of these valves can lead to reoperation and progressive heart failure. We investigated the frequency and predictors of MV bioprosthesis early degeneration within three years following MV replacement surgery. *Methods*. In this retrospective cohort study, we retrieved the data of consecutive patients who underwent bioprosthetic MV replacement through midsternotomy at Tehran Heart Center between 2013 and 2019. Based on the reviewed parameters of the bioprosthetic MV in the follow-up echocardiography, the patients were divided into two groups to compare the variables respecting early degeneration. Finally, the predictors of early degeneration were recognized using the Cox regression hazards model. *Results*. We reviewed and analyzed data of 177 patients from our hospital database. The mean age of the patients was 63.9 ± 11.7 years and 100 (56.5%) were women. 39 (22.0%) patients had experienced early degeneration and two (1.1% of the total) had died during the follow-up period. Patients in the degeneration group tended to have a history of stroke and renal failure, although not statistically significant. The sole independent predictor of early degeneration of bioprosthetic MV was a high MV mean gradient in the first postoperative echocardiography study (HR = 11.01, 95% CI: 4.80–25.24; $P < 0.001$). *Conclusion*. About 22.0% of our patients had echocardiographic criteria for early degeneration, and according to our results, increased MV gradients (without considering the reason) in the first postoperative echocardiography were the sole independent predictor for it. Careful valve selection can be essential in reducing early degeneration.

1. Introduction

Valvular heart disease (VHD) is a frequent cardiovascular condition worldwide [1–3]. Either structural or functional, valvular abnormalities are important public health problems leading to a shorter life span and reduced quality of life [1, 4]. Aortic and mitral valve (MV) diseases are the two most common types of VHD, and degenerative mitral valve regurgitation (MR) is the most common valve problem in industrialized countries [5]. Meanwhile, mitral stenosis (MS), mainly due to rheumatic fever, is still the leading cause in developing countries.

According to the new surgical guidelines for treating VHDs, surgical repair and replacement are still the accepted methods in managing VHD despite the increased use of transcatheter heart valve replacement [6, 7]. Bioprosthetic valve replacement is a standard treatment for VHDs, and its use has increased in the recent past as more replacement interventions have become available [8, 9]. The primary reason for this trend is better clinical outcomes due to better

hemodynamic profiles and reduced need for anticoagulants due to lower thrombogenicity than mechanical valves [10]. However, bioprosthetic valves have limited durability and are prone to early degeneration, leading to several problems, such as heart failure, that might limit their use [8, 10, 11]. Therefore, recognizing predictors of early bioprosthetic valve degeneration is essential to select the best candidates for bioprosthesis valve replacement. Current guidelines and proposed standard definitions of dysfunction and degeneration outline the importance of imaging. Imaging modalities such as echocardiography play a crucial role in understanding valve degeneration and malfunction, identifying transvalvular gradients, leaflet thickening, thrombosis, calcification, and restricted or reduced leaflet motion. [12] We conducted this retrospective cohort study using the data from our center's database to determine the frequency and predictors of early degeneration in bioprosthetic mitral valves in patients who underwent mitral valve replacement in our hospital.

2. Methods

2.1. Participants and Setting. For this retrospective cohort study, we reviewed the data of 294 consecutive patients who underwent mitral valve replacement through mid-sternotomy and received bioprosthetic valves between 2013 and 2019 at Tehran Heart Center, a university-affiliated tertiary center [13]. The baseline, surgical, and follow-up data were retrieved from our cardiac surgery database [14]. The baseline data included demographics, clinical, laboratory, surgical, and transthoracic echocardiography. Classic cardiovascular risk factors, including hypertension, diabetes mellitus, dyslipidemia, and smoking, were evaluated and recorded according to the respective guidelines. In accordance with the research practices at our center, all patients consented to using their clinical data for research purposes at the time of hospitalization; therefore, no additional consent was required for the observational study. The study protocol was approved by the Ethics Committee and the Research Council of Tehran Heart Center separately.

