Results of aortic valve replacement in aortic stenosis and moderate functional mitral regurgitation

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ABSTRACT

Background: Referral and admission echocardiography (ECHO) in patients scheduled for aortic valve replacement (AVR) with aortic stenosis (AS) may differ in the assessment of moderate functional mitral regurgitation (FMR).

Aims: Our study aimed to determine truly moderate FMR and evaluate its impact on survival.

Methods: We conducted an observational study of patients referred for AVR with AS and no, mild, or moderate FMR between 2014 and 2019. Patients were assigned into three groups: (1) no/mild (N-FMR); (2) moderate-FMR on one ECHO (either at referral or on admission) termed incidental (I-FMR); (3) moderate FMR in two studies (both at referral and on admission) termed permanent (PM-FMR).

Results: The referral and admission assessment were performed median 35 days apart. Of the 679 elective patients who underwent elective isolated AVR, 516 patients had N-FMR, 102 patients had I-FMR, and 61 patients had PM-FMR. Median follow-up was 46 months (22.5–58.5); max 73.3. Thirty-day mortality was 2.5% vs. 1% vs. 8.2% (N-FMR vs. I-FMR vs. PM-FMR, respectively; $P = 0.01$). Five-year survival was 84.1% in N-FMR vs. 88.5% in I-FMR vs. 60.6% in the PM-FMR group, where it was the lowest ($P < 0.001$). In multivariable modeling, PM-FMR increased mortality (hazard ratio [HR], 1.88 [1.05–3.37]; $P = 0.03$). I-FMR had no effect on mortality (HR, 0.67 [0.32–1.37]; $P = 0.28$). Five-year survival after excluding 30-day mortality was 86.3% vs. 89.4% vs. 66.0%; (N-FMR vs. I-FMR vs. PM-FMR, respectively; $P = 0.02$). PM-FMR increased late mortality (HR, 2.17 [1.14–4.15]; $P = 0.01$).

Conclusions: In patients undergoing isolated AVR for AS, the presence of permanent moderate FMR significantly impacts 30-day and mid-term survival.

Key words: aortic stenosis, aortic valve replacement, mitral regurgitation

INTRODUCTION

Aortic stenosis (AS) is the most common acquired valve disorder in Europe and North America affecting almost 5% of the elderly population. Mitral regurgitation (MR) has an estimated prevalence of 3% in the general population. Both diseases separately affect more than 176 million people worldwide [1, 2]. This is a growing trend, and it is partly due to increased life expectancy and better access to medical care. Simultaneous replacement of both aortic and mitral valves significantly increases morbidity and mortality [3–6]. Moderate functional MR during aortic valve replacement (AVR) is often treated conservatively, as the trend toward MR improvement or non-progression was observed. However, the optimal treatment in this cohort with moderate functional mitral regurgitation is still debatable and the outcome is unknown [7]. To operate or not on moderate FMR during AVR for AS is still mostly the surgeon's decision. To facilitate this process additional evidence is required. Echocardiographic (ECHO) assessment of moderate functional mitral regurgitation (FMR) may provide various results related to the patient's clinical condition and volume overload status [8, 9]. Routine assessment before surgery may miss truly moderate functional mitral regurgitation,

WHAT'S NEW?

Moderate functional mitral regurgitation in patients with aortic stenosis scheduled for aortic valve replacement is generally treated conservatively because there is no strong evidence of survival benefit. Routine assessment based on just one echocardiography imaging before surgery may miss truly moderate survival-affecting functional mitral regurgitation, which is variable in nature. To our knowledge, it is the first study considering influence of time on moderate functional mitral regurgitation in patients with aortic stenosis. To diagnose permanent moderate mitral regurgitation, which truly affects survival, one needs to confirm it on two separate occasions at different time points. The incidental finding of functional mitral regurgitation in patients with aortic stenosis is not per se a predictor of decreased survival but permanent moderate functional mitral regurgitation in patients with aortic stenosis is a strong predictor of impaired survival.

which is variable in nature. FMR, whose diagnosis is usually based on just one ECHO imaging, may not affect survival after AVR [10].

To precisely identify patients with truly moderate FMR, we evaluated patients with AS referred to our department for AVR with and without moderate FMR. Then on admission, we checked once again if they had moderate FMR and assigned them into three groups: without FMR, with moderate MR in one assessment (incidental FMR), and moderate MR seen in both evaluations (permanent FMR). Our study aimed to assess the influence of incidental, moderate, and permanent moderate FMR on the outcomes of AVR for AS.

METHODS

Study population and clinical variables

We retrospectively analyzed the cardiac surgical database of patients operated between 2014 and 2019 in the Department of Cardiac Surgery at the Medical University of Silesia in Katowice, Poland. Institutional Review Board was consulted, and patient consent was waived (PCN/CBN/0052/KB/118/22, 2022-06-15). Baseline clinical and procedural data and outcomes at follow-up were entered into prespecified electronic case report forms. Follow-up status was assessed by personal contact or by consulting the National Registry of Cardiac Surgical Procedures (www.krok.csioz.gov.pl), which contains the mortality data acquired from the National Health Fund.

