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Manuscript title: The impact of transcatheter aortic valve implantation (TAVI) on mitral regurgitation — a single center study

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Abstract

Background: *The coexistence of mitral regurgitation (MR) and severe aortic stenosis (AS) has been associated with worse outcomes in patients undergoing transcatheter aortic valve implantation (TAVI). Herein, the aim was to assess the etiology and degree of MR in an unselected TAVI population and investigate the impact of MR reduction at mid-term follow-up.*

Methods: *Patients subjected to TAVI as a treatment for severe AS in a single center were retrospectively analyzed. The primary endpoint was the MR reduction after TAVI. The secondary endpoint was all-cause mortality and heart failure hospitalization at a 3-year follow-up.*

Results: *Patients undergoing TAVI (n = 283) in the years 2017–2019 were screened for the presence of hemodynamically significant MR. Sixty-nine subjects (24.4%) with severe (16, 23.2%) and moderate (53, 76.8%) MR were included. The primary MR was predominant (39 subjects, 56.5%). The median age of the patients was 82 years. MR improved in 25 patients (36.2%, $p < 0.001$). Baseline severe MR was more prone to reduce (8 subjects, 50%) than moderate (17 subjects, 32.1%, $p = 0.04$). The primary MR improved in 14 patients (35.9%), while secondary in 11 patients (36.7%, $p = 1$). Patients showing MR reduction had lower mortality (8 vs. 29.55%, $p = 0.047$) and were less frequently hospitalized (20 vs. 45.45%, $p = 0.03$) at 3-year follow-up.*

Conclusions: *Hemodynamically significant MR improves after TAVI regardless of its etiology. Moreover, MR reduction after TAVI is associated with better clinical outcomes.*

Keywords: aortic stenosis, mitral regurgitation, TAVI, transcatheter aortic valve implantation, TAVR, transcatheter aortic valve replacement

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Introduction

Mitral regurgitation (MR) and severe aortic stenosis (AS) coexist in one-third of the patients, reaching up to 48% in the elderly [1, 2]. Patients with severe MR have often been excluded from randomized TAVI (transcatheter aortic valve implantation) trials [3]. In this setting, the MR is usually secondary to the AS (functional MR), while the primary MR (organic) is less common [2, 4]. The co-occurrence of severe AS and significant MR has been associated with worse outcomes [5–9].

TAVI is offered as a treatment in patients with severe AS at intermediate and high surgical risk [10–12].

A significant improvement in MR severity is well documented and was detected in more than 50% of the patients following TAVI [7, 8]. Nevertheless, the aim was to assess changes in MR in an Eastern European population of unselected TAVI patients with a relatively high prevalence of rheumatic valve disease.

Methods

Study design and population

This was a retrospective analysis of consecutive patients subjected to TAVI as a treatment for severe AS between January 2017 and December 2019 in a single center. Patients with at least moderate MR were included. Nonsignificant MR and previous mitral valve (MV) intervention were excluded from the study.

The primary endpoint was MR reduction following TAVI, and the secondary endpoint was all-cause mortality and heart failure hospitalization at a 3-year follow-up. The outcome reporting complied with standardized VARC-2 (Valve Academic Consortium) consensus definitions [13].

Echocardiography

MR was assessed at baseline, discharge, and at 3 and 6–12 months after the procedure. Philips iE33 and Cx50 systems (Philips Ultrasound, Bothell, Washington, United States) were used for transthoracic echocardiography (TTE). Loops and images were stored in the DICOM format.

TTEs were acquired by cardiologists, certified by the European Association of Cardiovascular Imaging (EACVI). The deferred image analyses were performed by two experienced cardiologists, blinded to clinical data, using ComPACS (Medimatic S.R.L., Genova, Italy) and QLAB (Philips Medical Systems, Andover, Massachusetts, United States) workstations.

Baseline moderate and severe MR were considered clinically significant. MR was classified as primary (i.e. organic/structural) or secondary (i.e. functional/non-structural) according to EACVI (European Association of Cardiovascular Imaging) recommendations [14]. Postprocedural MR reduction of at least one grade was recognized as an improvement. When quantitative evaluation of MR was not feasible, qualitative parameters were taken into account.

Ethical issues

Due to the retrospective character, the ethical review and approval were waived for this study. However, the institutional board was informed and acknowledged the analysis. The investigation conforms with the principles outlined in the 1964 Declaration of Helsinki and its later amendments.