2.2. Interventions and Outcomes. Experienced cardiac surgeons performed mitral valve replacements. The routine surgical method can be described briefly as opening the left atrium with an incision parallel to the interatrial groove, cross-clamping the aorta, and infusing cardioplegia to replace the mitral valve. The following steps included resecting the anterior leaflet of the MV and replacing the valve.

The primary study endpoint was the early degeneration within three years following MV replacement based on the echocardiographic features. We describe valve early degeneration by the following criteria during patient follow-up visits: (1) increased MV mean gradient more than 5 mmHg in stable hemodynamic status compared to predischarge echocardiography study; (2) any transvalvular mitral regurgitation more than mild (in the previous echocardiography study); (3) degenerative changes of MV bioprosthesis leaflets visible in echocardiography images (including motion abnormality, thickening, calcification, pannus formation, and thrombosis); (4) Peak E velocity >1.9 m/s; and (5) Doppler velocity index (DVI) more than 2.2. Our exclusion criteria were the destruction of the endocarditis process, isolated clot formation, paravalvular leakage without any degeneration features, and unreliable echocardiography results due to confounders such as high heart rate. The secondary study endpoint was all-cause mortality. The routine follow-up visits at our center are conducted 1, 6, and 12 months after the operation and then repeated annually.

2.3. Variables and Measurements. Experienced cardiologists performed all baseline and follow-up echocardiographic assessments using commercially available ultrasound machines (Vivid S60 and (GE Healthcare, USA) and Philips Affiniti (Koninklijke Philips N.V, the Netherlands)). Postoperative echocardiography was performed one week after the surgery when the patient had stable hemodynamics. Transesophageal echocardiography was utilized to confirm the results when required. Different parameters were obtained, such as left atrial and left ventricle dimensions, left ventricular ejection fraction, right ventricular size and function, pulmonary artery pressure, and bioprosthetic valve function and characteristics. The echocardiographic diagnosis of left atrial enlargement was based on a transverse dimension greater than 4.0 cm in the parasternal long-axis view. The trans-tricuspid pressure gradient was calculated using the modified Bernoulli equation ($4v2$), where v is the maximum velocity of the tricuspid valve regurgitant jet. Right atrial pressure (RAP) was estimated by the respiratory variation in the diameter of the inferior vena cava and was categorized as 5, 10, or 15 mmHg. Right ventricular systolic pressure (RVSP) was calculated by adding the trans-tricuspid pressure gradient to the RAP estimate, and values of more than 40 mmHg were defined as pulmonary hypertension. The bioprosthetic valve mean gradients were calculated in three cycles in normal sinus rhythm and five cycles in AF rhythm cases using continuous wave Doppler and the simplified Bernoulli equation. The mean gradients of more than five mmHg were defined as increased. Increased postoperative gradient was assessed compared to suggested MV gradients after the MVR surgery [15–17]. The Doppler velocity index (DVI) was assessed by measuring the ratio of mitral valve velocity-time integral (VTI) and systolic left ventricular outflow tract (LVOT) VTI that were measured using pulsed wave (PW) Doppler. Measures more than 2.2 were considered abnormal. The appearance and leaflet thickness of mitral bioprosthetic valves were checked precisely to detect any degenerative changes. We evaluated paravalvular leak, or transvalvular MR, by color Doppler, and any transvalvular regurgitation more than mild was defined as abnormal. The prosthetic mitral valve's EOA was calculated from the continuity equation: EOA = CSALVOT × (LVOT VTI ÷ PrMV VTI), where EOA is in cm^2,

LVOTVTI is the subaortic velocity-time integral, and PrMV VTI is the velocity-time integral obtained by CW Doppler through the mitral prostheses, both in cm. Subsequently, it was divided by the body surface area (BSA) to obtain an effective orifice area index to rule out patient prosthesis mismatch (PPM). Values of less than 1.2 were considered abnormal and indicated PPM. The pressure half-time method (PHT) was measured by tracing the deceleration slope of the E-wave on the Doppler spectral display of transmitral flow. Measures more than 130 msec were considered abnormal.