The study included 679 elective patients referred for surgical AVR for severe AS, with no or up to moderate FMR from our satellite cardiology centers. On admission, an ECHO assessment was performed to confirm FMR status. Both studies were conducted by experienced echocardiographers at satellite centers and on admission to our center. The degree of functional mitral regurgitation was determined using integrative criteria in accordance with the current guidelines at the time of the patient's assessment [2, 11, 12]. Patients were retrospectively assigned into three cohorts based on the presence of moderate FMR:

1. No/mild FMR (N-FMR) — the patients without moderate FMR;
2. Incidental moderate FMR (I-FMR) — the patients with moderate FMR observed in one transthoracic ECHO only, either the referral or admission study;
3. Permanent moderate FMR (PM-FMR) — the patients with moderate FMR present in two echocardiographic studies i.e. referral and admission transthoracic echocardiogram (TTE).

Endpoints

The primary endpoint was mid-term survival after AVR for AS in relation to the presence of preoperative incidental or permanent FMR. PM-FMR was defined as a moderate MR occurring in both referral and admission ECHO studies. I-FMR was identified when moderate FMR was noticed only in one ECHO study — either referral or admission. Thirty-day mortality was also reported. The other clinical and echocardiographic patient characteristics were included in survival analysis.

Statistical analysis

Data were presented as median with interquartile range (IQR) or number with proportion as appropriate. Quantitative data were compared using the Kruskal-Wallis one-way analysis of variance on ranks with post-hoc Dunn's method for non-normally distributed data and one-way analysis of variance with post-hoc Holm-Sidak method for normal distribution. The frequencies were compared with the chi-square test or Fisher's exact test when feasible. The Kaplan-Meier curves were used to depict estimated long-term survival. The influence of various factors on survival was assessed with a log-rank test. To adjust for other confounders, parsimonious multivariable modeling with Cox regression was performed for overall mortality and postoperative mortality of 30-day survivors. Cox regression was used to seek univariable predictors of survival, and all patients' characteristics presented in the Table 1 were tested. The multivariable model was built with Cox regression with the stepwise backward conditional method of variable inclusion using the factors with score statistics <0.1 on univariable testing. The 30-day and 5-year survival rates following AVR with PM-FMR were presented. P <0.05 was considered significant. Statistical analysis was performed with SPSS version 22 (IBM, Armonk, NY, US).

