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Evolution of concomitant moderate and moderate to severe functional mitral regurgitation following aortic valve surgery for severe aortic stenosis

Evolucija istovremene umerene i umerene do teške funkcionalne mitralne regurgitacije nakon operacije teške stenoze aortnog zaliska

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Abstract

Background/Aim. Functional mitral regurgitation (FMR) is a common entity in patients with aortic stenosis (AS) undergoing aortic valve replacement (AVR). The aim of this study was to examine evolution of moderate and moderate to severe FMR after an isolated AVR, to identify prognostic indicators for persistent MR postoperatively, and to offer the recommendation regarding surgical intervention for moderate and moderate to severe FMR at the time of AVR for AS. **Methods.** We retrospectively reviewed 39 consecutive patients with moderate and moderate to severe FMR at the time of isolated AVR from January 2007 to December 2013. We collected preoperative and postoperative echocardiographic data to determine the evolution of FMR after AVR. Patients were divided into the persistent (n = 14) and improved FMR group (n = 25). Secondary division was into the prosthesis-patient mismatch (PPM, n = 7) and non prosthesis-patient mismatch group (non PPM, n = 32 patients). Late follow-up echocardiography was completed in 100% (39/39) of patients. **Results.** FMR improved postoperatively (MR < 2+) in 64% (25/39) of patients, while 36% (14/39) of patients had persistent MR ≥ 2). In comparison to the persistent group, the patient with improved FMR had significant decrease in the left ventricular end-diastolic diameter, left ventricular end-systolic diameter, posterior wall and septum thickness postoperatively. The same indicators of reverse remodeling were found in the non PPM group in comparison to the PPM group. The incidence of postoperative FMR improvement was higher in the non PPM group (65.6%, p = 0.001) in comparison to thePPM group (42.9%, p = 0.125). The mean follow-up duration was 39.5 ± 23.5 months. **Conclusion.** In accordance with previous studies, this study also showed improvement in FMR following AVR surgery. Improvement in MR degree was associated with echocardiographic parameters of reverse left ventricular remodeling. Conservative approach is advisable in patients with moderate and moderate to severe FMR, believing that repair or replacement is unnecessary at the time of AVR for severe AS. PPM could prevent downgrading of FMR, stressing out the importance of choosing the prosthesis of adequate size.

Key words:
mitral valve insufficiency; aortic valve stenosis; cardiovascular surgical procedures; postoperative period.

Apstrakt

Uvod/Cilj. Funkcionalna mitralna regurgitacija (FMR) je čest entitet kod bolesnika sa stenozom aortnog zaliska (AS), kojima je indikovana zamena aortnog zaliska (ZAZ). Cilj ove studije bio je da ispita evoluciju umerene i umerene do teške FMR nakon izolovane ZAZ, da identifikuje prognostičke indikatore za perzistentnu MR posle operacije, i da ponudi preporuku za operaciju umerene i umerene do teške FMR u vreme ZAZ zbog AS. **Metode.** Retrospektivno je ispitano 39 konsekutivnih bolesnika sa umerenom i umerenom do teškom FMR u trenutku izolovane ZAZ, od januara 2007. do decembra 2013. Godine. Prikljupljeni su preoperativni i postoperativni ehokardiografski podaci da bi se analizirala evolucija FMR nakon ZAZ. Bolesnici su bili podeljeni na perzistentnu grupu (n = 14) i grupu sa smanjenom FMR (n = 25). Naknadna podela je bila na grupu sa bolesnik-proteza diskrepancom (PPD, n = 7) i *non* bolesnik-proteza diskrepancom (*non* PPD, n = 32). Udaljeno ehokardiografsko praćenje je kompletirano kod 100% (39/39) bolesnika. **Rezultati.** Kod 64% (25/39) bolesnika, FMR je bila smanjena postoperativno (MR < 2+), a kod 36% (14/39) bolesnika je perzistirala (MR ≥ 2+). Za razliku od perzistentne grupe, bolesnici sa smanjenom FMR su nakon