Statistical analysis

The tests for the assessment of normality were: Lilliefors, Shapiro-Wilk, Jarque–Bera and Kolmogorov–Smirnov. When any of these rejected the hypothesis of a normal distribution, non-parametric calculations were used. Continuous variables with normal distribution were presented as mean and standard deviation (SD). Non-normally distributed variables were reported as median and interquartile range (IQR). Categorical variables were presented as numbers and percentages (%). Unpaired samples t-test for normally distributed variables and Wilcoxon rank-sum test for non-parametric variables were used. Fisher's exact test and Pearson's chi-squared tests for unpaired categorical data were applied. Event-free survival was estimated using the Kaplan-Meier method. The log-rank test was used to compare subgroups stratified according to MR reduction. Statistical analyses were performed by use of Statistica 13.3 (Tibco Software Inc., Palo Alto, California, United States). A two-tailed p-value less than 0.05 was considered significant.

Results

Clinical data

Patients undergoing TAVI in years 2017–2019 (n = 283) were screened for the presence of hemodynamically significant MR. Two hundred fourteen subjects were excluded due to insignificant MR or previous MV surgery. Finally, 69 patients (24.4%) were included, 16 with severe and 53 with moder-

ate MR. Etiology of MR was classified either as primary (39, 56.5%) or secondary (30, 43.5%). All subjects underwent follow-up visits. The study flowchart is presented in Figure 1.

The median age of the patients was 82 years, overweight women predominated in the study group (45, 65.2%). Subjects had advanced heart failure symptoms and an intermediate operative risk profile. The majority of patients had high-gradient AS (43, 62.3%). However, 17 patients (24.6%) had low-flow, low-gradient AS with reduced ejection fraction (EF) and 9 (13%) low-flow, low-gradient AS with preserved EF.

Self-expandable valves were mostly used (54, 78.3%). CoreValve/Evolut R/Evolut Pro valves (Medtronic, Dublin, Ireland) were commonly implanted (29, 42%), followed by SymetisAcurate/Acurateneo2(Boston Scientific, Ecublens, Switzerland; 21, 30.4%) and Portico (St. Jude Medical, Minneapolis, MN, USA; 2, 2.9%). Balloon-expandable Sapien XT/Sapien 3 (Edwards Lifescience, Irvine, CA, USA) valves were used in 15 (21.7%) subjects. There were no perioperative deaths. Six patients (8.7%) required pacemaker implantation, two subjects (2.9%) suffered a non-disabling stroke and one (1.5%) a non-fatal tamponade.

The clinical, biochemical, echocardiographic and procedural data are summarized in Tables 1–3.

Primary endpoint

The quantitative evaluation of MR was feasible in 47 subjects (68.12%), with the others, a reliable qualitative appraisal was possible. MR improved in 25 patients (36.2%, $p < 0.001$, Figure 2). Baseline severe MR was more prone to reduce (8 subjects, 50%) than moderate (17 subjects, 32.1%, $p = 0.04$). The primary MR decreased in 14 patients (35.9%), while secondary in 11 patients (36.7%, $p = 1$). In 3 subjects MR increased from moderate to severe, unrelated to TAVI myocardial infarction (MI), pacemaker-induced asynchrony, and significant paravalvular leak, respectively.

Patients with MR reduction suffered less frequently from chronic obstructive pulmonary disease (0 vs. 15.9%, $p=0.04$) and chronic kidney disease (48 vs. 79.5%, $p = 0.01$). In this subgroup the preprocedural MI was less common (12 vs. 36.4%, $p = 0.04$). Moreover, there was a visible trend towards non-smoking (4% vs. 15.9%, $p = 0.09$) as well (Table 1).

In patients responding to TAVI with MR reduction, a lower postprocedural pulmonary systolic artery pressure (19.6 vs. 36.2mmHg, $p = 0.02$) and less common incidence of severe tricuspid regurgitation (12 vs. 36.4%, $p = 0.01$) were noticed, despite the lack of preprocedural differences (Tables 2 and 4). In addition, a trend of ejection fraction increase (3.9 vs 1.1%, $p = 0.09$) was detected in this subgroup.