Table 1. Baseline characteristics

Variable	N-FMR (n = 516)	I-FMR (n = 102)	PM-FMR (n = 61)	*P*-value
Clinical characteristics				
Age, years, median (IQR)	66.00 (60.00–73.00)[a,b]	70.00 (64.75–74.00)[c]	75.00 (69.00–77.00)	<0.001
Male sex, n (%)	297 (42.4)	53 (52.0)	25 (41.0)	0.02
BSA, m^2, median (IQR)	1.87 (1.72–2.02)	1.87 (1.74–2.02)	1.83 (1.69–1.94)	0.21
NYHA, n (%)				0.35
NYHA I	44 (8.5)	5 (4.9)	2 (3.3)	—
NYHA II	327 (63.4)	73 (71.6)	38 (62.3)	—
NYHA III	138 (26.7)	24 (23.5)	20 (32.8)	—
NYHA IV	7 (1.4)	0 (0)	1 (1.6)	—
Hypertension, n (%)	424 (82.2)	85 (83.3)	55 (90.2)	0.29
Diabetes mellitus, n (%)				0.13
With insulin	37 (7.2)	10 (9.8)	5 (8.2)	—
With oral agents	109 (21.1)	20 (19.6)	21 (34.4)	—
COPD, n (%)	31 (6.0)	7 (6.9)	2 (3.3)	0.63
Renal failure, n (%)	22 (4.5)	13 (13.8)	4 (7.3)	<0.01
Creatinine level, mg/dl, median (IQR)	0.88 (0.76–1.02)[a]	0.93 (0.78–1.11)	0.91 (0.80–1.08)	0.04
GFR preop, ml/min/1.73 m^2, median (IQR)	81.00 (68.00–90.00) n = 516[a,b]	73.50 (60.00–84.25) n = 102	73.00 (56.50–84.00) n = 61	<0.001
Troponin T, ng/ml, median (IQR)	0.012 (0.008–0.020) n = 516[a, b]	0.015 (0.009–0.024) n = 102	0.016 (0.009–0.026) n = 61	0.04
Current smoker, n (%)	70 (13.6)	5 (4.9)	4 (6.6)	0.09
Hyperlipidemia, n (%)	341 (66.1)	78 (76.5)	42 (68.9)	0.12
Atrial fibrillation, n (%)	55 (10.7)	20 (19.6)	14 (23.0)	0.01
EuroSCORE II, %, median (IQR)	1.24 (0.85–1.88)[a, b]	1.62 (1.05–2.50)[c]	2.35 (1.28–4.14)	<0.001
Coronary angiography results, n (%)				0.51
No lesions	452 (88)	90 (88)	48 (79)	
Single vessel disease	47 (9.1)	7 (6.9)	9 (15)	
Double vessel disease	12 (2.3)	4 (3.9)	3 (4.9)	
Triple vessel disease	5 (1.0)	1 (1.0)	1 (1.6)	
PCI in the past, n (%)	57 (11)	19 (19)	5 (8.2)	0.06
CAD (PCI or angio- result), n (%)	101 (20)	26 (26)	15 (25)	0.31
Previous MI, n (%)	32 (6.2)	11 (11)	7 (12)	0.12
Admission echocardiography				
Bicuspid aortic valve, n (%)	171 (33.1)	25 (24.5)	10 (16.4)	0.01
Aortic insufficiency (AI), n (%)				0.15
No	244 (47.3)	49 (48.0)	25 (41.0)	—
Mild	168 (32.6)	24 (23.5)	24 (39.3)	—
Moderate	104 (20.2)	29 (28.4)	12 (19.7)	—
Mitral regurgitation (MR), n (%)				<0.001
No	266 (51.6)	20 (19.6)	0 (0)	—
Mild	250 (48.4)	50 (49.0)	0 (0)	—
Moderate	0 (0)	32 (31.4)	61 (100)	—
LA, mm, median (IQR)	40.00 (36.00–44.00) n = 396	43.00 (40.00–47.00) n = 74	44.00 (40.00–47.75) n = 44	<0.001
LVESV, ml, median (IQR)	50.8 (38.12–64.90) n = 461[a, b]	58.9 (44.13–73.15) n = 97	66.0 (45.35–91.26) n = 56	<0.001
LVEDV, ml, median (IQR)	118.2 (97.33–145.00) n = 462[a, b]	126.0 (111.00–153.66) n = 97	134.50 (111.25–163.01) n = 56	<0.01
Ejection fraction, %, median (IQR)	55.0 (50.00–60.00)[a, b]	55.0 (49.50–60.00)	55.0 (41.00–60.00) n = 61	<0.001
Mean aortic gradient, mm Hg, median (IQR)	47.0 (39.00–58.00) n = 514	48.0 (38.00–60.00)	46.0 (42.00–62.00) n = 61	0.49
Peak aortic gradient, mm Hg, median (IQR)	81.0 (69.00–95.75)	87.0 (68.00–101.50) n = 101	83.0 (71.50–102.5) n = 61	0.28
Pulmonary hypertension, n (%)	50 (9.7)	17 (16.7)	19 (31.1)	<0.001
LF, %	212 (49.6) n = 427	41 (44.6) n = 92	23 (46.9) n = 49	0.66

[a](N-FMR vs. I-FMR) <0.05; [b](N-FMR vs. PM-FMR) <0.05; [c](I-FMR vs. PM-FMR) <0.05

Abbreviations: AS, aortic stenosis; BSA, body surface area; COPD, chronic obstructive pulmonary disease (long-term use of bronchodilators or steroids for lung disease); ESV, end-systolic volume; EDV, end-diastolic volume; GFR, glomerular filtration rate (ml/min/1.73 m^2); I-FMR incidental moderate functional mitral regurgitation; N-FMR, without or mild functional mitral regurgitation; LA, left atrium; LF, low flow (stroke volume <35 ml/m^2); LV, left ventricle; NYHA, New York Heart Association; PM-FMR, permanent moderate functional mitral regurgitation

