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Dynamics of Concomitant Functional Mitral Regurgitation in Patients with Aortic Stenosis Undergoing TAVI

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Background: The aim of this study was to investigate the echocardiographic features of functional mitral regurgitation (MR) in patients with aortic stenosis (AS) pre- and post-trans catheter aortic valve implantation (TAVI).

Methods: The study subjects consisted of 79 patients with severe AS, who underwent TAVI. The echocardiographic parameters related to MR severity prior to TAVI and the change in these parameters and MR severity within one month after implantation were retrospectively evaluated.

Results: The mean left ventricular ejection fraction (LVEF) was 53 ± 12%, and the mean MR severity was 1.2 ± 0.7. Among the baseline parameters, age (p = 0.019, r = 0.264), LV mass (p = 0.017, r = 0.269), deceleration time (DT) (p = 0.019, r = -0.266), left atrial diameter (p = 0.003, r = 0.325), were related to pre-procedure MR severity. After TAVI, the grade of MR (1.2 ± 0.7 vs. 0.8 ± 0.6, p < 0.001) and MR duration (43 ± 19% vs. 31 ± 23%, p < 0.001) were significantly decreased. The grade of pre-procedural MR (p < 0.001) was a predictor of residual MR after TAVI. However, there was not a significant change in the left ventricular echocardiographic parameters after TAVI [LVEF (53 ± 12 vs. 52 ± 11, p = 0.285), and LV mass (302 ± 84 vs. 306 ± 76 g, p = 0.495)].

Conclusions: In patients with severe AS, functional MR is related to age, LV mass, DT and left atrial diameter. TAVI improves MR in these patients, even before LV remodelling occurs.

Key Words: Aortic stenosis • Mitral regurgitation • Trans catheter aortic valve implantation (TAVI)

INTRODUCTION

Functional mitral regurgitation (MR) in patients with severe aortic stenosis (AS) is a common finding and may be related to poor prognosis.[1,2] In cases of severe AS, functional MR may be the result of increased left ventricular afterload due to aortic valve obstruction and left ventricular remodelling. In addition, fluid overload and coexisting coronary artery disease may also contribute to left ventricular dilatation and progression of functional MR.[3]

While it is assumed that degenerative MR is less likely to change after aortic valve treatment, functional MR is deemed to have a better prognosis.[4,5] Nevertheless, limited information is available on how patients with functional MR benefit from isolated aortic valve intervention, and what the predictors of MR improvements are. Therefore, the decision about concomitant treatment of the mitral valve at the time of aortic valve intervention/surgery remains undecided.[6] Unnecessary intervention with the mitral valve at the time of aortic valve surgery may increase mortality and morbidity.[7] Recent advances in trans catheter aortic valve implantation (TAVI), during which concomitant mitral valve treat-

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ment is usually not available, makes identification of patients with likely improvement of MR even more important. As the outcome of functional MR after TAVI is not yet well-established.[8-12] Identification of echocardiographic predictors of residual MR would be helpful.

The aim of the present study was to investigate the mechanisms of functional MR in patients referred for TAVI and the predictors of post-procedural change.

METHODS

Patients with severe AS who underwent TAVI at King's College Hospital between January 2007 and January 2012 were evaluated in a retrospective manner. We excluded patients with myxomatous or rheumatic mitral valve disease, but patients with mitral annular calcification, which is common, were included. Patients with poor diagnostic test imaging quality, which precluded precise analysis of MR, were also excluded. Mitral regurgitation was noted and graded in our study subject as follows: absent in 15 patients, grade 1 in 78 patients, grade 2 in 25 patients, grade 3 in 12 patients and grade 4 in 9 patients.

Seventy-nine patients underwent TAVI via the transapical (n = 37) or transfemoral approach (n = 42). In all procedures, the Edwards SAPIEN™ transcatheter heart valve (Edwards Lifesciences, Irvine, CA, USA) was used and inserted under general anaesthesia with the guidance of fluoroscopy and transesophageal echocardiography as described previously.[13,14]

Patients were evaluated in a retrospective manner. Basal clinical characteristics, including a history of hypertension, diabetes mellitus, atrial fibrillation, coronary artery disease, cerebrovascular event, peripheral artery disease, renal dysfunction, chronic obstructive airway disease and the functional capacity of the patients (according to New York Heart Association classification), were recorded from the patients' files and are documented in Table 1. The usage of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker was also recorded.