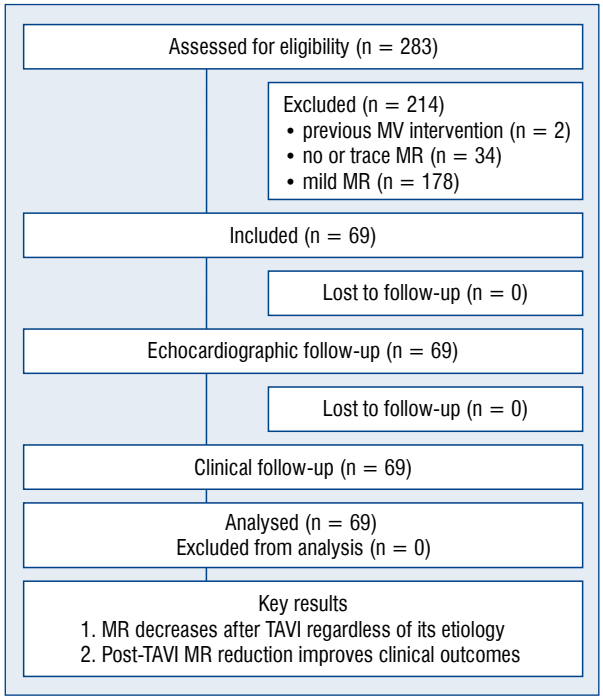

Figure 1. Study flowchart; MR — mitral regurgitation; MV — mitral valve; TAVI — transcatheter aortic valve implantation

A sub-analysis comparing moderate and severe MR showed no significant differences (Tables 1–4). Severe MR was more pronounced in patients with dilated annuli (31.4 vs. 35.6mm, $p = 0.02$) and larger atria (27.3 vs. 31.3cm^2, $p = 0.04$).

Secondary endpoint

The overall mortality at 3 years was 21.7%. Subjects showing MR improvement had lower mortality (8 vs. 29.55%, $p = 0.047$) and heart failure hospitalization rate (20 vs. 45.45%, $p = 0.03$) compared to those without MR reduction. However, regardless of MR improvement, patients had similar composite endpoint of all-cause mortality or heart failure hospitalization (28 vs. 50%, $p = 0.078$) at a 3-year follow-up (Figure 3).

Discussion

In the present study, moderate or severe MR was present in about one-fourth (24.4%) of the patients undergoing TAVI and was of primary origin in more than half (56.5%) of the cases. The

Table 1. Clinical characteristics

	Total n = 69	Moderate MR n = 53 (76.8%)	Severe MR n = 16 (23.2%)	p	No MR reductionn = 44 (63.8%)	MR reductionn = 25 (36.2%)	p
Age, median (IQR), years	82 (80–85)	82 (80–85)	82 (79.75––84.25)	0.743	82 (79.5–84.5)	83.5 (80.25––85)	0.188
Female, n (%)	45 (65.2)	33 (62.3)	12 (75)	0.389	27 (61.4)	18 (72)	0.437
BMI, mean (SD), kg/m^2	27.5 (47)	27.7 (4.9)	27 (4.6)	0.648	28.2 (5.2)	26.2 (3.6)	0.141
NYHA class III––IV, n (%)	53 (76.8)	40 (75.5)	13 (81.3)	0.598	36 (81.8)	17 (68)	0.456
Diabetes, n (%)	21 (30.4)	17 (32.1)	4 (25)	0.444	12 (27.3)	9 (36)	0.972
Hypertension, n (%)	60 (87)	45 (84.9)	15 (93.8)	0.107	38 (86.4)	22 (88)	0.096
Nicotynism, n (%)	8 (11.6)	8 (15.1)	0	0.695	7 (15.9)	1 (4)	0.73
Prior PCI, n (%)	23 (33.3)	17 (32.1)	6 (37.5)	0.607	14 (31.8)	9 (36)	0.038
Priormyocardialinfarction, n (%)	19 (27.5)	14 (26.4)	5 (31.3)	0.081	16 (36.4)	3 (12)	0.357
Prior CABG, n (%)	9 (13)	9 (17)	0	0.717	7 (15.9)	2 (8)	0.312
Atrialfibrilation, n (%)	36 (52.2)	27 (50.9)	9 (56.3)	0.640	25 (56.8)	11 (44)	0.197
COPD, n (%)	7 (10.1)	6 (11.3)	1 (6.3)	0.613	7 (15.9)	0	0.035
Hemoglobin, mean (SD), g/dl	11.7 (1.8)	11.8 (1.9)	11.2 (1.2)	0.262	11.7 (1.6)	10.3 (1.5)	0.856
Chronic kidney disease (eGFR < 60ml/min/m^2), n (%)	47 (68.1)	36 (67.9)	11 (68.8)	0.957	35 (79.5)	12 (48)	0.007
eGFR, median (IQR), ml/min/m^2	51 (40–64)	53 (42–64)	49.50 (40––60.75)	0.664	50.5 (40–58)	60 (42–67)	0.25
Creatinine, median (IQR), umol/l	96 (84–113)	97 (84–113)	93 (87–112)	0.971	98.5 (85–118.25)	93 (81–108)	0.274
NT–proBNP, median (IQR), pg/ml	3740 (1985––10403)	3583 (2069––10279)	4127 (1404––11114)	0.973	3467 (1976––10155)	4766 (2028––10155)	0.512
NT–proBNP > 3000 pg/ml, n (%)	35 (50.7)	26 (49.1)	9 (56.3)	0.759	22 (50)	13 (52)	0.764
Pacemaker, n (%)	19 (27.5)	13 (24.5)	6 (37.5)	0.316	12 (27.3)	7 (28)	0.954
Bundle branchblock, n (%)	13 (18.8)	11 (20.8)	2 (12.5)	0.468	9 (20.5)	4 (16)	0.658
STS–PROM, median (IQR), %	4.77 (3.4––6.1)	4.43 (3.2––4.95)	4.57 (3.5––5.9)	0.738	4.99 (3.92–5.7)	4.23 (3.54––4.95)	0.774
EuroScore II, median (IQR), %	5.32 (4.29––7.9)	4.94 (4.03––7.5)	5.51 (4.39––7.9)	0.569	4.9 (3.65–7.6)	5.46 (4.17––7.61)	0.644