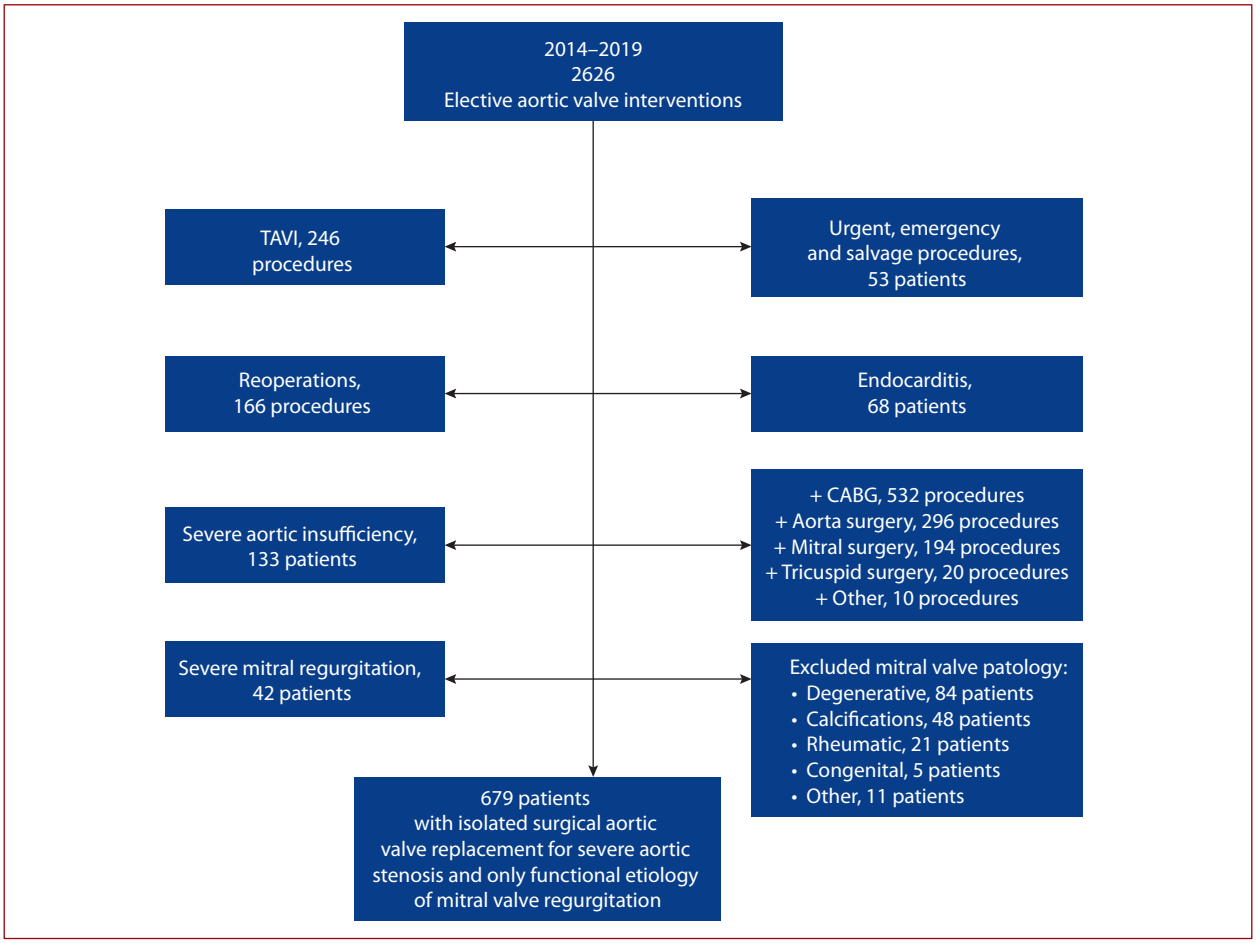

Figure 1. Study flowchart

Abbreviations: CABG, coronary artery bypass grafting; TAVI, transcatheter aortic valve implantation

RESULTS

Baseline and surgical characteristics

Of the initial 2626 patients after aortic valve intervention, we excluded patients with urgent, emergency, and salvage surgery (n = 53), patients treated by transcatheter aortic valve implantation (n = 246), reoperations (n = 166), and endocarditis (n = 68). Patients with concomitant procedures: coronary artery bypass grafting (n = 532), aorta surgery (n = 296), mitral surgery (n = 194), tricuspid surgery (n = 20), and other procedures (n = 10) were excluded too. Moreover, patients with severe aortic insufficiency (n = 133), severe mitral regurgitation (n = 42), or any other than functional mitral valve pathology (n = 170) were also not considered (Figure 1).

Six hundred seventy-nine elective patients who between 2014 and 2019 underwent isolated AVR for aortic stenosis in our institution, with up to moderate functional mitral regurgitation, were included in the analysis. Moderate FMR was present in 93 patients on referral ECHO imaging, 131 patients on admission ECHO, and in 61 patients in both ECHO studies. As for cohorts, 516 patients were in the N-FMR group (297 men), 102 patients in the I-FMR group (53 men), and 61 patients in the PM-FMR group (25 men) (Figure 2). Median time between the referral and admission TTE studies was 35 days (interquartile range [IQR], 25–49).

Patients with N-FMR (66 [60–73]) were younger than patients with I-FMR (70 [65–74]) and PM-FMR (75 [69–77]); P <0.01. On admission, echocardiography patients with N-FMR had smaller ventricles with lower end-systolic volume (ESD) (50 [38–65] ml) than those with I-FMR (59 [44–73] ml) and PM-FMR (66 [45–91] ml); P<0.01. They also had smaller end-diastolic volume (EDV) in N-FMR (118 [97–145] ml) than in I-FMR (126 [111–154] ml) and in PM-FMR (134 [111–163] ml, respectively; P <0.01). The highest prevalence of atrial fibrillation (AF) was in PM-FMR (23%) vs. N-FMR (10.7%) and I-FMR (19.6%), (P = 0.01). The prevalence of pulmonary hypertension defined as systolic pulmonary arterial pressure (PAP) above 30 mm Hg was also highest in the PM-FMR group (31.1%) than in the N-FMR (9.7%) and I-FMR (16.7%) groups; P <0.01.

