Impact of transcatheter aortic valve implantation on coexistent mitral regurgitation parameters

Authors: Piotr Scisło, Kajetan Grodecki, Bartosz Rymuza, Karol Zbroński, Janusz Kochman, Radosław Wilimski, Zenon Huczek

Article type: Original article

Received: July 2, 2020.
Accepted: October 30, 2020.
Published online: November 6, 2020.
ISSN: 0022-9032
e-ISSN: 1897-4279

This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives 4.0 International License (CC BY-NC-ND 4.0), allowing third parties to download articles and share them with others, provided the original work is properly cited, not changed in any way, distributed under the same license, and used for noncommercial purposes only. For commercial use, please contact the journal office at kardiologiapolska@ptkardio.pl.
Impact of transcatheter aortic valve implantation on coexistent mitral regurgitation parameters

Piotr Scisło¹, Kajetan Grodecki¹, Bartosz Rymuza¹, Karol Zbroński¹, Janusz Kochman¹, Radosław Wilimski², Zenon Huczek¹

¹I Chair and Department of Cardiology, Medical University of Warsaw
²Department of Cardiac Surgery, Medical University of Warsaw

Short title: Mitral regurgitation after TAVI

Corresponding author:

Piotr Scislo, MD, PhD
I Chair and Department of Cardiology, Medical University of Warsaw
Banacha 1a St.
02-097 Warsaw
mail: scislo@wum.edu.pl
tel. +48 22 5992612
fax +48 22 5991234

Conflict of interest: none declared.
What’s new?

The data assessing the impact of transcatheater aortic valve implantations (TAVI) on coexisting mitral regurgitation (MR) are still lacking. We assessed the impact of the TAVI on MR during a 1-year follow-up using effective regurgitation orifice (MR-ERO) and regurgitation volume (MR-Vol). It was demonstrated that TAVI has no significant impact on the MR-ERO regardless of the aetiology of regurgitation. The procedure reduces, however, MR-Vol in both functional and non-functional mitral regurgitation.
Abstract

Background: The data assessing the impact of transcatheter aortic valve implantations (TAVI) on coexisting mitral regurgitation (MR) are still inconsistent.

Aims: The study aimed to evaluate the impact of TAVI on coexistent MR depending on its aetiology.

Methods: From 311 patients treated with TAVI, we selected 48 patients with coexistent MR: functional (FMR; n=26) or non-functional (nFMR; n = 22). The impact of the procedure on MR was quantitatively assessed during a 1-year follow-up using mitral regurgitation effective regurgitation orifice (MR-ERO) and volume (MR-Vol).

Results: No change of MR-ERO was observed after a one-year follow-up in all MR patients (0.20 cm² [IQR 0.17 - 0.23 cm²] vs 0.17 cm² [0.14 - 0.20 cm²]; $P = 0.054$). No change in MR-ERO was observed neither in FMR (0.21 cm² [0.17 - 0.27 cm²] vs.0.19 cm² [0.14 - 0.25 cm²] cm², $P = 0.142$) nor nFMR (0.17 cm² [IQR 0.12 - 0.23 cm²] vs 0.17 cm² [IQR 0.10 - 0.20 cm²], $P = 0.238$) cohorts. Reduction of MR-Vol was observed in the overall MR population after TAVI (32 ml/b [IQR 28 – 36 ml/b] vs. 26 ml/b [IQR 22 – 28 ml/b], $P = 0.002$). Similarly, reduction of MR-Vol was noted for both FMR (33 ml/b [IQR 26 - 42 ml/b] vs. 26 ml/b [20 – 40 ml/b], $P = 0.042$) and nFMR (30 ml/b [IQR 20 – 46 ml/b] vs. 24 ml/b [15 – 33 ml/b], $P = 0.015$) cohorts.

Conclusions: TAVI has no impact on the MR-ERO regardless of the aetiology of regurgitation. The procedure reduces, however, MR-Vol in both FMR and nFMR.