2.4. Statistical Analysis. The study population was divided into two groups based on early degeneration for comparison. Categorical data were presented as frequency (percentage) and were compared using a chi-square test. Continuous data were presented as the mean ± standard deviation or median (interquartile range (IQR)) and were compared using the Pearson chi-square, Fisher's exact test, and Mann-Whitney*U* test where applicable. Univariate and multivariate Cox proportional hazard regression analyses were performed to identify the predictors of early degeneration. For multivariate Cox regression analysis, variables with $p < 0.2$ were included in the regression model with the backward selection method. The predictors of early degeneration were reported as hazard ratios with 95% confidence intervals (95% CI). All statistical analyses were computed using SPSS version 22.0 (IBM, Armonk, New York).

3. Results

3.1. Baseline Characteristics. In the present study, we reviewed the data of 294 patients who received a bioprosthetic mitral valve in our center. Almost 117 patients (39.7%) did not complete the follow-up (including 24 (8.1%) patients who died within one year after surgery) and were excluded from the analysis. Finally, data from 177 patients were included in this analysis. The mean age of the included patients was 63.9 ± 11.7 years and 100 (56.5%) were women. 39 (22.0%) patients developed early degeneration and two (1.1% of the total) died during the follow-up period. 23 patients had regurgitative degeneration (according to degenerative echocardiographic changes) and 16 had stenotic degeneration (increased gradient, DVI, and Peak E velocity). There was no significant difference between the patients with and without degeneration in age and gender. However, patients who developed early degeneration were more likely to have a history of stroke or chronic renal failure ($P = 0.011$ and $P = 0.072$, respectively). Mitral valve insufficiency was the patients' most common reason for surgery (about 60%). Ten patients had a history of mitral valve replacement, and redo surgery was done for them due to a malfunctioning preliminary prosthesis. Two patients had a history of previous mitral valve repair and two others had a previous coronary artery bypass graft (CABG) history. There was no other significant difference between the two groups (patients who developed early degeneration and those who did not) in the baseline characteristics (Table 1).

3.2. Operation Outcomes. The most common type of surgery was valve replacement alone (39.0%), and in the rest of the patients, it was accompanied by coronary artery bypass grafting or other types of cardiac surgery (Table 2). No significant difference was detected between the two groups regarding the perioperative characteristics, total ICU stay duration, and ventilation time. Atrial fibrillation was the most common in-hospital complication (40.1%), followed by prolonged ventilation (14.7%) and pleural effusion (13.6%). However, there was no significant difference between the patients with and without early degeneration, except for tamponade, that only occurred in 2 patients within the early degeneration group ($P = 0.048$).

In the first postoperative echocardiography within the first or the second day after surgery, paravalvular leaks tended to be more frequent in the early degeneration group, but there was no other significant difference between the two study groups (Table 3).

3.3. Follow-Up Outcomes. The mean duration between surgery and the last echocardiography was 2.1 ± 0.7 years, with no significant difference between the subgroups. Patient-prosthesis mismatch was observed in 77 (43.5) but with no difference between the subgroups. Paravalvular leak and transvalvular mitral regurgitation were significantly higher in the early degeneration group. Most of the echocardiographic indices were significantly worse in the early degeneration group, as described in Table 4.

In the multivariable Cox regression model, the variables eligible to enter were age, renal failure, previous cerebrovascular accidents, total ICU stay duration, use of anticoagulants preoperatively, paravalvular mitral regurgitation, clot formation, and increased MV gradient in the first postoperative echocardiography. The only variable that remained significant and could independently predict early degeneration of the bioprosthetic mitral valve was increased MV gradient in the first postoperative echocardiography (HR = 11.01, 95% CI: 4.80–25.24; $P < 0.001$).

4. Discussion

In the present study, we observed a 22% occurrence of early degeneration of MV bioprosthesis within three years following the replacement surgery as detected by transthoracic echocardiography. Among the baseline clinical and echocardiographic characteristics, only an increased MV gradient in the first postoperative echocardiography was detected as an independent predictor for early degeneration regardless of its etiology.