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operacije imali značajnu redukciju dijametra leve komore na kraju dijastole, dijametra leve komore na kraju sistole, debljine zadnjeg zida i septuma. Isti indikatori reverznog remodelovanja su nađeni i kod *non* PPD grupe u poređenju sa PPD grupom. Incidenca smanjenja postoperativne FMR je bila veća kod *non* PPD grupe (65,6%, p = 0,001) u odnosu na PPD grupu (42.9%, p = 0,125). Srednje vreme ehokardiografskog praćenja bolesnika je bilo 39.5 ± 23.5 meseci. **Zaključak.** U skladu sa prethodnim studijama, ova studija takođe pokazuje poboljšanje FMR nakon ZAZ. Smanjenje stepena MR je udruženo sa ehokardiografskim parametrima reverznog remodelovanja leve komore. Preporučuje se konzervativan pristup bolesnicima sa umerenom i umereno do teškom FMR, sa stavom da je rekonstrukcija ili zamena nepotrebna u trenutku ZAZ zbog AS. PPD može da spreči smanjenje FMR, te se naglašava značaj izbora proteze odgovarajuće veličine.

Ključne reči:
zalistak, mitralni, insuficijencija; zalistak, aortni, stenoza; hirurgija, kardiovaskularna, procedure; postoperativni period.

Introduction

Mitral regurgitation (MR) is a frequent coexisting dysfunction in patients with severe aortic valve stenosis (AS). Some degree of MR is found in as much as 61% to 90% of patients undergoing aortic valve replacement (AVR) for AS [1].

Functional mitral regurgitation (FMR) has been reported in as high as 75% of patients who undergo AVR [2].

According to the guidelines, mitral valve (MV) surgery is reasonable for patients with chronic severe secondary MR who are undergoing AVR, and MV repair may be considered for patients with chronic moderate secondary MR who are undergoing other cardiac surgery [3]. As long as there are no morphological leaflet abnormalities, mitral annulus dilatation or marked abnormalities of left ventricular (LV) geometry, surgical intervention on MV is in general not necessary and non-severe secondary MR usually improves after aortic valve treatment [4].

Although mitral valve surgery at the time of AVR may increase perioperative mortality and morbidity, the effect of residual MR on survival, quality of life and development of heart failure is important too.

Data from the Society for Thoracic Surgery (STS) database (2002–2006) reported an overall unadjusted mortality of 3.2% following AVR in a population of 6,292 patients at 809 centers worldwide. Double valve replacement is, as expected, associated with a significantly higher operative risk with a postoperative mortality at 11–12%, emphasizing that careful patient selection is imperative [5]. Gillinov et al. [5] suggested that MV repair during double valve surgery might be beneficial compared to mitral replacement, with a long-term reduction in mortality (34% versus 46%), without increased perioperative mortality. Talwar et al. [6] reported that MV repair with AVR provided significantly better event-free survival than double valve replacement.

Schubert et al. [7] emphasized that in patients whose MR improved postoperatively, 5-year survival was 73.5%, compared with 65.4% in patients whose MR did not improve (p = 0.06). Survival was worse in patients whose MR worsened (46.7%; p < 0.01). Barreiro et al. [8] found that patients with persistent or worsening MR after AVR tended to have a lower 5-year survival. Vanden Eynden et al. [9] found a trend towards better 10-year survival in patients with improved postoperative MR.

The aim of this study was to examine evolution of moderate and moderate to severe functional MR after isolated AVR, and to identify prognostic indicators for persistent MR postoperatively. Also, we intended to set a recommendation – should FMR be operated simultaneously with AVR.

Methods

Patient selection

From January 2007 to December 2013, a total of 1,104 patients underwent isolated AVR for severe AS, at the Dedinje Cardiovascular Institute, Belgrade, Serbia. From this group we excluded patients with: morphologic abnormalities of the mitral apparatus, calcification or fibrosis of leaflets, chordae rupture, leaflet prolaps, significant coronary artery stenosis, aortic disease, previous open heart procedures, and congenital disease. After these exclusions, 39 patients were enrolled in the study.

We conducted a retrospective study of 39 consecutive patients. Patient's demographics, clinical characteristics and preoperative and postoperative echocardiographic data were collected in a retrospective manner for the entire cohort.

Primarily, patients were stratified into two groups based on improvement or no improvement of their FMR at the last follow-up echocardiogram after AVR. Persistent FMR group (14 patients, 36%) remained in moderate and moderate to severe grade (2+ and 3+) after AVR. Improved FMR group (25 patients, 64%) had a reduction in MR grade (less than 2+) after AVR.