All patients underwent transthoracic echocardiograms (TTE) as part of their work-up for TAVI. These TTE's were evaluated for this study to investigate the mechanisms of MR. In patients who subsequently underwent TAVI (n = 79/57%), the TTE immediately before the procedure and the first TTEs performed within the first month after clinical stabilization were also assessed. For all TTEs, a Philips iE33 echocardiography system with an S5 probe (Andover, MA, USA) was used.

The degree of MR was based on the recommendations of the American Society of Echocardiography, by a vena contracta width, and by ratio of the planimetric regurgitant jet area to the left atrial area.[15] It was graded into five different categories (0: none, 1: trace, 2: mild, 3: moderate, 4: severe). We evaluated mild MR further in 2 different categories as trace and mild for a more precise evaluation (Vena contract < 0.1 mm: trace, Vena contracta ≥ 0.1 mm but < 0.3 mm: mild). The severity of aortic stenosis was determined by measurement of the aortic valve peak and mean gradients using the modified Bernoulli equation and calculation of the aortic valve area (AVA) by continuity equation.[15] Bi-plane Simpson's method or 3-D Echo (when available) were used to measure the end-diastolic and end-systolic left ventricular (LV) volumes and ejection fraction (EF). LV mass was calculated by using the cubed formula.[16] The left atrial (LA) area and mitral regurgitant jet area were measured by planimetry in the apical 4-chamber views.[17] Systolic pulmonary artery pressure (PAP) was calculated by estimation of right ventricular systolic pressure using tricuspid regurgitation velocity plus the estimated right atrial pressure. E wave, A wave, mitral deceleration time (DT) and E wave duration were measured using pulsed wave Doppler. Duration of MR and duration of aortic valve forward flow was calculated from continuous wave Doppler as the percentage of RR interval. Mitral tenting height was calculated by measuring the distance between coaptation points of the mitral leaflets and the line extending through annular hinge points in the parasternal long axis view at end systole.[18] Mitral annulus systolic and diastolic diameters were measured in parasternal long axis view at end systole and end diastole, respectively. Mitral annulus calcification (MAC) was graded visually as mild, moderate or severe.[19] Mild MAC was defined as calcification involving one-third or less of the annulus. When the calcification involved more than one-third but less than two-thirds of the annulus, it was graded as moderate. When the calcification included more than two-thirds of the annulus, it is defined as severe MAC.

We reviewed the echocardiographic parameters related to MR severity prior to TAVI, and the change in these parameters and MR severity less than one month after valve implantation.

Statistical analysis

Continuous variables were given as mean ± standard deviation, and categorical variables were defined as percentages. Data were tested for normal distribution using the Kolmogorov-Smirnov test. Continuous variables with normal distribution were compared by Student's t-test, and non-normally disturbed variables by Mann-Whitney U Test. The $\chi 2$ test was used for categorical variables between two groups. The dependent variables were analysed using paired t-test, and Spearman's correlation coefficient was used for correlation analysis. All tests of significance were two-tailed, and statistical significance was defined as $p < 0.05$. The SPSS statistical software (SPSS 15.0 for Windows, Inc., Chicago, IL, USA) was used for all statistical calculations.

RESULTS

The baseline clinical and echocardiographic characteristics of the study patients (n = 79) are shown in Table 1. Mean age was 84 ± 5 years, the mean LVEF was 51% and degree of MR was 1.2 ± 0.7.