Bioprosthetic valves are more popular than in the past because of the fewer risks linked to anticoagulation medications after mechanical valve implantation. Their new generations also have more reasonable durability [18–21]. Due to their risks, bioprosthetic valves are currently preferred in older patients, but the evidence is growing that implanting these valves in younger patients can also be accompanied by better clinical outcomes and survival rates [4]. On the other hand, despite the continuous progress in

Table 1: Baseline characteristics of the study population and comparison between patients with and without bioprosthetic mitral valve early degeneration.

Characteristics	Total ($n = 177$)	Normal ($n = 138$)	Degeneration ($n = 39$)	P value*
Age, years	63.9 ± 11.7	63.0 ± 12.6	66.8 ± 7.0	0.08
Male gender, *n* (%)	77 (43.5)	57 (41.3)	20 (51.3)	0.27
Body surface area, m^2	1.70 ± 0.18	1.70 ± 0.18	1.70 ± 0.17	0.96
BMI, kg/m^2	25.9 ± 4.7	25.8 ± 4.6	26.2 ± 5.2	0.64
Diabetes mellitus, *n* (%)	32 (18.0)	26 (18.8)	6 (15.4)	0.62
Hypertension, *n* (%)	69 (39.1)	52 (37.7)	17 (43.6)	0.50
Dyslipidemia, *n* (%)	48 (27.1)	38 (27.5)	10 (25.6)	0.81
Smoking, n (%)				
Current	15 (8.5)	10 (7.2)	5 (12.8)	0.51
Former	18 (10.2)	14 (10.1)	4 (10.3)	
Opium, n (%)				
Current	9 (5.1)	8 (5.8)	1 (2.6)	0.87
Former	4 (2.3)	3 (2.2)	1 (2.6)	
History of CVA, *n* (%)	22 (12.4)	12 (8.7)	10 (25.6)	0.01
History of MI, *n* (%)	21 (11.9)	17 (12.3)	4 (10.3)	0.73
Renal failure, *n* (%)	5 (2.8)	2 (1.4)	3 (7.7)	0.07
Previous MVR	10 (5.6)	6 (4.3)	4 (10.3)	0.23
COPD, *n* (%)	15 (8.5)	12 (8.7)	3 (7.7)	0.84
CAD, n (%)				
None	52 (29.4)	40 (29.0)	12 (30.8)	
Minimal	27 (15.3)	19 (13.8)	8 (20.5)	0.36
Single vessel	28 (15.8)	24 (17.4)	4 (10.3)	
Double vessel	17 (9.6)	12 (8.7)	5 (12.8)	
Triple vessel	24 (13.6)	17 (12.3)	7 (17.9)	
Atrial fibrillation, *n* (%)	76 (42.9)	57 (41.3)	19 (48.7)	0.41
EF, %	46.7 ± 9.6	47.1 ± 9.4	46.2 ± 10.2	0.51
Mitral insufficiency, n (%)				
None	5 (2.8)	5 (3.6)	0 (0)	
Trivial	3 (1.7)	2 (1.4)	1 (2.6)	0.20
Mild	18 (10.2)	17 (12.3)	1 (2.6)	
Moderate	39 (22.0)	29 (21.0)	10 (25.6)	
Severe	106 (59.9)	79 (57.2)	27 (69.2)	
Mitral stenosis, n (%)				
None	82 (46.3)	62 (44.9)	20 (51.3)	
Mild	7 (4.0)	5 (3.6)	2 (5.1)	0.13
Moderate	18 (10.2)	11 (8.0)	7 (17.9)	
Severe	62 (35.0)	52 (37.7)	10 (25.6)	
Diastolic dysfunction, *n* (%)	8 (4.5)	5 (3.6)	3 (7.7)	0.38
LVH, *n* (%)	49 (28.8)	38 (29.0)	11 (28.2)	0.92
Serum creatinine, mg/dl	0.99 ± 0.49	0.98 ± 0.51	1.02 ± 0.39	0.67
FBS, mg/dl	98.2 ± 24.3	98.7 ± 26.5	96.4 ± 13.8	0.54
Hemoglobin, g/dl	13.3 [12.1, 14.4]	13.5 [12.4, 14.6]	12.7 [11.5, 14.0]	0.01
Preoperative anticoagulants, *n* (%)	61 (34.5)	43 (31.2)	18 (46.2)	0.08
Aspirin, *n* (%)	86 (48.6)	63 (45.7)	23 (59.0)	0.14
Preoperative status, n (%)				
Elective surgery	165 (93.2)	130 (94.2)	35 (89.7)	0.40
STEMI	7 (4.0)	5 (3.6)	2 (5.1)	
NSTEMI	5 (2.8)	3 (2.2)	2 (5.1)	