Continuous variables are represented as mean (SD) and median (IQR); categorical variables are presented as numbers (%). BMI — body mass index; CABG — coronary artery bypass grafting; COPD — chronic obstructive pulmonary disease; eGFR — estimated glomerular filtration rate; MR — mitral regurgitation; NT–proBNP — N–terminal pro B–type natriuretic peptide; NYHA — New York Heart Association; PCI — percutaneous coronary intervention; STS–PROM — Society of Thoracic Surgery – predicted risk of mortality

Table 2. Baseline echocardiographic variables

	Total n = 69	Moderate MR n = 53 (76.8%)	Severe MR n = 16 (23.2%)	p	No MR reduction n = 44 (63.8%)	MR reduction n = 25 (36.2%)	p
Chambers							
LVEDD, median (IQR), mm	50 (45–55)	50 (45–54)	48 (39.25––57.75)	0.507	49 (45–53)	51.5 (41–55.5)	0.637
LVEF, median (IQR), %	55 (40–60)	52.5 (40––60)	59 (44.7–65)	0.210	53 (39–65)	55 (40–60)	0.537
Left atrium area, mean (SD), c^m2	30.4 (6.4)	27.3 (6.2)	31.2 (6.32)	0.044	30.5 (6.7)	30.1 (5.9)	0.789
Aortic valve							
Peak aortic gradient, mean (SD), mmHg	71.2 (29.2)	71.4 (30.8)	72 (28.9)	0.878	75.6 (32.1)	64.6 (25.5)	0.274
Mean aortic gradient, mean (SD), mmHg	43.7 (17.3)	43.9 (17.2)	43.2 (18.3)	0.906	45.2 (19)	41.0 (13.8)	0.363
Aortic valve area, median (IQR), cm^2	0.64 (0.5––0.9)	0.7 (0.5––0.9)	0.57 (0.5–0.77)	0.443	0.67 (0.5––0.8)	0.6 (0.6–0.9)	0.329
Aortic valve area index, median (IQR), cm^2/m^2	0.42 (0.32––0.49)	0.43 (0.36––0.53)	0.37 (0.29––0.45)	0.143	0.39 (0.35––0.48)	0.45 (0.32–0.54)	0.488
Moderate to severe AR, n (%)	38 (55.1)	28 (52.8)	10 (62.5)	0.117	25 (56.8)	13 (52)	0.938
Mitral valve							
Mitral annulus, mean (SD), mm	34.8 (6.3)	31.4 (8.4)	35.6 (5.4)	0.024	35.6 (5.6)	33.3 (7.39)	0.170
Mean mitral gradient, median (IQR), mmHg	2 (1.5–3)	2 (1.5–3)	3 (2.15–4.25)	0.529	2 (1.45–3)	2 (1.55–4)	0.643
MR etiology							
Primary, n (%)	39 (56.5)	30 (56.6)	9 (56.3)	1	25 (56.8)	14 (56)	1
Secondary, n (%)	30 (43.5)	23 (43.4)	7 (43.8)		19 (43.2)	11 (44)	
MR vena contracta, median (IQR), cm	0.53 (0.32––0.79)	0.4 (0.25––0.54)	1.03(0.85–1.08)	< 0.001	0.53 (0.31––0.73)	0.53 (0.33–0.92)	0.727
MR EROA, median (IQR), cm^2	0.3(0.15––0.57)	0.2(0.1––0.31)	0.71 (0.57––0.82)	< 0.001	0.28 (0.1––0.46)	0.33 (0.17–0.57)	0.267
MR regurgitant volume, median (IQR), ml	49 (40–66)	43.5 (36––51)	78 (69–84)	< 0.001	48 (41–64)	51 (40–66)	0.617
Tricuspid valve							
Moderate to severe TR, n (%)	33 (47.8)	25 (47.2)	8 (50)	0.609	24 (54)	9 (36)	0.172
Pulmonary systolic artery pressure, mean (SD), mmHg	45.7 (17.9)	45.5 (29.8)	46.5 (20.9)	0.898	47 (27.7)	41.0 (13.8)	0.350