Secondarily, we formed additional two groups of patients, based on the value of indexed Effective Orifice Area (EOAi), of the implanted aortic prosthesis. The EOA was derived from the manufacturer's published values of projected *in vivo* EOA. This value was indexed to body surface area to yield the indexed effective orifice area of the valve. Prosthesis-patient mismatch group (PPM) (7 patients, 18%) had EOAi ≤ 0.85 cm^2/m^2. Non prosthesis-patient mismatch group (non PPM) (32 patients, 82%) had EOAi > 0.85 cm^2/m^2.

The values, distributions and frequencies of preoperative and postoperative variables between groups were compared, to determine if any significant differences were associated with postoperative improvement or worsening of functional MR.

AVR was performed using mechanical St. Jude Medical™ Hemodynamic Plus Aortic Valve in 36 patients, and St. Jude Medical™ Biocor™ Pericardial Stented Tissue Valve in 3 patients.

Our study was approved by the Institutional Review Board of the Dedinje Cardiovascular Institute, with a waiver of the requirement for an individual patient consent.

Echocardiography and grading of mitral regurgitation

All studied patients went through preoperative and postoperative transthoracic echocardiography, a complete M-mode, bidimensional and Doppler echocardiographic assessment according to the European Association of Echocardiography and the American Society of Echocardiography guidelines [10].

The diagnosis of a severe AV stenosis was established by preoperative echocardiography.

Grading of MR was as follows: 0 for no regurgitation, 0.5 for trace, 1+ for mild, 2+ for moderate, 3+ for moderate-severe, and 4+ for severe, as defined by the American Society of Echocardiography. Grading was done by preoperative transtoracic echocardiography [7, 10].

Follow-up

Postoperative echocardiography was routinely performed before discharge. Late follow-up echocardiograms were obtained on the patients at variable intervals and at the discretion of the patients' individual cardiologists. Late follow-up echocardiographic data were obtained for 100% (39/39) of patients. We use the latest echocardiography findings for the comparison.

Statistical Analysis

All data are expressed as mean ± standard deviation (SD) or as absolute values and percentages. Statistical analysis was done using the Student's independent *t*-test, paired-samples *t*-test, χ^2 or Fisher's exact test and Wilcoxon's signed-rank test. Statistical significance was defined as a two-tailed *p* value less than 0.05. SPSS for Windows, version 20.0 (SPSS Inc, Chicago, IL) was used for statistical analysis.

Results

Improved FMR group versus persistent FMR group

In the cohort of 39 patients, 25 improved FMR and 14 had persistent FMR postoperatively. There was no difference in the preoperative demographic, clinical and echocardiographic parameters between groups, except left ventricle ejection fraction (LVEF). Persistent FMR patients had lower preoperative values of LVEF (41.79 ± 17.93% vs. 53.6 ± 14.76%, p = 0.033) (Table 1). The mean late follow-up duration was 42.64 ± 20.72 months in the persistent FMR group, and 37.72 ± 25.13 months in the improved FMR group (p = 0.537).

Table 1
Comparison of the baseline patient characteristics in respect to function mitral regurgitation (FMR) persistence

Variables	Persistent FMR (n = 14)	Improved FMR (n = 25)	*p* value
Age (years), mean ± SD	59.36 ± 12.57	64.08 ± 9.45	0.192
Female sex, n (%)	6 (42.9)	17 (68)	0.126
BSA (m^2), mean ± SD	1.79 ± 0.17	1.84 ± 0.16	0.363
BMI (kg/m^2), mean ± SD	25.17 ± 3.61	26.60 ± 5.27	0.373
Atrial fibrillation, n (%)	1 (7.1)	5 (20)	0.391
NYHA functional class, n (%)			
II	13 (92.9)	24 (96)	1.000
III	1 (7.1)	1 (4)	
TAV, n (%)	13 (92.9)	22 (88)	1.000
AVA (cm^2), mean ± SD	0.69 ± 0.18	0.61 ± 0.17	0.200
Peak gradient (mmHg), mean ± SD	90.57 ± 32.73	109.08 ± 29.07	0.076
Mean gradient (mmHg), mean ± SD	54.86 ± 20.21	70.72 ± 25.44	0.053
LVEDD (mm), mean ± SD	57.86 ± 11.45	52.40 ± 5.92	0.115
LVESD (mm), mean ± SD	41.50 ± 12.46	35.20 ± 7.19	0.052
Septum thickness (mm), mean ± SD	11.86 ± 1.79	12.04 ± 1.88	0.769
Posterior wall thickness (mm), mean ± SD	11.86 ± 1.56	11.72 ± 1.46	0.785
LA (mm), mean ± SD	41.86 ± 4.80	43.00 ± 4.55	0.465
LVEF (%), mean ± SD	41.79 ± 17.93	53.6 ± 14.76	0.033
TR grade, n (%)			
0	7 (50)	14 (56)	
I	3 (21.4)	5 (20)	1.000
II	4 (28.6)	6 (24)	
RVSP (mmHg), mean ± SD	47.33 ± 8.45	44.00 ± 10.95	0.529
EAOi (cm^2/m^2), mean ± SD	1.15 ± 0.39	1.13 ± 0.29	0.846