*$P < 0.05$ was considered statistically significant. BMI: body mass index; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; EF: ejection fraction; LVH: left ventricular hypertrophy; MI: myocardial infarction; NSTEMI: non-ST segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

bioprosthetic valves, valve dysfunction and degeneration remain the fundamental issue of this type of valve [12]. Recent studies have suggested immune response as a contributor to valve degeneration. This response is possibly due to tissue damage and absorption of plasma protein on the bioprosthesis surface [22, 23].

Imaging is central in investigating the implanted valve function, and echocardiography is an affordable and

Table 2: Perioperative characteristics and surgical complications of the study population and their comparison between patients with and without bioprosthetic mitral valve early degeneration.

Characteristics	Total ($n = 177$)	Normal ($n = 138$)	Degeneration ($n = 39$)	P value*
Type of surgery				
Valve replacement	69 (39.0)	56 (40.6)	13 (33.3)	
Valve replacement + CABG	45 (25.4)	33 (23.69)	12 (30.8)	0.70
Valve + CABG + other	18 (10.2)	15 (10.9)	3 (7.7)	
Valve + other	45 (25.4)	34 (24.6)	11 (28.2)	
Manufacturer of the valve, n (%)				
Perimount	117 (66.1)	91 (65.9)	26 (66.7)	
Hancock I	13 (7.3)	11 (8.0)	2 (5.1)	
Hancock II	29 (16.4)	23 (16.7)	6 (15.4)	0.63
Biocor	12 (6.8)	9 (6.5)	3 (7.7)	
Epic	3 (1.7)	1 (0.7)	2 (5.1)	
Magna	2 (1.1)	2 (1.4)	0 (0)	
St. Jude	1 (0.6)	1 (0.7)	0 (0)	
Size of the valve, n (%)				
24	1 (0.6)	0	1 (2.6)	
25	4 (1.7)	4 (2.2)	0 (0)	
27	89 (50.3)	64 (46.4)	25 (64.1)	0.14
29	61 (34.5)	50 (36.2)	11 (28.2)	
31	20 (11.3)	18 (13.0)	2 (5.1)	
33	2 (1.1)	2 (1.4)	0 (0)	
In hospital anticoagulant, n (%)	171 (96.6)	133 (96.4)	38 (97.4)	0.75
Aspirin, n (%)	152 (85.9)	121 (87.7)	31 (79.5)	0.20
Total ICU stay, hour	67.0 [26.3, 109.0]	69.0 [27.8, 110.7]	68.5 [30.1, 135.5]	0.72
Total ventilation duration, hour	13.0 [10.5, 18.0]	13.3 [10.5, 18.9]	16.3 [11.9, 26.3]	0.10
Cross clamp time, minutes	72.5 ± 32.7	72.3 ± 34.1	73.2 ± 27.7	0.87
ICU readmission, n (%)	12 (6.8)	9 (6.5)	3 (7.7)	0.80
Reintubation, n (%)	15 (8.5)	11 (8.0)	4 (10.3)	0.65
Packed cell transfusion, n (%)	105 (59.3)	79 (57.2)	26 (66.7)	0.29
In-hospital complications				
Atrial fibrillation, n (%)	71 (40.1)	56 (40.6)	15 (38.5)	0.81
Pericardial effusion, n (%)	12 (6.8)	9 (6.5)	3 (7.7)	0.80
Pleural effusion, n (%)	24 (13.6)	16 (11.6)	8 (20.5)	0.15
Cardiac arrest, n (%)	2 (1.1)	2 (1.4)	0 (0)	0.99
Tamponade, n (%)	2 (1.1)	0 (0)	2 (5.1)	0.05
Pneumonia, n (%)	2 (1.1)	2 (1.4)	0 (0)	0.99
Prolonged ventilation, n (%)	26 (14.7)	18 (13.0)	8 (20.5)	0.25
Hemodialysis, n (%)	1 (0.6)	0 (0)	1 (2.6)	0.22
Reoperation due to valvular dysfunction, n (%)	1 (0.6)	0 (0)	1 (2.6)	0.22
Death, n (%)	2 (1.1)	1 (0.7)	1 (2.6)	0.40