Continuous variables are represented as mean (SD) and median (IQR); categorical variables are presented as numbers (%). AR — aortic regurgitation; EROA — effective regurgitant orifice area; LVEDD — left ventricular end–diastolic dimension; LVEF — left ventricular ejection fraction; MR — mitral regurgitation

Table 3. Procedure, complications and outcomes

	Total n = 69	Moderate MR n = 53 (76.8%)	Severe MR n = 16 (23.2%)	p	No MR reduction n = 44 (63.8%)	MR reduction n = 25 (36.2%)	p
Procedure							
Self–expandablevalves, n (%)	54 (78.3)	39 (73.6)	15 (93.8)	0.094	34 (77.3)	18 (72)	0.772
Transfemoralaccess, n (%)	66 (95.7)	50 (94.3)	16 (100)	1	43 (97.7)	23 (92)	0.288
Complications							
Highest creatinine, median (IQR), umol/l	109 (92––131)	109 (92––131)	107 (90.8––130.8)	0.915	113.5 (94.5––137.3)	104 (90–124)	0.127
Acute kidney injury, n (%)	12 (17.4)	10 (18.9)	2 (12.5)	0.566	9 (20.5)	3 (12)	0.381
Lowest hemoglobin, mean (SD), g/dl	10 (14.5)	10.1 (1.8)	11.2 (1.2)	0.479	9.9 (1.7)	10.3 (1.56)	0.329
Blood transfusion, n (%)	13 (18.8)	12 (22.6)	1 (6.3)	0.147	9 (20.5)	4 (16)	0.658
Pacemaker, n (%)	6 (8.7)	3 (5.7)	3 (18.8)	0.109	4 (9.1)	2 (8)	0.888
Stroke, n (%)	2 (2.9)	2 (3.8)	0	—	2 (4.5)	0	—
Tamponade, n (%)	1 (1.5)	1 (1.9)	0	—	1 (6.25)	0	—
Death, n (%)	0	0	0	N/A	0	0	N/A
Myocardial infarction, n (%)	0	0	0	N/A	0	0	N/A
Outcomes							
All–causemortality, n (%)	15 (21.7)	11 (20.8)	4 (25)	0.732	13 (29.5)	2 (8)	0.047
Heart failure hospitalization, global, n (%)	25 (36.2)	18 (34)	7 (43.8)	0.478	20 (45.5)	5 (20)	0.03
All–cause mortality or heart failure hospitalization, n (%)	29 (42.1)	21 (39.6)	8 (50)	0.778	22 (50)	7 (28)	0.078

Continuous variables are represented as mean (SD) and median (IQR); categorical variables are presented as numbers (%). MR — mitral regurgitation