Note: Results are presented as mean ± standard deviation or as absolute values (percentages).
BSA – body surface area; BMI – body mass index; TAV – tricuspid aortic valve; AVA – aortic valve area; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; LA – left atrial diameter; LVEF – left ventricular ejection fraction; TR – tricuspid regurgitation; RVSP – right ventricular systolic pressure; EAOi – effective orifice area index.

Persistent FMR group – before versus after AVR

Following aortic valve replacement, peak and mean transvalvular pressure gradients reduced significantly. Gradients measured across aortic prostheses were significantly lower than gradients measured across severely stenosed native valve. The remaining echocardiographic parameters did not change significantly (Table 2).

Improved FMR group – before versus after AVR

Following aortic valve replacement, peak and mean transvalvular pressure gradients reduced significantly. Gradients measured across aortic prostheses were significantly lower than gradients measured across severely stenosed native valve. In addition, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), septum thickness, left ventricular posterior wall thickness, also reduced significantly (Table 3). In other words, there was a significant reverse remodeling of the LV in this group of patients.

PPM group versus non PPM group

In the cohort of 39 patients, 32 were in the non PPM group (EOAi > 0.85 cm^2/m^2), and 7 were in the PPM group (EOAi ≤ 0.85 cm^2/m^2). There was no difference in the preoperative demographic, clinical and echocardiographic parameters between groups, except the patients' age. The PPM patients were older than the non PPM ones (71.00 ± 6.16 vs. 60.50 ± 10.68, respectively; p=0.017) (Table 4). The mean late follow-up duration was 36.47 ± 20.12 months in the non PPM group, and 53.29 ± 33.63 months in the PPM group (p = 0.086).

Table 2

Changes in echocardiographic data after aortic valve replacement (AVR) in the persistent functional mitral regurgitation (FMR) group

Variables	Preoperative	Late follow-up	*p* value
Peak gradient (mmHg), mean ± SD	90.57 ± 32.73	29.14 ± 8.74	0.001
Mean gradient (mmHg), mean ± SD	54.86 ± 20.21	15.93 ± 5.18	0.001
LVEDD (mm), mean ± SD	57.62 ± 11.88	57.69 ± 11.82	0.861
LVESD (mm), mean ± SD	41.31 ± 12.95	40.92 ± 13.87	0.687
Septum thickness (mm), mean ± SD	11.92 ± 1.85	11.46 ± 1.94	0.190
Posterior wall thickness (mm), mean ± SD	11.92 ± 1.61	11.46 ± 1.90	0.111
LA (mm), mean ± SD	41.77 ± 4.99	42.15 ± 4.69	0.457
LVEF (%), mean ± SD	41.92 ± 18.66	41.62 ± 15.75	0.824
TR grade, n (%)			
0	7 (50)	6 (46.2)	
I	3 (21.4)	2 (15.4)	0.739
II	4 (28.6)	5 (38.5)	
RVSP (mmHg)	44.00 ± 6.48	39.75 ± 9.00	0.582

Note: Results are presented as mean ± standard deviation (SD) or as absolute values (percentages).
LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; LA – left atrial diameter; LVEF – left ventricular ejection fraction; TR – tricuspid regurgitation; RVSP – right ventricular systolic pressure.