*$P < 0.05$ was considered statistically significant. CABG: coronary artery bypass graft; ICU: intensive care unit.

accurate diagnostic tool [12]. By assessing various valve parameters, including mean gradient, cusp motility, and thickness, echocardiography can have an acceptable sensitivity and specificity in detecting valve degeneration when combined with clinical characteristics [24]. Our study's rate of early degeneration was acceptable, with no association with age, and it can be compared to other studies that reported a degeneration rate of 18–27% with different follow-up periods [20, 25–27]. Considering that we have mainly used the first and second generation of the MV prosthesis, using the third generation bioprosthesis in the future may be accompanied by a lower rate of degeneration [18]. Nevertheless, novel imaging modalities such as 18F-sodium fluoride PET/CT have recently been suggested as an improve degeneration detection [28].

The current data on bioprosthetic valve degeneration are conflicting, and several predictors have been introduced so far [20, 22, 26, 27, 29]. In our study, age at the implantation time was not related to early degeneration of the bioprosthesis, although the mean age of the patients with early degeneration was about 3.5 years higher than those who did not develop it. However, older studies in the literature introduced age as a predictor of survival [19, 25, 30], and durability was lower in younger patients [31].

Patients who developed early degeneration were more likely to have a history of stroke or chronic renal failure, suggesting that they may have multiple risk factors that make them more susceptible to early degeneration. These risk factors include inflammation, metabolic disorders, and other conditions such as hypercalcemia and

Table 3: Postoperative echocardiographic characteristics of the study population and comparison between patients with and without bioprosthetic mitral valve early degeneration.

Postoperative echocardiographic characteristics	Total ($n = 177$)	Nondegenerative ($n = 138$)	Degeneration ($n = 39$)	P value*
Mitral valve peak gradient	11.06 ± 3.4	10.89 ± 3.48	11.71 ± 2.90	0.20
Mitral valve mean gradient	5.21 ± 1.7	5.14 ± 1.81	5.49 ± 1.47	0.27
Clot formation, *n* (%)	2 (1.1)	0 (0)	2 (5.1)	0.05
Increased mitral valve gradient, *n* (%)	53 (59.9)	23 (16.7)	30 (76.9)	0.01
Pressure half time	78.8 ± 22.9	77.5 ± 21.7	83.6 ± 26.7	0.21
Doppler velocity index	1.9 ± 0.4	1.86 ± 0.40	1.95 ± 0.44	0.33
Paravalvular leak, n (%)				
None	160 (90.4)	127 (94.1)	33 (89.2)	
Trivial	3 (1.7)	1 (0.7)	2 (5.4)	0.10
Mild	7 (4.0)	6 (4.4)	1 (2.7)	
Moderate	1 (0.6)	1 (0.7)	0 (0)	
Moderate to severe	1 (0.6)	0 (0)	1 (2.7)	
Transvalvular mitral regurgitation, n (%)				
None	71 (40.1)	58 (43.0)	13 (35.1)	
Trivial	29 (16.4)	25 (18.5)	4 (10.8)	0.22
Mild	68 (38.4)	50 (37.0)	18 (48.6)	
Mild to moderate	4 (2.3)	2 (1.5)	2 (5.4)	

*$P < 0.05$ was considered statistically significant. LVED: left ventricular end-diastolic; LVES: left ventricular end-systolic; PAP: pulmonary arterial pressure; PHT: pressure half-time.

Table 4: Follow-up echocardiographic characteristics of the study population and comparison between patients with and without bioprosthetic mitral valve early degeneration.