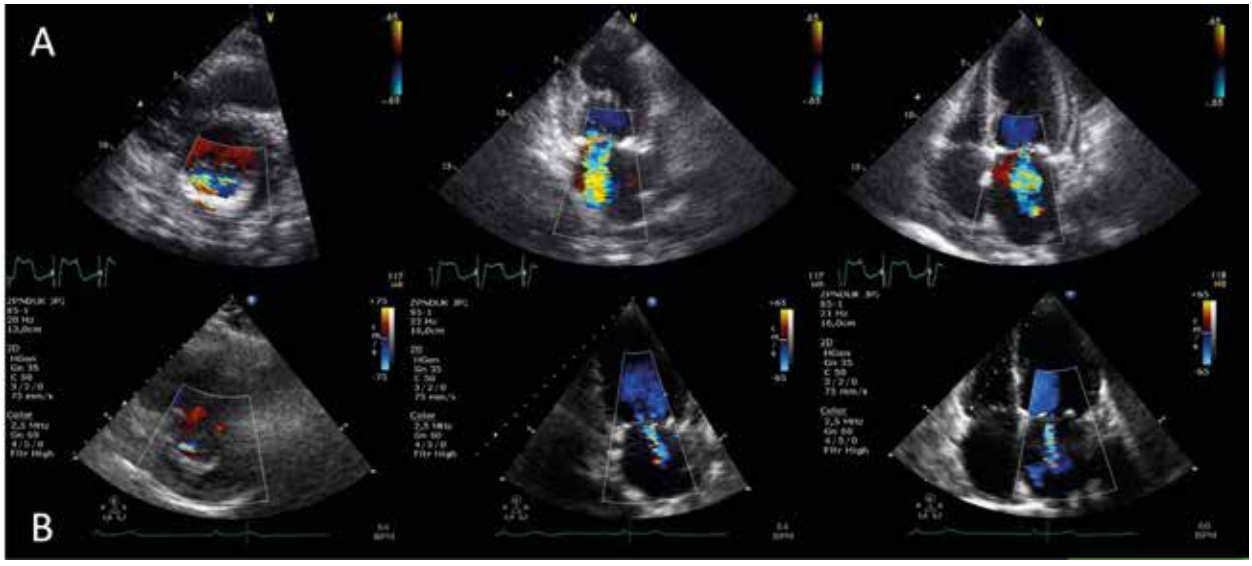

Figure 2. Transthoracic echocardiography, color Doppler imaging. Baseline (A) and 5 months follow-up (B). Parasternal short-axis view (left), two-chamber view (center), four-chamber view (right). Reduction of mitral regurgitation (moderate to mild)

Table 4. Follow–up echocardiographic variables

	Total n = 69	Moderate MR n = 53 (76.8%)	Severe MR n = 16 (23.2%)	p	No MR reduction n = 44 (63.8%)	MR reduction n = 25 (36.2%)	p
Chambers							
LVEDD, median (IQR), mm	47.5. (44––52.8)	48 (44.5––53)	45 (42–48)	0.193	47.5 (44.75––52)	47.5 (43–53.8)	0.79
Postprocedural LVEDD reduction, mean (SD), mm	2.2 (3.92)	1.6 (4.4)	2.7 (7.5)	0.516	0.7 (3.9)	3.8 (6.2)	0.032
LVEF, median (IQR), %	55 (45–60)	55 (45–60)	60 (48.3––62)	0.48	55 (45–60)	60 (50–65)	0.102
Postprocedural LVEF improvement, mean (SD), %	2.1 (9.1)	3.3 (13.1)	0.1 (10.2)	0.075	1.1 (9)	3.9 (17.1)	0.086
Aortic valve							
Peak aortic gradient, median (IQR), mmHg	11.6 (9––14.7)	11.6 (9––5.8)	10.2 (9–13)	0.164	11.6 (9–16)	11.6 (8.4–14.4)	0.62
Mean aortic gradient, mean (SD), mmHg	7.2 (2.8)	6.2 (2.1)	7.4 (2.9)	0.143	7.5 (2.7)	6.6 (2.9)	0.18
Effective orifice area, median (IQR), cm^2	1.9 (1.7–2.2)	2 (1.7–2.1)	1.9 (1.7––2.2)	0.481	2 (1.6–2.2)	1.9 (1.8–2.2)	0.66
Effective orifice area index, median (IQR), cm^2/m^2	1.1 (0.9–1.4)	1.2 (0.9––1.5)	1.1 (0.8––1.4)	0.652	1.2 (0.9–1.3)	1.1 (1–1.4)	0.895
Moderate to severe PVL, n (%)	8 (11.6)	5 (9.4)	3 (18.8)	0.143	5 (11.4)	3 (12)	0.834
Mitral valve							
Mitral annulus, mean (SD), mm	34 (5.9)	33.4 (7.4)	36.1 (5.4)	0.12	35.1 (5.5)	32.6 (6.9)	0.21
Peak mitral gradient, median (IQR), mmHg	5.8. (4.8––7.8)	5.8 (4.8––7.5)	9 (6.3–14.4)	0.075	5.8 (4.8–7)	5.8 (4–7.8)	0.99
Mean mitral gradient, median (IQR), mmHg	2 (1.12–3)	2 (1.1–3)	3 (2.2–4.75)	0.138	2 (1.15––3.25)	1.5 (1.15–3)	0.561
MR vena contracta, median (IQR), cm	0.35 (0.22––0.55)	0.29 (0.19––0.43)	0.61 (0.35––0.94)	< 0.001	0.52 (0.41––0.71)	0.22 (0.17–0.28)	< 0.001
MR EROA, median (IQR), cm^2	0.22 (0.15––0.34)	0.19 (0.15––0.28)	0.36 (0.26––0.51)	0.001	0.33 (0.25––0.44)	0.16 (0.13–0.19)	< 0.001
MR regurgitant volume, median (IQR), ml	33 (19–46)	28.5 (18––44)	44 (33–66)	0.006	47 (38–63)	20 (15–28)	< 0.001
Tricuspid valve							
Moderate to severe TR, n (%)	19 (27.5)	13 (24.5)	6 (37.5)	0.16	16 (36.4)	3 (12)	0.01
Pulmonary systolic artery pressure, mean (SD), mmHg	30.2 (25.2)	29.3 (24.1)	33 (29.3)	0.468	36.2 (24.8)	19.6 (22.8)	0.015