When we evaluated the baseline echocardiographic features related to grade of MR using vena contracta

Table 1. Baseline characteristics of study patients

Parameters (N = 79)	
Age, yrs	84 ± 5
Gender, male	51%
Hypertension	66%
Diabetes mellitus	23%
NYHA class (I-IV)	2.5 ± 0.5
Presence of AF	28%
CAD	67%
PAD	28%
CKD	27%
COPD	37%
Prior MI	14%
Prior PCI	19%
Prior CABG	20%
Prior CVE	14%

Table 1. Continued

Parameters (N = 79)	
Echocardiography	
Left ventricular parameters	
Ejection fraction (%)	53 ± 12
LVEDD (cm)	4.7 ± 0.7
LVESD (cm)	3.1 ± 0.8
LVEDV	106 ± 44
LVESV	53 ± 35
IVS (cm)	1.39 ± 0.19
PW (cm)	1.29 ± 0.17
LV mass (gr)	302 ± 84
Left atrial parameters	
LA diameter (cm)	4.3 ± 0.5
LA area	26 ± 6
Doppler echocardiography	
Mitral regurgitation degree	1.2 ± 0.7
Mitral regurgitation duration %	43 ± 19
Mitral tenting height(cm)	0.47 ± 0.23
Mitral annulus (diastolic) (cm)	3.1 ± 0.5
Mitral annulus (systolic) (cm)	2.4 ± 0.5
Mitral E velocity (cm/s)	103 ± 33
Mitral A velocity (cm/s)	98 ± 36
DT (ms)	224 ± 75
Mitral inflow E duration %	34 ± 8
MAC (presence)	61%
MAC severity (median)	0.85 ± 0.79 [1 (0-3)]
AVA	0.66 ± 0.16
Aortic ejection duration %	36 ± 5
Maximum aortic gradient (mmHg)	84 ± 24
Mean aortic gradient (mmHg)	48 ± 15
Aortic regurgitation	1.6 ± 0.8
sPAP (mmHg)	41 ± 14
Medications	
ACEi	47%
Statin	65%

A significant p value was accepted as < 0.05.
ACEi, Angiotensin converting enzyme inhibitor; AF, atrial fibrillation; AVA, aortic valve area; CABG, coronary artery bypass graft; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVE, cerebrovascular event; DT, deceleration time; IVS, interventricular septum; LA, left atrium; LV, left ventricle; LVEDD, left ventricular end diastolic diameter; LVEDV, left ventricular end diastolic volume; LVESD, left ventricular end systolic diameter; LVESV, left ventricular end systolic volume; MAC, mitral annulus calcification; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral arterial disease; PAP, pulmonary artery pressure; PCI, percutaneous coronary intervention; PW, posterior wall.

width and jet area, and the MR duration, we found that age was positively correlated with MR degree (p = 0.019, r = 0.264). Other than age, baseline LV mass (p = 0.017, r = 0.269), DT (p = 0.019, r = -0.266), and LA diameter (p = 0.003, r = 0.325), were associated with a higher grade of MR (Table 2).

Baseline LVEF (p = 0.012, r = -0.290), LV mass (p = 0.043, r = 0.236), DT (p < 0.001, r = -0.483), and aortic ejection duration (p = 0.003, r = 0.341) were related to increased duration of MR. Neither the presence of MAC, or the degree of MAC showed a statistically significant correlation with any of the MR severity parameters (Table 2).

At the pre-procedural evaluation of the 79 patients who underwent TAVI, MR was absent in 9 patients, grade 1 in 48 patients, grade 2 in 18 patients, and grade 3 in 4 patients. TAVI was not performed in any patients with grade 4 MR. In our study population, the procedure was successful in all of the patients except 1, who died secondary to a major vascular complication 7 days after the procedure.