Follow-up echo characteristic	Total ($n = 177$)	Normal ($n = 138$)	Degeneration ($n = 39$)	P value
Years between surgery and last echo, year	2.1 ± 0.7	2.1 ± 1.7	2.2 ± 0.8	0.55
Patient-prosthesis mismatch, *n* (%)	77 (43.5)	58 (43.3)	19 (48.7)	0.55
Mitral valve peak gradient	11.9 ± 3.8	11.5 ± 3.5	13.2 ± 4.5	0.01
Mitral valve mean gradient	5.1 ± 1.7	4.78 ± 1.50	6.38 ± 1.80	0.01
Paravalvular leak, n (%)				
None	170 (96.0)	135 (97.8)	35 (89.7)	
Trivial	2 (1.1)	2 (1.4)	0 (0)	
Mild	2 (1.1)	1 (0.7)	1 (2.6)	0.03
Mild to moderate	1 (0.6)	0 (0)	1 (2.6)	
Moderate	1 (0.6)	0 (0)	1 (2.6)	
Severe	1 (0.6)	0 (0)	1 (2.6)	
Transvalvular mitral regurgitation, n (%)				
None	64 (35.6)	53 (38.4)	10 (25.6)	
Trivial	24 (13.6)	20 (14.5)	4 (10.3)	
Mild	74 (41.8)	65 (47.1)	10 (25.6)	0.01
Mild to moderate	9 (5.1)	0 (0)	9 (23.1)	
Moderate	3 (1.7)	0 (0)	3 (7.7)	
Moderate to severe	2 (1.1)	0 (0)	2 (5.1)	
Severe	1 (0.6)	0 (0)	1 (2.6)	
PAP	33.8 ± 10.5	33.2 ± 10.6	35.2 ± 9.9	0.33
LVES dimension, mm	35.2 ± 7.4	34.4 ± 7.2	37.7 ± 7.4	0.01
LVED dimension, mm	50.1 ± 6.5	49.4 ± 6.3	52.6 ± 6.6	0.01
Left atrial size	47.3 ± 8.5	46.5 ± 8.0	50.4 ± 9.7	0.01
Mitral valve area index	1.19 ± 0.25	1.19 ± 0.25	1.20 ± 0.22	0.78
Effective orifice area	2.13 ± 1.61	2.17 ± 1.84	2.01 ± 0.34	0.62
Last peak e velocity	1.59 ± 0.31	1.57 ± 0.32	1.66 ± 0.26	0.25
PHT	100.6 ± 36.9	96.6 ± 31.3	114.4 ± 49.8	0.05
Doppler velocity index	2.19 ± 0.61	2.10 ± 0.44	2.49 ± 0.93	0.02
Right ventricular dysfunction, n (%)				
None	25 (14.1)	21 (15.2)	4 (10.3)	
Mild	109 (61.6)	81 (58.7)	28 (71.8)	0.44
Moderate	40 (22.6)	33 (23.9)	7 (17.9)	
Severe	3 (1.7)	3 (2.2)	0 (0)	

Table 4: Continued.

Follow-up echo characteristic	Total ($n = 177$)	Normal ($n = 138$)	Degeneration ($n = 39$)	P value
Left atrial dilation, n (%)				
None	18 (10.2)	17 (12.3)	1 (2.6)	
Mild	55 (3.1.1)	45 (32.6)	10 (25.6)	0.07
Moderate	49 (27.7)	39 (28.3)	10 (25.6)	
Severe	55 (31.1)	37 (26.8)	18 (46.2)	

*$P < 0.05$ was considered statistically significant. LVED: left ventricular end-diastolic; LVES: left ventricular end-systolic; PAP: pulmonary arterial pressure; PHT: pressure half-time.

hyperphosphatemia. Accordingly, calcific degeneration of cusp tissue is responsible for almost 75% of bioprosthetic valve failures [32]. Other factors such as diabetes, dyslipidemia, and hypertension were not significant predictors in our study, despite their possible role in early degeneration, as described in previous studies [32–35].