The aortic valve gradients and prevalence of concomitant moderate aortic regurgitation did not differ between groups. Patients did not differ in Canadian Cardiovascular Society Scale (CCS) and New York Heart Association (NYHA) Functional Classification. The prevalence of hypertension diabetes, chronic obstructive pulmonary disease (COPD), extracardiac atherosclerosis, and smoking were similar

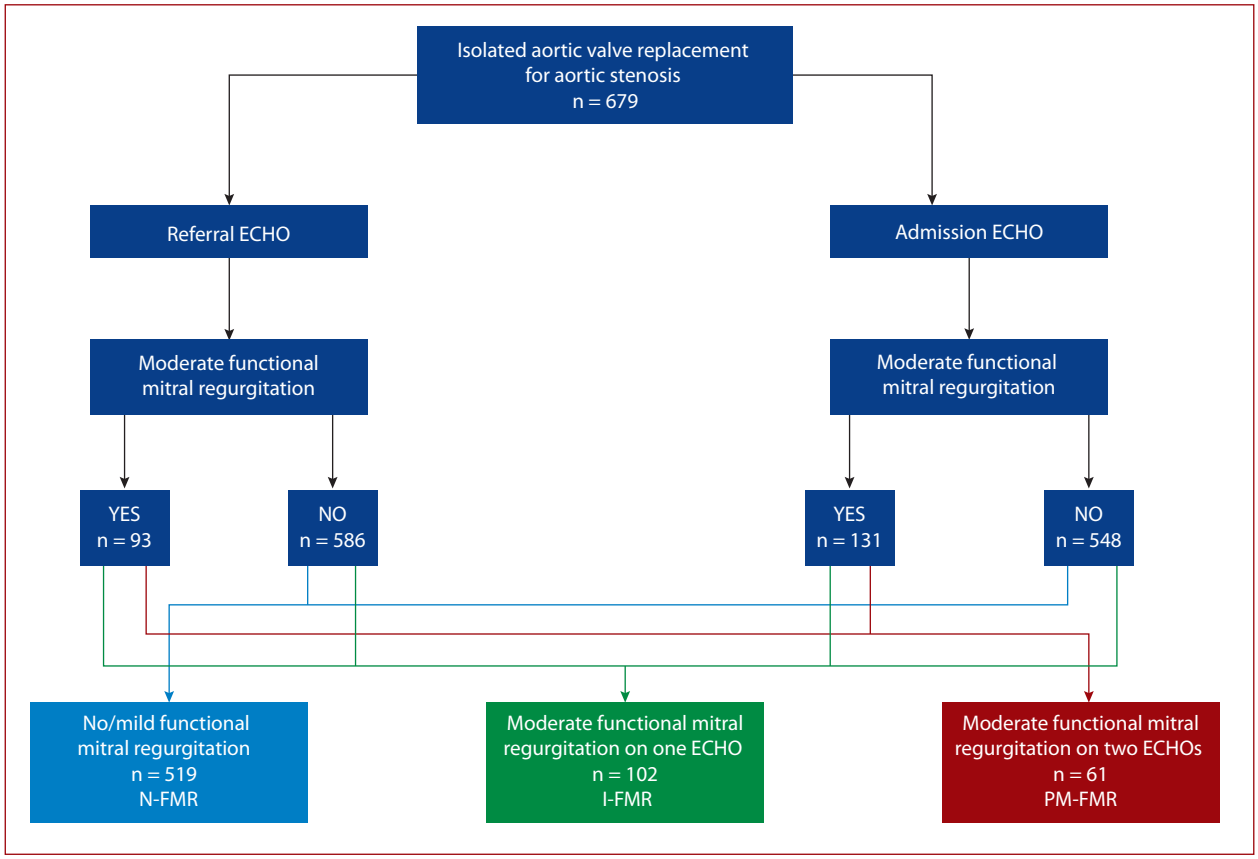

Figure 2. Flowchart of patients with functional mitral regurgitation
Abbreviations: ECHO, echocardiography; other — see Table 1