Table 3

Changes in echocardiographic data after AVR in the improved functional mitral regurgitation (FMR) group

Variables	Preoperative	Late follow-up	*p* value
Peak gradient (mmHg), mean ± SD	109.08 ± 29.07	27.48 ± 7.25	0.001
Mean gradient (mmHg), mean ± SD	70.72 ± 25.44	14.60 ± 4.6	0.001
LVEDD (mm), mean ± SD	52.40 ± 5.92	50.00 ± 3.38	0.014
LVESD (mm), mean ± SD	35.20 ± 7.19	32.08 ± 5.11	0.006
Septum thickness (mm), mean ± SD	11.96 ± 1.88	10.71 ± 1.40	0.001
Posterior wall thickness (mm), mean ± SD	11.67 ± 1.47	10.75 ± 1.07	0.003
LA (mm), mean ± SD	43.00 ± 4.55	41.68 ± 4.00	0.063
LVEF (%), mean ± SD	53.60 ± 14.76	57.40 ± 7.79	0.140
TR grade, n (%)			
0	14 (56)	12 (48)	
I	5 (20)	8 (32)	
II	6 (24)	4 (16)	0.714
III	0	1 (4)	
RVSP (mmHg), mean ± SD	44.00 ± 12.02	37.38 ± 3.89	0.123

Note: Results are presented as mean ± standard deviation (SD) or as absolute values (percentages).
LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; LA – left atrial diameter; LVEF – left ventricular ejection fraction; TR – tricuspid regurgitation; RVSP – right ventricular systolic pressure.

Table 4

Comparison of the baseline patient characteristics in respect to EOAi

Variables	Non PPM (n = 32)	PPM (n = 7)	*p* value
Age (years), mean ± SD	60.50 ± 10.68	71.00 ± 6.16	0.017
Female sex, n (%)	18 (56.3%)	5 (71.4%)	0.678
BSA (m^2), mean ± SD	1.82 ± 0.18	1.85 ± 1.00	0.664
BMI (kg/m^2), mean ± SD	25.89 ± 4.97	26.98 ± 3.67	0.588
Atrial fibrillation, n (%)	4 (12.5%)	2 (28.6%)	0.290
NYHA functional class, n (%)			
II	31 (96.9%)	6 (85.7%)	0.331
III	1 (3.1%)	1 (14.3%)	
TAV, n (%)	28 (87.5%)	7 (100%)	1.000
AVA (cm^2), mean ± SD	0.62 ± 0.15	0.73 ± 0.27	0.350
Peak gradient (mmHg), mean ± SD	105.16 ± 32.53	90.00 ± 22.95	0.251
Mean gradient (mmHg), mean ± SD	66.19 ± 25.84	59.71 ± 18.98	0.536
LVEDD (mm), mean ± SD	54.41 ± 9.31	54.14 ± 4.53	0.943
LVESD (mm), mean ± SD	37.63 ± 10.51	36.71 ± 5.62	0.826
Septum thickness (mm), mean ± SD	11.97 ± 1.88	12.00 ± 1.73	0.968
Posterior wall thickness (mm), mean ± SD	11.72 ± 1.57	12.00 ± 1.00	0.654
LA (mm), mean ± SD	42.56 ± 4.98	42.71 ± 2.50	0.938
LVEF (%), mean ± SD	49.69 ± 17.73	47.86 ± 12.20	0.797
TR grade, n (%)			
0	16 (50)	5 (71.4)	
I	6 (18.8)	2 (28.6)	0.255
II	10 (31.3)	0 (0)	
MR grade, n (%)			
2+	23 (71.9)	6 (85.7)	0.653
3+	9 (28.1)	1 (14.3)	

Note: Results are presented as mean ± standard deviation (SD) or as absolute values (percentages).
EAOi – effective orifice area index; BSA – body surface area; BMI – body mass index; TAV – tricuspid aortic valve; AVA – aortic valve area; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; LA – left atrial diameter; LVEF – left ventricular ejection fraction; TR – tricuspid regurgitation; MR – mitral regurgitation.

Table 5

Changes in echocardiographic data after aortic valve repeacement (AVR) (EOAi ≤ 0.85 group)

Variables	Preoperative	Late follow-up	*p* value
Peak gradient (mmHg), mean ± SD	90.00 ± 22.95	31.86 ± 10.61	0.002
Mean gradient (mmHg), mean ± SD	59.71 ± 18.98	17.14 ± 6.52	0.002
LVEDD (mm), mean ± SD	53.00 ± 3.69	52.17 ± 4.62	0.419
LVESD (mm), mean ± SD	35.50 ± 5.01	35.83 ± 5.19	0.721
Septum thickness (mm), mean ± SD	11.80 ± 1.79	11.00 ± 1.41	0.374
Posterior wall thickness (mm), mean ± SD	12.00 ± 1.00	11.60 ± 0.89	0.374
LA (mm), mean ± SD	42.67 ± 2.73	42.83 ± 1.72	0.867
LVEF (%), mean ± SD	49.17 ± 12.81	52.50 ± 10.84	0.102
TR grade, n (%)			
0	5 (71.4)	3 (50)	
I	2 (28.6)	2 (33.3)	0.157
II	0 (0)	1 (16.7)	
MR grade, n (%)			
≥ 2+	7 (100)	3 (57.1)	0.125
< 2+	0 (0)	4 (42.9)	