Key words: aortic stenosis, mitral regurgitation, transcatheter aortic valve implantation
Introduction

Mitral regurgitation (MR) frequently coexists with aortic stenosis and its prevalence in patients referred for transcatheter aortic valve implantation (TAVI) ranges between 2 and 33% [1, 2]. While reports on MR improvement after surgical aortic valve replacement (SAVR) are inconsistent (varying between 27 and 82%), the data assessing the impact of TAVI on coexisting MR are still incomplete - most of the papers utilize simplified, qualitative or grade-only, analysis of mitral regurgitation [3-5]. Echocardiographic evaluation of regurgitation is, however, far more complex and should be based on a quantitative, parametric approach [6, 7].

Admittedly, attempts to implement new MR quantification protocols based on 2-dimensional (2D) as well as 3-dimensional (3D) echocardiography are made [8]. However, even the most recognized of novel 3D-derived techniques such as 3D vena contracta area and 3D surface proximal isovelocity surface area (PISA) need to be further validated before widespread introduction into the practice [9]. Heretofore, the most widely used parameters are effective regurgitation orifice (MR-ERO) and regurgitation volume (MR-Vol) – derived with the PISA method. Despite several limitations such as the inherent assumption of hemispherical PISA shape or difficult assessment of multi-jet regurgitations, they remain the most acknowledged in daily clinical practice [10, 11]. We, therefore, sought to quantitatively assess the impact of TAVI on coexistent MR using both MR-ERO and MR-Vol.

Material and methods

Study population

We screened echocardiographic data of 311 consecutive patients treated with TAVI for severe aortic stenosis (aortic valve area < 1.0 cm²) between 2010 and 2017 [12]. A total of 53 patients with coexistent moderate-to-severe MR at baseline were identified. Further, 5 patients were excluded due to death before completing a 1-year follow-up. The final study
sample included 48 patients with complete baseline and follow-up echocardiographic data. No data beyond 1-year has been analyzed. Accordingly, to the guidelines, the functional MR (FMR) was present in 26 (54.2%) patients, whereas the non-functional MR (nFMR) in 22 (45.8%). [7]

Patients were treated with transfemoral, transapical, or transcarotid TAVI with implantation of self-expanding, balloon-expandable, or mechanically expandable valves. Procedures were performed in hybrid operating rooms under general anesthesia with conscious sedation or local anesthesia. All patients were referred for TAVI after detailed evaluation by Heart Team.

**Echocardiographic examination**

The echocardiographic assessment was performed at the local core laboratory by a single accredited echocardiographer (P.S.) with over 20 years of experience, using Philips iE33 and Epiq 7C with s5-1/x5-1 probes (Supplementary Table 1). All digital data were stored on Philips Xcelera PACS and analyzed further on Philips QLAB 9-11 and Pixmeo OsiriXMD. The routine echocardiographic measurements were done according to the current guidelines and left ventricle ejection fraction (LVEF) was measured by biplane Simpson’s method. [13, 14] During the assessment, the blood pressure was in the normal range.

The mitral valve assessment was made according to the recommendations of the European Association of Echocardiography and based on a 2D echocardiographic calculation of MR-ERO and MR-Vol by proximal isovelocity surface area (PISA) method. For these analyses, the apical four-chamber view was used as a basal projection, the area of interest was optimized by lowering imaging depth and reducing the Nyquist limit to 15 - 40 cm/s. The radius of the PISA was measured at mid-systole using the first-aliasing zone. The same view was used for continuous-wave doppler data acquisition. MR-ERO and MR-Vol were obtained
using the standard formula. [7] The analysis was provided by our core-lab dedicated to the valvular heart disease program.

The cohort was further divided by the MR aetiology into functional mitral regurgitation (FMR) and non-functional mitral regurgitation (nFMR) groups. FMR was defined as abnormal leaflet function secondary to the impaired ventricular function resulting from left ventricle remodeling most frequently due to ischemic heart disease or dilatated cardiomyopathy. Patients with other MR aetiologies (calcification, degeneration) were included in the nFMR group. FMR was classified as: mild when MR-ERO < 0.1 cm² or MR-Vol < 15 ml; severe when MR-ERO > 0.2 cm² or MR-Vol > 30 ml. NFMR was classified as: mild if MR-ERO < 0.2 cm² or MR-Vol < 30 ml; severe if MR-ERO > 0.4 cm² or MR-Vol > 60 ml [7]. All patients received pharmacological therapy according to the current guidelines [12].