Table 2. Operative data

Variable	N-FMR (n = 516)	I-FMR (n = 102)	PM-FMR (n = 61)	*P*-value
CBP time, min, median (IQE)	65.00 (55.00–80.00)	62.00 (51.00–76.25)	62.00 (53.50–70.00)	0.17
X-clamp time, min, median (IQE)	51.00 (42.25–62.00)	48.00 (41.00–61.00)	48.00 (41.00–55.50)	0.06
Stentless valve, n (%)	15 (3)	4 (3)	0 (0)	<0.01
Biological valve, n (%)	338 (65)	78 (77)	52 (85.0)	
Mechanical valve, n (%)	163 (32)	20 (20)	9 (15)	
Prothesis size, mm, median (IQE)	23.00 (21.00–23.00)	23.00 (21.00–23.00)	23.00 (21.00–23.00)	0.12
Bleeding, ml, median (IQE)	550.00 (400.00–750.00), n = 512	550.00 (350.00–700.00), n = 99	507.50 (378.75–686.25), n = 58	0.39

Abbreviations: CPB time, cardiopulmonary bypass time; X-clamp time, cross-clamp time; other — see Table 1

between the groups. The presence of coronary artery disease had no influence on survival in our cohort ($P = 0.57$ in the log-rank test), and the need for concomitant coronary artery bypass grafting (CABG) was an exclusion criterion.

The baseline demographic data and clinical characteristics of the study population are summarized in Table 1.

After analyzing operative data, we found no difference in the implanted prosthesis size, cardiopulmonary bypass time (CPB), or cross-clamp time (x-clamp). Mechanical aortic valves were mostly implanted in N-FMR followed by I-FMR and PM-FMR (32% vs. 20% vs. 15%). Biological valves, on the other hand, were implanted mostly in PM-FMR (66% vs. 77% vs. 85%); $P < 0.01$ (Table 2). The incidence of postoperative bleeding was similar between groups.

Clinical outcomes

Follow-up was 100% complete with a median of 46 (22.5–58.5) months, max. 73.3. Thirty-day mortality was significantly highest in PM-FMR 8.2% (5 patients) vs. N-FMR 2.5% (13 patients) and I-FMR 0.9% (1 patient); ($P = 0.02$).

Five-year survival was 84.1% vs. 88.5% vs. 60.6% for N-FMR vs. I-FMR vs. PM-FMR, respectively, ($P < 0.01$) (Figure 3). After adjusting for other confounders multivariable analysis revealed PM-FMR as an independent risk factor impacting survival (HR, 1.88 [1.05–3.37]; $P = 0.03$), (Table 3). I-FMR did not affect survival (HR, 0.67 [0.32–1.37] months; $P = 0.67$). Other predictors of mortality included pulmonary hypertension (estimated systolic PAP >30 mm Hg) (HR, 1.82 [1.07–3.08]; $P = 0.02$), preoperative troponin T

Table 3. Univariable and multivariable analysis of mortality predictors after aortic valve replacement

	Univariable analysis			Multivariable analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
LF	1.59	0.97–2.62	0.06			
COPD	1.96	0.94–4.08	0.07			
Diabetes mellitus (vs. no diabetes)						
Oral agents	1.40	0.84–2.34	0.19	1.20	0.71–2.02	0.49
Insulin	2.54	1.31–4.89	<0.01	2.38	1.22–4.65	0.01
Atrial fibrillation	1.89	1.10–3.23	0.02			
Bicuspid aortic valve	0.57	0.32–1.00	0.05			
Pulmonary hypertension	2.06	1.24–3.41	<0.01	1.82	1.07–3.08	0.03
Age, years	1.02	0.99–1.04	0.06			
Log (pre-op troponin T), ng/ml	1.40	1.12–1.74	<0.01	1.29	1.02–1.64	0.03
GFR pre-operation, ml/min/1.73 m^2	0.98	0.97–0.99	0.001	0.98	0.97–1.00	0.07
FMR (vs. N-FMR)						
I-FMR	0.80	0.39–1.63	0.56	0.67	0.32–1.37	0.28
PM-FMR	2.75	1.61–4.70	<0.001	1.88	1.05–3.37	0.03