Note: Results are presented as mean ± standard deviation (SD) or as absolute values (percentages).
EAOi – Effective orifice area index; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; LA – left atrial diameter; LA – left atrial diameter; TR – tricuspid regurgitation; MR – mitral regurgitation.

PPM group – before versus after AVR

Following aortic valve replacement, peak and mean transvalvular pressure gradients reduced significantly. Gradients measured across aortic prostheses were significantly lower than gradients measured across severely stenosed native valve. The remaining echocardiographic parameters did not changed significantly. MR grade remained ≥ 2+ in 57.1% of patients, and reduced below 2+ in 42.9% ($p = 0.125$) (Table 5).

Non PPM group – before versus after AVR

Following aortic valve replacement, peak and mean transvalvular pressure gradients reduced significantly. Gradients measured across aortic prostheses were significantly lower than gradients measured across severely stenosed native valve. In addition, LVEDD, LVESD, septum thickness, left ventricular posterior wall thickness, also reduced significantly. In other words, there was a significant reverse remodeling of the left ventricle in this group of patients. Another important finding was that MR grade reduced below 2+ in the majority of patients (65.6%) (p = 0.001) (Table 6).

Table 6

Changes in echocardiographic data after aortic valve repeacement (AVR) (EOAi > 0.85 group)

Variables	Preoperative	Late follow-up	*p* value
Peak gradient (mmHg), mean ± SD	105.16 ± 32.53	27.25 ± 6.92	0.001
Mean gradient (m, mean ± SD mHg), mean ± SD	66.19 ± 25.84	14.63 ± 4.32	0.001
LVEDD (mm), mean ± SD	54.41 ± 9.31	52.72 ± 8.70	0.030
LVESD (mm), mean ± SD	37.63 ± 10.51	34.97 ± 10.58	0.005
Septum thickness (mm), mean ± SD	11.97 ± 1.88	10.97 ± 1.68	0.001
Posterior wall thickness (mm), mean ± SD	11.72 ± 1.57	10.91 ± 1.49	0.001
LA (mm), mean ± SD	42.56 ± 4.98	41.66 ± 4.50	0.113
LVEF (%), mean ± SD	49.69 ± 17.73	51.91 ± 13.88	0.281
TR grade, n (%)			
0	16 (50)	15 (46.9)	0.906
I	6 (18.8)	8 (25)	
II	10 (31.3)	8 (25)	
III	0 (0)	1 (3.1)	
MR grade, n (%)			
≥ 2+	32 (100)	11 (34.4)	0.001
< 2+	0 (0)	21 (65.6)	

Note: Results are presented as mean ± standard deviation (SD) or as absolute values (percentages).
EAOi – effective orifice area index; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; LA – left atrial diameter; LVEF – left ventricular ejection fraction; TR – tricuspid regurgitation; MR – mitral regurgitation.

Discussion

AVR for severe AS decreases left ventricular afterload and initiate reverse remodeling of the left ventricle. Those effects are expected to have positive influence on the mitral valve mechanics, abolishing secondary MR dysfunction without structural abnormalities of the mitral apparatus. Nevertheless, this evolution is frequently not achieved.

Barreiro et al. [8] observed that 82% of patients with functional MR improved postoperatively. Vanden Eynden et al. [9] found that isolated ischaemic and functional MR were the only preoperative factors predictive of MR improvement after AVR. In our study, 64% (25/39) of patients improved FMR postoperatively.

Harling et al. [11] quantitatively demonstrated that, within their review, the structural remodeling resulting from severe AS regresses following AVR, as demonstrated by a reduction in LV mass and LVED diameter. Several studies identified factors associated with evidence of ventricular remodeling, such as higher preoperative LV mass, larger LV diastolic diameter and enddiastolic volume being independent predictors of improvement in MR following AVR. They suggest that, where there is potential for reverse remodeling to occur, a more significant improvement in MR will be seen following AVR [12–14].