There was a significant decrease in maximum (83 ± 25 mmHg vs 17 ± 6 mmHg, p < 0.001) and mean (47 ± 15 mmHg vs. 8 ± 3 mmHg, p < 0.001) aortic gradients as well as in PAP (42 ± 14 mmHg vs. 38 ± 12 mmHg, p = 0.02) in the echocardiographic examinations performed within one month after the procedure. When we compared the echocardiographic parameters before and within one month after TAVI, we found a significant decrease in MR degree (1.2 ± 0.7 vs. 0.8 ± 0.6, p < 0.001), and MR duration (43 ± 19 vs. 31 ± 23, p < 0.001) (Table 3). After TAVI, MR disappeared in 12 of 48 patients (25%) who had pre-procedural grade 1 MR. Furthermore, MR severity decreased in 15 out of 18 patients (83%) with pre-procedural grade 2 MR, and in all patients (n = 4) with pre-procedural grade 3 MR. Mitral E wave duration increased significantly after TAVI (34 ± 8 vs. 37 ± 10, p = 0.01) (Table 3). In 4 patients, MR severity increased only modestly after TAVI. When we investigated the possible causes of this increase, we observed that all of these patients had coronary artery disease (CAD) or pulmonary arterial hypertension. However, the number of patients with an increase in MR after the procedure was not enough to make a multivariate analysis to search for an independent impact of significant atherosclerosis on the response of MR to TAVI.

Table 2. Baseline echocardiographic parameters related to severity of mitral regurgitation prior to implantation

Parameters	Mitral regurgitation degree		Mitral regurgitation duration%	
	r	p	r	p
Age	0.264	0.019	0.229	0.050
Ejection fraction	-0.177	0.120	-0.290	0.012
LV mass (gr)	0.269	0.017	0.236	0.043
E wave duration(%)	-0.166	0.154	-0.064	0.595
DT	-0.266	0.019	-0.483	< 0.001
AVA	-0.180	0.116	-0.203	0.087
Aortic ejection duration%	0.005	0.963	0.341	0.003
Maximum aortic gradient	0.063	0.583	-0.078	0.507
Mean aortic gradient	0.091	0.427	-0.042	0.723
Aortic regurgitation	-0.059	0.609	-0.054	0.650
LA diameter (A-P)	0.325	0.003	0.038	0.748
LA area	0.129	0.259	-0.012	0.918
Mitral tenting height	0.121	0.288	0.140	0.234
Mitral annulus (diastolic)	-0.018	0.877	-0.055	0.642
Mitral annulus (systolic)	0.128	0.263	0.077	0.516
MAC severity	0.109	0.337	0.071	0.547
sPAP (mmHg)	0.076	0.537	0.200	0.115

Spearman rank correlation. A significant p value was accepted as < 0.05. p values between 0.05-0.1 represent a nonsignificant tendency.
AVA, aortic valve area; DT, deceleration time; LA, left atrium; LV, left ventricle; MAC, mitral annulus calcification; sPAP, systolic pulmonary artery pressure.

The relation between baseline echocardiographic parameters to reduction in MR severity after TAVI is presented in Table 4. Pre-procedural MR degree (p < 0.001, r = 0.653), and MR duration (p = 0.05, r = 0.232) were related to the amount of reduction in severity. Other than these parameters, older age (p = 0.006, r = 0.312) was also related to the amount of reduction in MR severity. Mitral annulus calcification was not related with the response of MR to TAVI. The route of implantation (transapical vs. transfemoral) did not affect MR degree after TAVI (0.47 ± 0.85 vs. 0.38 ± 0.85; p = 0.594). Additionally, the presence of coronary artery disease was not related to the change in MR after TAVI (0.47 ± 0.79 vs. 0.41 ± 0.80; p = 0.742. On the other side, presence of peripheral artery disease (PAD) was related to a lesser reduction of MR after the procedure (0.56 ± 0.74 vs. 0.09 ± 0.83; p = 0.02). However, in multivariate analysis, although PAD was related to less reduction in MR, if we