Abbreviations: COPD, chronic obstructive pulmonary disease; other — see Table 1

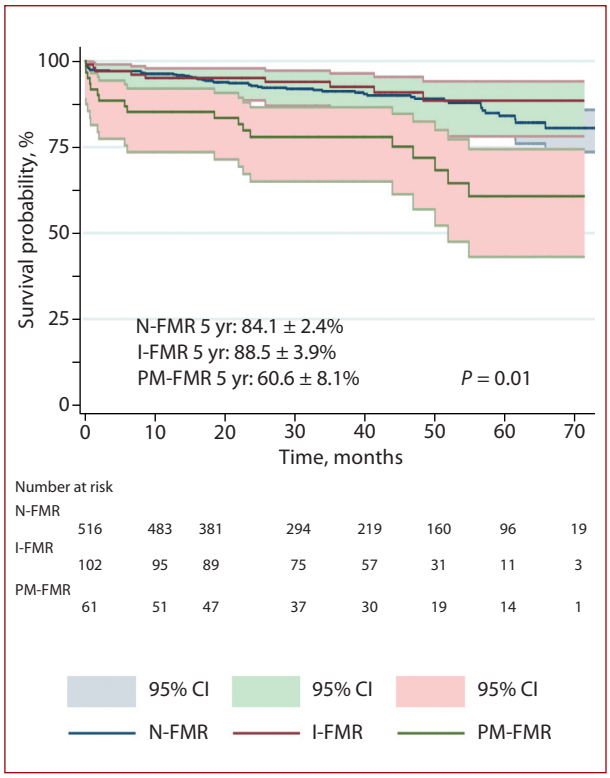

Figure 3. Kaplan-Meier survival estimates for patients after AVR for AS with no-moderate functional mitral regurgitation (N-FMR) vs. incidental moderate FMR (I-FMR) vs. permanent FMR (PM-FMR)

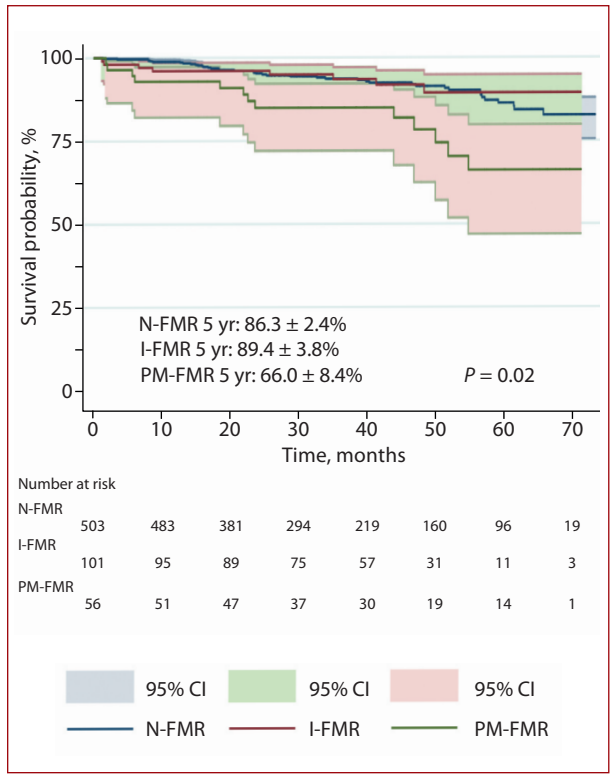

Figure 4. Kaplan-Meier 30-day landmark analysis for patients after AVR for AS with no-moderate functional mitral regurgitation (N-FMR) vs. incidental moderate FMR (I-FMR) vs. permanent FMR (PM-FMR)

(HR, 1.29 [1.02–1.64]; *P* = 0.03), and diabetes on insulin (HR, 2.38 [1.22–4.65]; *P* = 0.01).

After excluding 30-day mortality, the five-year survival rate was still inferior in the PM-FMR group (86.3% N-FMR vs. 89.4% I-FMR vs. 66.0% PM-FMR; P = 0.02) (Figure 4). In multivariable modeling, PM-FMR remained a strong predictor of mortality (HR, 2.17 [1.14–4.15]; *P* = 0.02), together with preoperative troponin T (HR, 1.40 [1.09–1.80]; *P* <0.01), and pulmonary hypertension (HR, 1.85 [1.03–3.35]; *P* = 0.04), (Table 4).

DISCUSSION

The current guidelines on valvular heart diseases help to decide when to operate on secondary mitral regurgitation caused by coronary artery disease or related to atrial fibrillation [1], but there is a paucity of data on when to intervene in secondary mitral regurgitation related to aortic stenosis [2, 13]. The problem is important, as mitral regurgitation concurrent with aortic stenosis is common [14]. Recently, the Japanese multicenter registry CURRENT showed that a relatively high proportion (80%) of patients in whom

Table 4. Univariable and multivariable analysis of mortality predictors after aortic valve replacement excluding 30-day mortality

	Univariable analysis			Multivariable analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Age, years	1.02	0.99–1.05	0.10			
EuroSCORE II	1.14	1.02–1.27	0.02			
GFR pre-operation, ml/min/1.73 m^2	0.98	0.97–0.99	<0.01			
Bicuspid aortic valve	1.33	0.96–1.84	0.08			
Pulmonary hypertension	2.12	1.20–3.75	0.01	1.86	1.03–3.35	0.04
Log (pre-op troponin T), ng/ml	1.40	1.09–1.79	<0.01	1.41	1.10–1.80	<0.01
FMR (vs. N-FMR)						
I-FMR	0.94	0.44–2.00	0.87	0.83	0.38–1.78	0.64
PM-FMR	2.59	1.39–4.84	<0.01	2.17	1.14–4.15	0.02

Abbreviations: see Tables 1 and 3

moderate-to-severe MR was left untreated had a lower degree of MR after AVR. Moreover, additional mitral valve repair did not improve survival in this group [15]. To assess precisely whether FMR can influence symptoms severity, risk of LV failure, and most importantly survival is very difficult. Literature findings are inconsistent [5, 16]. The variability of secondary MR makes clinical assessment based on one ECHO imaging insufficient [17]. The FMR mechanism is heterogeneous, and there is no single strong parameter to predict precisely its severity [10], for instance, an increase in preload deteriorates FMR and can induce congestive heart failure [17–19]. Such conditions are not permanent, and the decision about the type of valve surgery is usually based just on one ECHO report.