Statistical analysis

Data were tested for normality using the Shapiro–Wilk test. Continuous variables are expressed as mean (standard deviation) or median (interquartile range [IQR]), as appropriate. Categorical variables are presented as absolute numbers (percentage). Unpaired continuous variables were compared using the Student’s t-test or nonparametric Mann-Whitney U-test, as appropriate. Paired variables (pre- vs postprocedural) were compared with the Wilcoxon signed-rank test. Categorical variables were compared using a Chi-square test or Fisher exact test as appropriate. Spearman rank correlations were performed to examine the relationship between echocardiographic indices. Intra-observer variability for MR parameters was measured in a sample of 10 random patients using an interclass correlation coefficient (ICC). Medcalc for Windows (version 18.11 MedCalc Software, Ostend, Belgium) was used for statistical analysis, and all probability values reported are two-sided. P-value of 0.05 was considered statistically significant.
Results

Patients and baseline characteristics

The study population included 48 patients with coexistent MR, who underwent TAVI. FMR was identified in 26 (54%) patients, while nFMR was found in 22 (46%) patients. No differences in demographic data and comorbidities were found between patients with FMR and nFMR as presented in Table 1. There were no discrepancies between cohorts regarding types of implanted transcatheter heart valves (THVs; Table 2). In FMR group larger sizes of THVs were used when compared to nFMR, however, it was dictated strictly by the individual characteristic of the patients and did not influence indexed aortic valve area (iAVA 1.04 cm$^2$/m$^2$ [IQR 0.93 - 1.1 cm$^2$/m$^2$] vs 0.98 cm$^2$/m$^2$ [IQR 0.94 - 1.07 cm$^2$/m$^2$], $P = 0.417$). In none of the patients postprocedural valvular or paravalvular leak greater than mild was observed.

Left Ventricle Ejection Fraction after TAVI

Overall, LVEF increased after TAVI in all MR patients included into the study (50% [IQR 38 – 56 %] vs 56% [IQR 49 – 61 %], $P = 0.005$). This was driven mainly by the significant postprocedural LVEF increase in FMR group (35% [IQR 22 – 47 %] vs. 43% [IQR 35 – 57 %], $P = 0.007$). Only slight change of LVEF was observed in nFMR cohort (60% [IQR 55 – 63 %] vs. 63% [IQR 55 – 65 %], $P=0.307$; Figure 1).

Mitral Regurgitation Effective Orifice Area after TAVI

No significant change of MR-ERO was observed after a one-year follow-up in all MR patients (0.20 cm$^2$ [IQR 0.17 - 0.23 cm$^2$] vs 0.17 cm$^2$ [0.14 - 0.20 cm$^2$]; $P = 0.054$). Consequently, no significant change in MR-ERO was observed neither in FMR (0.21 cm$^2$ [0.17 - 0.27 cm$^2$] vs.0.19 cm$^2$ [0.14 - 0.25 cm$^2$], $P = 0.142$) nor nFMR (0.17 cm$^2$ [IQR 0.12 - 0.23 cm$^2$] vs 0.17 cm$^2$ [IQR 0.10 - 0.20 cm$^2$], $P = 0.238$; Figure 2) cohorts.
The grade of MR, when classified by the MR-ERO, did not change in 28 (58.3%) of overall MR patients, reduced in 17 (35.5%), and increased in 3 (6.2%). The MR grading remained unchanged in 10 (38.5%) FMR patients, while grade reduction occurred in 13 (50%) cases and grade increase in 3 (11.5%). In the nFMR cohort, no change in the MR grade was observed in 18 (81.8%) patients and downgrade was noted in 4 (18%).