Table 3. Changes in echocardiographic parameters following TAVI implantation

Parameters	Prior TAVI	Post TAVI	p value
Left ventricular parameters			
Ejection fraction (%)	53 ± 12	52 ± 11	0.285
LVEDD (cm)	4.7 ± 0.7	4.7 ± 0.7	0.828
LVEDV	106 ± 44	106 ± 40	0.776
LVESV	53 ± 35	53 ± 32	0.826
IVS (cm)	1.39 ± 0.19	1.37 ± 0.16	0.151
PW (cm)	1.29 ± 0.17	1.27 ± 0.16	0.207
LV mass (gr)	302 ± 84	306 ± 76	0.495
LA area	25.7 ± 6.2	24.8 ± 5.7	0.145
Doppler echocardiography			
Mitral regurgitation degree	1.2 ± 0.7	0.8 ± 0.6	< 0.001
Mitral regurgitation duration %	43 ± 19	31 ± 23	< 0.001
Mitral E velocity (cm/s)	103 ± 33	108 ± 30	0.091
DT (ms)	225 ± 75	223 ± 66	0.867
E wave duration	34 ± 8	37 ± 10	0.010
Maximum aortic gradient (mmHg)	83 ± 25	17 ± 6	< 0.001
Mean aortic gradient (mmHg)	47 ± 15	8 ± 3	< 0.001
sPAP (mmHg)	41 ± 14	38 ± 12	0.021

Paired t test; A significant p value was accepted as < 0.05. p values between 0.05-0.1 represent a non-significant tendency.
DT, deceleration time; IVS, interventricular septum; LA, left atrium; LV, left ventricle; LVEDD, left ventricular end diastolic diameter; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; PAP, pulmonary artery pressure; PW, posterior wall; TAVI, transcatheter aortic valve implantation.

Table 4. The parameters related to reduction of mitral regurgitation in patients undergoing TAVI implantation

Parameters	MR reduction degree	
	r	p
Age	0.312	0.006
Ejection fraction	-0.093	0.426
LV mass	0.127	0.275
Mitral inflow E duration	-0.055	0.644
DT	-0.209	0.074
AVA	-0.212	0.070
Aortic ejection duration	0.073	0.531
Aortic regurgitation	-0.040	0.734
Mitral regurgitation degree (preop)	0.653	< 0.001
Mitral regurgitation duration (preop)	0.232	0.050
LA diameter (parasternal)	0.071	0.544
LA area	0.023	0.845
Mitral tenting	0.145	0.212
Mitral annulus (diastolic)	-0.008	0.948
Mitral annulus (systolic)	0.120	0.303
MAC severity	0.059	0.622
sPAP (mmHg)	0.171	0.170
Maximum aortic gradient (mmHg)	0.178	0.123
Mean aortic gradient (mmHg)	0.214	0.064

A significant p value was accepted as < 0.05. p values between 0.05-0.1 represent a non-significant tendency.
AVA, aortic valve area; DT, deceleration time; LA, left atrium; LV, left ventricle; MAC, mitral annulus calcification; sPAP, systolic pulmonary artery pressure.

take the criteria of at least 1 degree change in MR, only pre-procedural MR was an independent parameter to predict the change in MR (Table 5). We did not observe any significant relationship between other comorbidities and reduction in MR severity after TAVI.

DISCUSSION

The main findings of the present study are that age,

Table 5. Independent predictors of reduction of mitral regurgitation in multivariate linear regression analysis

Linear regression analysis	Dependent variable: reduction of mitral regurgitation	
Independent variables	*p value	Beta (standardized)
Age, years	0.382	0.085
Mitral regurgitation degree (preop)	< 0.001	0.608
PAD	0.025	-0.203
AVA	0.633	-0.054
Mean aortic gradient (mmHg)	0.656	0.050
Adjusted R^2	0.348	

AVA, aortic valve area; PAD, peripheral arterial disease.

LV hypertrophy and remodelling, as well as LV afterload are predictive of severity of concomitant MR in patients with severe AS. TAVI performed on these patients results in a significant reduction of functional MR. Furthermore, pre-procedural severity of MR and MR duration in pre-procedural echocardiographic assessment can help to predict the improvement in functional MR after the procedure.