The similar effect was observed in cardiac resynchronization therapy (CRT). Sitges et al. [15] reported that CRT induced acute and sustained reductions in functional MR in almost 50% of patients by initially improving LV systolic function and dyssynchrony; long-term reverse LV remodeling contributed to this sustained effect.

Our study confirmed the beneficial effect of LV reverse remodeling, with significant reduction in LVEDD, LVESD, septum thickness and left ventricular posterior wall thickness in patients with postoperatively improved FMR.

Numerous studies attempted to identify preoperative patient and echocardiographic characteristics that are predictive of postoperative evolution of MR. Alghamdi et al. [16] in their meta-analysis of 13 non-randomized studies found that progression factors of MR were: LV dysfunction, LA enlargement, atrial fibrillation (AF), peak AV gradient < 60 mmHg, increased LV mass index and increased tricuspid regurgitation (TR) velocity.

Brasch et al. [17] found that elevated left ventricular mass was the only statistically significant predictor of decreased postoperative MR. The only statistically significant predictor of postoperative MR in multivariate analysis, in a study by Joo et al. [18], was increased right ventricular systolic pressure. Unger et al. [13] published a study indicating that postoperative MR was likely to be improved in patients who had reduced left ventricular function and increased left ventricle size. Jeong et al. [19] demonstrated that patients with preoperative atrial fibrillation and an ejection fraction > 40% were more likely to suffer from residual postoperative MR. Sehovic et al. [20] identified deterioration predictors in patients with moderate-severe FMR: LVEDD > 54 mm, effective regurgitant orifice > 25 mm^2, regurgitation volume > 40 mL/beat, pulmonary artery systolic pressure > 40 mmHg, LA diameter > 45 mm.

When we compared patients with persistent and improved FMR, the only preoperative echocardiographic and patient characteristics difference was LVEF. Persistent FMR patients had lower preoperative values of LVEF (41.79 ± 17.93% vs. 53.6 ± 14.76%, $p = 0.033$).

The striking findings in our study were postoperative pressure differences between persistent and improved FMR groups. Postoperative peak gradient reduction was 61.4 mmHg (*t* test, $p = 6.881$) in the persistent FMR group and 81.6 mmHg (*t* test, $p = 13.282$) in the improved FMR group. Postoperative mean gradient reduction was 38.9 mmHg (*t* test, $p = 6.748$) in the persistent FMR and 56.1 mmHg (*t* test, $p = 10.653$) in the improved FMR group. Obviously, there was a robust reduction in transvalular gradients in the improved FMR group. This finding could be partially explained by lower preoperative values of LVEF in the persistent FMR group (low flow – low gradient effect).

Previous studies have reported that more than mild PPM, defined as an indexed EOA ≤ 0.85 cm^2/m^2, is associated with less symptomatic improvement, worse hemodynamics at rest and during exercise, less regression of left ventricular hypertrophy, and more cardiac events after AVR[21]. The impact of aortic prosthesis size, and thus of patient/prosthesis mismatch, on the evolution of FMR was addressed in our study. In addition to postoperative peak and mean gradient reduction, LVEDD, LVESD, septum thickness, left ventricular posterior wall thickness, also reduced significantly in patients without PPM. In other words, there was a significant reverse remodeling of the left ventricle in patients without PPM. Also, FMR grade reduced below 2+ in 65.6% of the non PPM patients, in comparison to 42.9% of the patients in the PPM group. It is worth of mentioning that we used the identical model of mechanical and tissue prostheses in all patients, eliminating the influence of different manufacturer design. In contrary, Waisbren et al. [22] reported that there was no independent relation of aortic prosthesis size with the change in MR.

Our patient selection was guided by restrictive criteria, forming a homogeneous FMR group. Nevertheless, the small number of patients limits the impact of our results, especially in comparing the non PPM and PPM groups (32 vs. 7, respectively).

Conclusion

In accordance with previous studies, our results also showed improvement in functional MR following AVR surgery, in majority of patients. The reverse remodeling of the LV positively correlates with postoperative FMR downgrading. PPM could be a condition that adversely affects reduction of FMR. We recommend conservative approach in patients with moderate and moderate to severe functional mitral regurgitation, believing that repair or replacement is unnecessary at the time of AVR for severe aortic stenosis. On the other hand, we strongly advocate against PPM in those patients, stressing out the importance of choosing the prosthesis of adequate size.

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