Previous studies have suggested PPM as a predictor of disturbed valve performance and an increased pressure gradient [35]. However, we did not observe any association between PPM and early degeneration in our patients. Nevertheless, a PPM was significantly higher than expected in both groups, with an average rate of 43.5% in all patients. Two main factors can contribute to the high PPM observed in these patients:

(1) Prolonged and suboptimal shipment duration and conditions from the manufacturer to our center can cause imperfect valve function after implantation. This might cause inferior outcomes compared to the Western centers despite similar valve types and patients and surgery conditions in our center.

(2) MS is significantly more prevalent in developing countries, including Iran, due to rheumatoid mitral valve diseases. This is while MS accounts for a negligible number of MV replacement surgeries in Western countries [3, 36]. Mitral stenosis prompts surgeons to choose a smaller valve size, which can cause higher PPM rates [37].

The metabolic status of the patient can also influence the bioprosthesis. In one study, renal failure was a predictor of structural valve failure in patients with aortic bioprosthesis [38]. Meanwhile, metabolic syndrome cannot be considered a definite predictor of survival and degeneration in patients with MV bioprosthesis due to conflicting results among the studies [29, 32, 39]. Although previously reported, we did not find any association between classic cardiovascular risk factors and early degeneration [38]. Our findings align with our previous study on the association between diabetes mellitus and complications following valvular heart surgery [40]. To fully understand this association, we believe several factors, such as blood glucose levels, hemoglobin A1c, duration of diabetes, and type of antiglycemic treatment, should be considered simultaneously to reach a precise conclusion.

4.1. Study Limitations. We performed a single-center study in a tertiary university hospital in Tehran, limiting our findings' interpretation due to center-specific bias. Also, we did not have access to all patients who underwent bioprosthetic MV replacement in our center, as some were not living in Tehran and did not continue their follow-up visits at our center. The retrospective design of our study was another limitation. Finally, we only studied early degeneration, and a more extended follow-up period may help better understand MV bioprosthesis's durability.

5. Conclusion

Based on the echocardiographic criteria, we observed an appropriate rate of early degeneration in bioprosthetic mitral valves. Moreover, regardless of its etiology, increased MV gradient in the first postoperative echocardiography was the sole independent predictor of early degeneration. Therefore, avoiding PPM and high early gradient by careful valve selection can be essential in reducing early degeneration. Also, age could not predict early degeneration. However, more data from large randomized controlled trials on this topic, particularly in younger patients, are warranted to reach a whole picture of bioprosthetic mitral valve replacement.

Abbreviations

BMI: Body mass index
BSA: Body surface area
CABG: Coronary artery bypass graft
CAD: Coronary artery disease
COPD: Chronic obstructive pulmonary disease
CVA: Cerebrovascular accident
CW: Continuous wave
DVI: Doppler velocity index
EF: Ejection fraction
EOA: Effective orifice area
HR: Hazard ratio
ICU: Intensive care unit
IQR: Interquartile range
LVED: Left ventricular end-diastolic
LVES: Left ventricular end-systolic
LVH: Left ventricular hypertrophy
LVOT: Left ventricular outflow tract
MI: Myocardial infarction
MR: Mitral regurgitation
MS: Mitral stenosis
MV: Mitral valve
NSTEMI: Non-ST segment elevation myocardial infarction
STEMI: ST-segment elevation myocardial infarction

PAP: Pulmonary arterial pressure
PHT: Pressure half-time method
PPM: Patient prosthesis mismatch
RAP: Right atrial pressure
RVSP: Right ventricular systolic pressure
VHD: Valvular heart disease
VTI: Velocity-time integral
THC: Tehran Heart Center.

Data Availability

The datasets regarding the current study are available from the corresponding author upon reasonable request.

Ethical Approval

The study protocol was approved by the Ethics Committee and the Research Council of Tehran Heart Center separately.

Consent

Informed consent was obtained from all participants.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

AZ, MS, and AS conceptualised and designed the study, ES, AH, ASh, and MS contributed to data curation, ASh and AA performed data analysis and interpreted the data, ASh and AA drafted the manuscript and revised the study, and AZ and AS performed scientific supervision.

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