Previous studies have shown that coexisting MR in patients with severe AS may be caused by intrinsic mitral valve disease or could be secondary to LV remodelling and increased LV afterload due to AS.[3,20,21] In our study, we also found that MR is associated with LV hypertrophy, AVA and LVEF in patients with severe AS. However, after TAVI, as the gradient at the aortic valve is acutely reduced, MR severity decreases independent of LV mass regression or improvement of LVEF. Furthermore, MR duration was also decreased significantly with the reduction in LV afterload. We used MR duration to assess the impact of increased LV afterload on MR. The coaptation defect which leads to MR in the setting of severe AS is partly a consequence of LV pressure overload of LV. These findings indicate that the increased LV afterload is an important contributor to the mechanism of MR. Thus, after TAVI, the favourable effects on MR severity occur acutely, even before reversal of LV remodelling.

The ability to predict a reduction of MR following isolated TAVI may be of particular importance in high-risk patients who otherwise would face double valve surgery or concomitant mitral valve intervention. Our results are consistent with previous studies investigating the impact of surgical aortic valve replacement on concomitant MR in patients with severe AS.[22-24] Most of these studies found a significant reduction of MR in cases of functional MR, but not in patients with degenerative or rheumatic MR.[4,5] The studies evaluating response of MR after TAVI also documented that the type of MR is important for the response of MR.[25,26] The probable mechanism for this difference in the response is that the reduction in LV size and pressure improves coaptation of the otherwise normal MV leaflets in case of functional MR. The reduction of left ventricular size is likely to be greater in patients with a flexible, non-calcified mitral valve ring. Durst et al. found that presence of MAC causing restriction leaflet mobility is the only variable related to the response of MR to TAVI.[26] However, mitral annular calcification occurs very frequently in patients with degenerative AS, and it is very rare to see a completely healthy mitral annulus structure in this patient population. We could not find a statistically significant relationship between presence and severity of MAC and postprocedural MR severity. Although shape and size of the mitral valve annulus is less likely to change in patients with MAC, MR is still likely to be reduced after TAVI as a result of reduction of left-ventricular pressures. The discrepancy related to the impact of MAC on MR between our study and the study by Durst et al. may be caused by different timing of echocardiographic evaluation. In their study, Durst et al. used the echocardiographic measurements three months after the procedure. In the immediate postprocedural period, the impact of the decrease in LV afterload may be more significant than MAC.

In the study by Toggweiler et al., the predictors of a decrease in MR after TAVI were transaortic mean gradient > 40 mmHg, functional MR and absence of pulmonary hypertension (PHT) and atrial fibrillation.[25] In our study, although we did not find a significant correlation between transaortic gradient and the reduction in MR, the significant relationship between AVA and post-procedural decrease in MR proves the importance of AS severity on MR. The absence of a significant relationship between pulmonary artery pressure and decrease in MR may be related to the absence of patients with severe PHT in our study population. The fact that pre-procedural MR severity was among the most powerful predictors of the decrease in MR severity after TAVI must be viewed in the context that patients with only mild MR do not have room for much reduction, and also that we excluded patients with organic MR, other than mitral annular calcification. Thus, more severe MR may, intuitively, show more reduction after TAVI. Several reports have shown that reduction in pure functional severe MR is possible.[27,28] However, since our practice is to exclude patients with grade 4 MR for TAVI, our study population did not include any such patients. Further studies are required to determine the outcome of severe functional MR after TAVI.

In general, we found a significant decrease in MR severity after TAVI procedure. However, an increase in MR was seen in 4 patients and the exact mechanism of this was unclear. Additionally, there was significant coro-

nary artery disease in all of these patients and ischemia during the procedure may play a role in the acute increase of MR severity.

Our results are in concordance with previous studies investigating the impact of TAVI using Edwards-Sapiens valves on concomitant MR.[11,12] The results of the PARTNER trial also showed a greater benefit with Edwards-Sapien valves in patients with significant MR.[29] Hekimian et al. investigated the effect of deep positioning on post-procedural MR severity in patients who received the Edwards-Sapien valve.[12] They did not find an association between the overlap of anterior mitral valve with the prosthesis and MR severity.