**Mitral Regurgitation Volume (MR-Vol) after TAVI**

In comparison to baseline values, significant reduction of MR-Vol was observed in the overall MR population after TAVI (32 ml/b [IQR 28 – 36 ml/b] vs. 26 ml/b [IQR 22 – 28 ml/b], \(P = 0.002\)). Similarly, reduction of MR-Vol was noted for both FMR (33 ml/b [IQR 26 – 42 ml/b] vs. 26 [20 – 40 ml/b], \(P = 0.042\)) and nFMR (30 ml/b [IQR 20 – 46 ml/b] vs. 24 ml/b [15 - 33 ml/b], \(P = 0.015\); Figure 3) cohorts.

The grade of MR, when classified by the MR-Vol, did not change in 26 (54.2%) of overall MR patients, reduced in 18 (37.5%), and increased in 4 (8.3%). The MR grading remained unchanged in 11 (42.5%) FMR patients, while grade reduction occurred in 13 (46.2%; Figure 4) cases and grade increase in 3 (11.5%). In the nFMR cohort, no change in the MR grade was observed in 15 patients (68.2%; Figure 5), the downgrade was noted in 6 (27.3%) and upgrade in 1 (4.5%).

**Correlations between MR-ERO/MR-Vol and LVEF**

No correlation between MR-ERO reduction and LVEF was found (rho -0.13; \(P = 0.35\)) in overall MR group. Additionally, such correlation was not found neither in FMR (rho -0.08; \(P = 0.68\)) nor nFMR (rho -0.2; \(P = 0.36\)) cohorts.
No correlation between MR-Vol reduction and LVEF was observed (rho -0.01; P = 0.94) in overall MR group. Similarly, such correlation did not occur in FMR (rho 0.01; P = 0.9) as well as nFMR (rho -0.13; P = 0.56) cohorts.

**Mitral Annulus Dimension (MAD) Change after TAVI**

The TAVI had no influence on mitral annulus dimension’s change both in FMR (39.6 mm [30.7 - 47.1 mm] vs. 39.9 mm [32.6 - 48.7 mm], P = 0.900), and also in nFMR groups (34 mm [IQR 27.7 - 43.7 mm] vs. 35.7 mm [IQR 30.5 - 41.5 mm], P = 0.500).

**Discussion**

The true impact of TAVI on coexistent MR is difficult to assess as their relationship is multifactorial. Firstly, the procedural success of TAVI itself may influence MR.

Secondly, postprocedural improvement of LVEF is an important factor to consider. In our study, we observed a significant increase of LVEF in FMR, but not in nFMR patients and the difference between cohorts may be explained with severe impairment of left ventricular function at baseline in the FMR group. These findings are consistent with previous studies, which described the remarkable functional recovery of the left ventricle in the setting primarily depressed LVEF [15, 16]. Whatsoever, we did not find a correlation between the MR-ERO/MR-Vol and LVEF – arguably due to the small number of patients underpowering statistical tests.

Finally, the improvement of MR may be dependent on its aetiology (FMR/nFMR). We observed a significant change of MR-ERO neither in FMR nor nFMR groups. However, MR grade classified by MR-ERO decreased more frequently in FMR than nFMR patients. Moreover, ERO is affected by the anatomy of the mitral valve (including leaflets, ring, subvalvular apparatus, and papillary muscles), while the configuration of the valvular ring
along with the geometry of the papillary muscles is dependent on the left ventricle shape. Mildly abnormal values of ERO in the FMR group, despite the significant increase of the LVEF following TAVI, may suggest that positive increment of the left ventricle mechanical function was not sufficient to induce anatomical changes of the mitral valve and subsequent improvement of the parameter [12]. Contrarily, MR-Vol was post-procedurally reduced in both FMR and nFMR cohorts. MR grade, based on MR-Vol, was reduced in 46.2% FMR and 27.3% of nFMR cases, while the grade of 42.5% and 68.2% of subjects, respectively, remained unchanged.

Observations stand in line with other papers, however, it is the first so detailed analysis [5, 16]. MR-Vol reduction followed a decrease of the regurgitation flow, even in the presence of unchanged ERO (for example as a consequence of left-ventricle end-systolic pressure decrease), potentially influencing thereby the long-term survival [18, 19].

LVEF increase following TAVI was observed in the FMR, but not nFMR patients. Moreover, TAVI had affected MR-ERO in neither of the groups. Finally, significant post-procedural reduction of the MR-vol noted in both cohorts did not change the overall grade of MR.