Continuous variables are represented as mean (SD) and median (IQR); categorical variables are presented as numbers (%). AR — aortic regurgitation; EROA, effective regurgitant orifice area; LVEDD — left ventricular end–diastolic dimension; LVEF — left ventricular ejection fraction; MR — mitral regurgitation; PVL — perivalvular leak

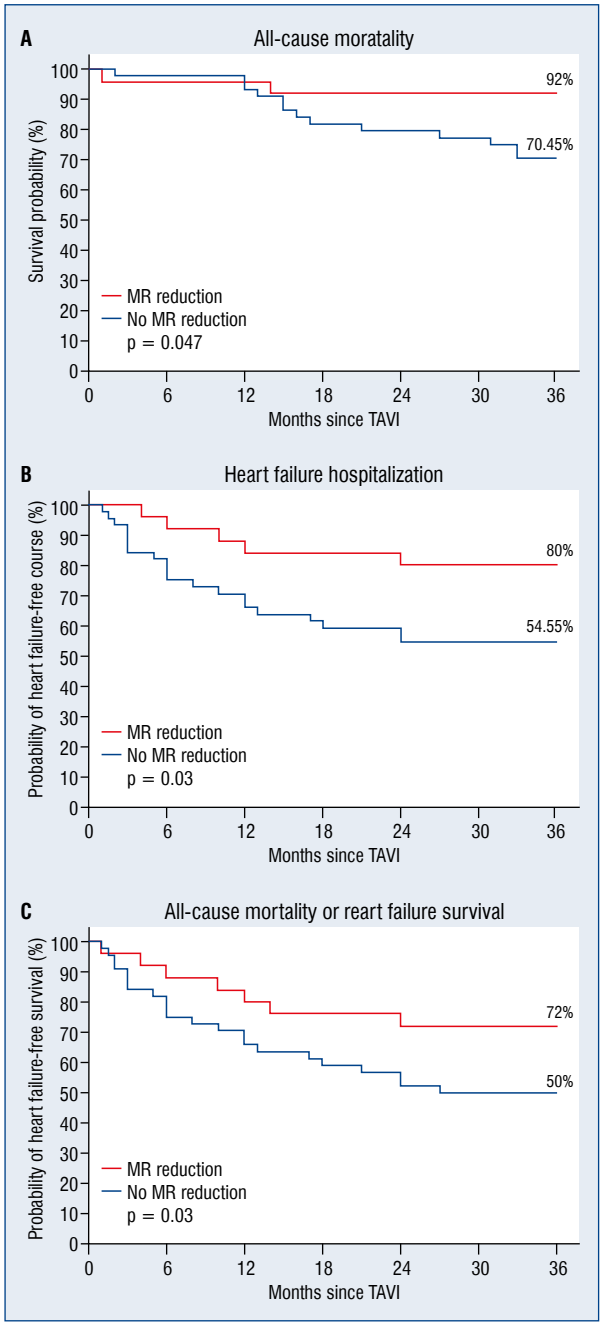

Figure 3. Kaplan-Meier curves for the secondary endpoints according to mitral regurgitation reduction at a 3-year follow-up; Abbreviations: MR, mitral regurgitation; TAVI, transcatheter aortic valve implantation

reduction of MR following TAVI was observed in about one-third (36.2%) of subjects, regardless of its etiology and type of bioprosthesis. In addition, persistent MR after valve implantation was not associated with worse clinical outcomes. The current findings seem to be important due to the lack of data on MR after TAVI in an unselected population with a high percentage of primary MR.