The small size of the study population and the single-centre, retrospective design are the main limitations of our study. However, TAVI is a relatively new treatment technique and is being performed in only selected centres. The other limitation is the semi-quantitative assessment of MR. We did not perform proximal isovelocity surface area (PISA) method to assess MR severity. However, PISA method also has its own limitations especially in patients with mitral annular calcification and eccentric regurgitant jets and aortic insufficiency.[30] We used vena contracta width which has been shown to be load-independent in previous studies[31,32] and the ratio of planimetric regurgitant jet area to left atrial area takes into account the increase in left atrial size in AS.[33] Inclusion of mostly mild to moderate MR in TAVI group is another limitation. Our TAVI group does not include grade 4 MR and the number of the patients with grade 3 MR (n = 4) was very low. Since pre-procedural MR severity was one of the most powerful predictors of post-procedural reduction in MR severity, the low number of higher grades of MR may be responsible for the relatively low r values in our study. Finally, we evaluated MR severity within one month of the TAVI procedure and therefore we are unable to state what might be the long term changes in MR severity.

CONCLUSIONS

In conclusion, a detailed transthoracic echocardiographic examination can provide much information about the likely success of TAVI, including the response of pre-procedural MR which appears to be related to the decrease in LV afterload rather than remodelling. These echocardiographic findings may be helpful in patient selection for TAVI in patients with severe AS and concomitant MR. However, further studies with larger patient populations are required to confirm these findings.

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REFERENCES

1. Takeda K, Matsumiya G, Sakaguchi T, et al. Impact of untreated mild-to moderate mitral regurgitation at the time of isolated aortic valve replacement on late adverse outcomes. *Eur J Cardiothorac Surg* 2010;37:1033-8.
2. Asimakopoulos G, Edwards MB, Taylor KM. Aortic valve replacement in patients 80 years of age and older: survival and cause of death based on 1100 cases: collective results from the UK Heart Valve Registry. *Circulation* 1997;96:3403-8.
3. Unger P, Dedobbeleer C, Van Camp G, et al. Mitral regurgitation in patients with aortic stenosis undergoing valve replacement. *Heart* 2010;96:9-14.
4. Barreiro CJ, Patel ND, Fitton TP, et al. Aortic valve replacement and concomitant mitral valve regurgitation in the elderly: impact on survival and functional outcome. *Circulation* 2005;112(suppl I):I-443-7.
5. Vanden Eynden F, Bouchard D, El-Hammasy I, et al. Effect of aortic valve replacement for aortic stenosis on severity of mitral regurgitation. *Ann Thorac Surg* 2007;83:1279-84.
6. Ruel M, Kapila V, Price J, et al. Natural history and predictors of outcome in patients with concomitant functional mitral regurgitation at the time of aortic valve replacement. *Circulation* 2006;114:541-6.
7. Mueller XM, Tevaearai HT, Stumpe F, et al. Long-term results of mitral-aortic valve operations. *J Thorac Cardiovasc Surg* 1998; 115:1298-309.
8. De Chiara B, Moreo A, De Marco F, et al. Influence of CoreValve revalving system implantation on mitral valve function: an echocardiographic study in selected patients. *Catheter Cardiovasc Interv* 2011;78:638-44.
9. Gotzmann M, Lindstaedt M, Bojara W, et al. Hemodynamic results and changes in myocardial function after transcatheter aortic valve implantation. *Am Heart J* 2010;159:926-32.
10. Tzikas A, Piazza N, van Dalen BM, et al. Changes in mitral regurgitation after transcatheter aortic valve implantation. *Catheter Cardiovasc Interv* 2010;75:43-9.