We have shown that moderate FMR found in one echocardiographic study but not confirmed on another occasion did not affect survival of patients subjected to AVR (HR, 0.67 [0.32–1.37]; $P = 0.67$). However, in the case of patients who were referred with moderate FMR, and the same moderate grade was confirmed on admission, it strongly and adversely affected their survival (HR, 1.88 [1.05–3.37]; $P = 0.03$). To our best knowledge, it is the first study in which moderate FMR was assessed over time to precisely define the patient population with permanent moderate FMR before AVR.

The worse survival rate in our PM-FMR cohort is consistent with the results found by Caballero-Borrego and colleagues in patients with moderate MR vs. no/mild MR [20].

Interestingly, there are studies where the early operative results were excellent with no mortality [16, 21]. In one of those, Jeong and colleagues did not find differences in cumulative survival at 10-year follow-up (95.1% no-MR vs. 83.6% MR group; $P = 0.10$) although they found some in cardiac-related mortality events [16]. On the other hand, Absil and colleagues noticed increased operative mortality and mid-term survival, but differences between MR 0–1 vs. MR 2–3 grades were not significant (60.9% vs. 55%) [5]. Also, no difference was reported by Barreiro et al. [6] with perioperative mortality of 3.8% vs. 7.1% ($P = 0.21$) and late survival of 40.8% vs. 41.4%; ($P = 1.0$). But the prevalence of functional etiology in that population was only 21.4%. Early mortality reported by Takeda et al. [22] in a group with no/trivial MR (1.7%) vs. a group with mild/moderate MR (2.9%) did not differ but was lower than in the current study. Most authors cited above relied on only one FMR ECHO assessment, and our data may explain the discrepancies in previous results.

Moreover, effective regurgitant orifice area (EROA) >10 mm^2 was previously associated with severe symptoms and higher pulmonary arterial pressure after mixed surgical AVR (SAVR) and transcatheter AVR (TAVI) [23]. TAVI and SAVR patient populations differ much in severity of comorbidities, but reports after TAVI in FMR correspond with SAVR results up to 24 months of follow-up [24–27].

Our permanent FMR patient population had more often their left atrium and ventricle enlarged, and more prevalent AF and pulmonary hypertension. Also, the patients with PM-FMR were significantly older than other groups. In fact, FMR presence related to higher age as the N-FMR group was the youngest. It may suggest that longer-lasting disease (AS) may more likely lead to FMR. The same may relate to LV volumes as the higher LV volumes correlated with FMR.

To avoid studying ischemic mitral regurgitation, we excluded from the study the patients who required myocardial revascularization, and the presence of coronary artery disease had no influence on survival in our cohort ($P = 0.57$ in the log-rank test).

The current guidelines on FMR related to AS suggest a conservative approach if no predictors of deterioration such as atrial fibrillation, enlarged left atrium, increased left ventricular mass index, pulmonary hypertension, or preoperative peak aortic valve gradient <60 mm Hg are present [15, 28–30]. Similar improvement or non-progression of FMR degree was also documented after TAVI [25, 31–33]. Even though, moderate FMR can improve, after isolated AVR, poor clinical outcomes were noticed in this cohort [16, 28, 22]. Moreover, persistent FMR on discharge can worsen survival after AVR [34].

Certain limitations of our study must be acknowledged. This was a retrospective analysis. In the current study, we focused on overall survival, and the information on the cause of death was unavailable. We did not assess other

clinical endpoints (e.g. late reoperations) or analyzed the postoperative follow-up ECHOs. Therefore, we cannot comment on the postoperative course of FMR.

The usual practice is that a decision on the treatment of FMR is based on one echocardiography study [35]. Meanwhile, our results show that only permanent FMR that was present on two TTEs affected the outcome. The incidental appearance of FMR on echocardiography that was not confirmed in another study did not influence survival. Thus, bearing in mind the dynamic nature of FMR, one should not make therapeutic decisions based on a single echocardiographic finding. We consider permanent moderate FMR in patients with AS scheduled for AVR a strong mortality predictor. The existence of PM-FMR in this patient population may indicate the need for additional mitral valve surgery, but this requires further studies.

Article information

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