Significant MR is present in 15-20% of patients undergoing TAVI [7, 8, 15]. Few studies analyzed multiple valvular heart disease; therefore current guidelines are limited on this topic [10]. In patients with coexisting severe AS and severe MR, there is agreement that despite higher operative risk, two-valve surgery is indicated [10]. Moreover, such coexistence frequently disqualified in patients from TAVI previously [16]. Several meta-analyses showed that MR improves in approximately 50% of patients after TAVI, especially in the presence of secondary MR [7–9, 17, 18]. However, the influence of TAVI on primary MR remains unclear. Muratori and Al-Hindwan reported significant primary MR regression after TAVI [19, 20]. In contrast, Rys associated the presence of the mitral calcifications with MR worsening following TAVI [21]. In the present group, the primary MR was barely predominant and improved after TAVI, similarly to secondary MR.

Several groups tried to indicate factors predicting MR improvement [7, 8, 22–24]. In a study by Mauri, the mitral annular dimension above 32mm predicted MR reduction [15]. Moreover, severe MR decreased more significantly than moderate in Nombela-Franco's population [7]. In the current study, larger mitral annuli were associated with more pronounced MR. However, there was no visible trend showing mitral annular diameter to be a predictor of MR reduction. Contrary to previous reports, it was not confirmed that AV gradient, pulmonary hypertension, atrial fibrillation, or use of balloon-expandable prostheses were linked with MR recovery [7]. In addition, 11.6% of TAVI patients with significant MR reported smoking. A similar percentage (10.1%) of patients suffered from chronic obstructive pulmonary disease (COPD) and required daily use of inhalers. It was noted herein, that there was a lower likelihood of MR reduction in smokers and COPD patients.

The mechanism of MR improvement after TAVI is mainly functional and closely related to LV (left ventricular) recovery. Early MR improvement can be explained by the reduction of mitral leaflet tethering secondary to postprocedural LV afterload decline [25]. Long-term, TAVI is associated with left ventricular (LV) reverse modelling, end-diastolic volume reduction, systolic and diastolic improvement [17, 26, 27]. In contrast to previous reports, it was not confirmed that baseline LV size was associated with MR severity [7]. Instead, MR reduction was associated with postprocedural LV size reduction. Several studies have shown a positive effect of TAVI (transcatheter aortic valve

implantation) on EF (ejection fraction) increase [18, 19, 26, 28]. A trend was detected towards post-TAVI EF gain in that group. Moreover, it was observed that patients responding to TAVI with MR reduction suffered noticeably less often from MI. Likely, the reverse remodeling that occurs after TAVI and leads to MR improvement does not occur in chambers affected by MI. The presence of residual perivalvular leak (PVL) is another factor that worsens MR due to LV volume overload [29]. In the present study, moderate to severe paravalvular leaks (8 subjects, 11,6%) were not related to MR intensity.

It was shown that a lack of MR reduction was associated with worse clinical outcomes, including mortality and rehospitalization rate. This is consistent with previous publications [8, 18, 19]. In addition, several papers have suggested an association between severe baseline MR and higher mortality [8, 15, 19]. Others disagreed with this association [28, 30]. However, in the present study, baseline MR severity was not associated with clinical outcomes.

Limitations

The main limitations of this study are the single-center design and its retrospective character. However, the data presented is from everyday clinical practice in a population of unselected TAVI patients.

A relatively small sample size prevented the development of a multivariable prediction model of MR reduction. A large, prospective and multicenter study would allow a more detailed evaluation.

Another limitation is the lack of quantitative measurements of MR in about third of subjects. Nevertheless, the integration of multiple parameters of MR severity allowed the evaluation of MR with high accuracy despite lacking utter quantitative data.

Conclusions

Hemodynamically significant MR improves after TAVI regardless of its etiology.

Mitral regurgitation reduction after TAVI improves clinical outcomes.

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