11. Samim M, Stella PR, Agostoni P, et al. Transcatheter aortic implantation of the Edwards-Sapien bioprosthesis: insights on early benefit of TAVI on mitral regurgitation. *Int J Cardiol* 2011;152: 124-6.
12. Hekimian G, Detaint D, Messika-Zeitoun D, et al. Mitral regurgitation in patients referred for transcatheter aortic valve implantation using Edwards Sapien prosthesis: mechanisms and early postprocedural changes. *J Am Soc Echocardiography* 2012;25: 160-5.
13. Vahanian A, Alfieri O, Al-Attar N, et al. Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European Association of Cardio-Thorasic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2008;29:1463-70.
14. Zamorano JL, Badano LP, Bruce C, et al. EAE/ASE recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease. *Eur J Echocardiogr* 2011; 12:557-84.
15. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two dimensional and Doppler echocardiography. *J Am Soc Echocardiogr* 2003;16:777-802.
16. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440-63.
17. Lancellotti P, Moura L, Pierard LA, et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). *Eur J Echocardiogr* 2010;11:307-32.
18 Calafiore AM, Gallina S, Di Mauro M, et al. Mitral valve procedure in dilated cardiomyopathy: repair or replacement? *Ann Thorac Surg* 2001;71:1146-53.
19. Jassal DS, Tam JW, Bhagirath KM, et al. Association of mitral annular calcification and aortic valve morphology: a substudy of the aortic stenosis progression observation measuring effects of rosuvastatin (ASTRONOMER) study. *Eur Heart J* 2008;12:1542-7.
20. Brener SJ, Duffy CI, Thomas JD, Stewart WJ. Progression of aortic stenosis in 394 patients: relation to changes in myocardial and mitral valve dysfunction. *J Am Coll Cardiol* 1995;25:305-10.
21. Timmis SB, Kirsh MM, Montgomery DG, Starling MR. Evaluation of left ventricular ejection fraction as a measure of pump performance in patients with chronic mitral regurgitation. *Catheter Cardiovasc Interv* 2000;49:290-6.
22. Vanden Eynden F, Bouchard D, El-Hamamsy I, et al. Effect of aortic valve replacement for aortic stenosis on severity of mitral regurgitation. *Ann Thorac Surg* 2007;83;1279-84.
23. Waisbren EC, Stevens LM, Avery EG, et al. Changes in mitral regurgitation after replacement of the stenotic aortic valve. *Ann Thorac Surg* 2008;86:56-63.
24. Tassan-Mangina S, Metz D, Nazeyllas P, et al. Factors determining early improvement in mitral regurgitation after aortic valve replacement for aortic valve stenosis: a transthoracic and transesophageal prospective study. *Clin Cardiol* 2003;26:127-31.
25. Toggweiler S, Boone RH, Rodes-Cabau J, et al. Transcatheter aortic valve replacement: outcomes of the patients with moderate or severe mitral regurgitation. *J Am Coll Cardiol* 2012;59:2068-74.
26. Durst R, Avelar E, McCarthy D, et al. Outcome and improvement predictors of mitral regurgitation after transcatheter aortic valve implantation. *J Heart Valve Dis* 2011;20:272-81.
27. Kisch S, D'Ancona G, Paranskaya L, et al. Staged transpercutaneous treatment of aortic valve pathology and mitral regurgitation: Institutional experience. *Catheter Cardiovasc Interv* 2013; 82:E552-63.
28. Sarı C, Aslan AN, Keleş T, Bozkurt E. Significant reduction in mitral regurgitation after transcatheter aortic valve implantation in a patient with severe degenerative aortic valve disease, moderate to severe mitral regurgitation, and normal ejection fraction. *Turk Kardiyol Dern Ars* 2012;40:527-31.
29. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597-607.
30. Gilard M, Eltchaninoff H, Iung B, et al. Registry of transcatheter aortic valve implantation in high risk patients. *N Engl J Med* 2012;366:1705-15.
31. Heinle SK, Hall SA, Brickner ME, et al. Comparison of vena contracta width by multiplane transesophageal echocardiography with quantitative Doppler assessment of mitral regurgitation. *Am J Cardiol* 1998;81:175-9.
32. Baumgartner H, Schima H, Kühn P. Value and limitations of proximal jet dimensions for the quantitation of valvular regurgitation: an in vitro study using Doppler flow imaging. *J Am Soc Echocardiogr* 1991;4:57-66.
33. Bhave NM, Lang RM. Quantitative echocardiographic assessment of native mitral regurgitation: two- and three-dimensional techniques. *J Heart Valve Dis* 2012;20:483-92.