Conclusions

In the studied cohort, TAVI has no significant impact on the mitral regurgitation effective regurgitant orifice (MR-ERO) regardless of the aetiology of insufficiency. The observation may be related to the organic origin of the regurgitation in (nFMR’s group) or insufficient positive remodelling of the left ventricle (FMR’s group) which is needed to change this parameter. [19] On the other side, the observation may be driven by a small number of patients in both groups.
TAVI reduces mitral regurgitation volume (MR-Vol) both in functional (FMR) and non-functional mitral regurgitation (nFMR), what could be a result of post-TAVI reduction of left-ventricle end-systolic pressure (velocity-time-integral reduction of MR).

Nevertheless, due to the holistic mitral regurgitation’s assessment defined by current guidelines, changes of MR parameters are not sufficient to reduce the grade of MR.

**Limitations**

It must be underlined that our study is inherent to its single-center, observational nature – therefore larger studies on the subject are necessary.

**Compliance with Ethical Standards**

The authors report no relationships that could be construed as a conflict of interest.

The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki, its later amendments, and the Review Board of the Medical University of Warsaw.
References:


Table 1. Baseline characteristics of analysed cohorts

<table>
<thead>
<tr>
<th></th>
<th>Mitral regurgitation</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>functional (n=26)</td>
<td>non-functional (n=22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13 (50)</td>
<td>10 (45.5)</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>80.7 (5.9)</td>
<td>79.7 (5.4)</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>BSA, m$^2$</td>
<td>1.83 (0.2)</td>
<td>1.75 (0.2)</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td>26.0 (4.4)</td>
<td>26.4 (4.3)</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td>14.7 (8.5-27)</td>
<td>18.7 (11-26)</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>EuroSCORE II</td>
<td>3.6 (2.8-4.3)</td>
<td>3.2 (2.6-3.9)</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11 (42.3)</td>
<td>9 (40.9)</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>18 (69.2)</td>
<td>19 (86.4)</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>4 (15.4)</td>
<td>7 (31.8)</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>14 (53.8)</td>
<td>6 (27.3)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Creatinine clearance, ml/min</td>
<td>45.8 (25.0)</td>
<td>50.6 (14.0)</td>
<td>0.44</td>
<td></td>
</tr>
<tr>
<td>ACEi or ARB</td>
<td>10 (38)</td>
<td>11 (50)</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>Previous MI</td>
<td>12 (46.2)</td>
<td>16 (72.7)</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>NYHA ≥2</td>
<td>23 (88.4)</td>
<td>20 (90.9)</td>
<td>0.76</td>
<td></td>
</tr>
<tr>
<td>Previous CABG</td>
<td>4 (15.4)</td>
<td>7 (31.8)</td>
<td>0.15</td>
<td></td>
</tr>
</tbody>
</table>

Data are n (%), median (IQR), or mean (SD)

ACEi – angiotensin-converting enzyme inhibitors; ARB – angiotensin II receptor blockers; BMI – body mass index; BSA – body surface area; CABG – coronary artery bypass grafting; COPD – chronic obstructive lung disease; MI – myocardial infarction; NYHA – New York Heart Association functional class;
### Table 2. Characteristics of TAVI valves used and results of the aortic procedure

<table>
<thead>
<tr>
<th>Mitral regurgitation</th>
<th>functional (n=26)</th>
<th>non-functional (n=22)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>THV type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medtronic Evolut R</td>
<td>8 (30.8)</td>
<td>11 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Medtronic CoreValve</td>
<td>6 (23.1)</td>
<td>4 (18.2)</td>
<td>0.65</td>
</tr>
<tr>
<td>Edwards Sapien XT</td>
<td>6 (23.1)</td>
<td>3 (13.6)</td>
<td></td>
</tr>
<tr>
<td>BS Lotus</td>
<td>2 (7.7)</td>
<td>3 (13.6)</td>
<td></td>
</tr>
<tr>
<td>Abbott Portico</td>
<td>3 (11.5)</td>
<td>1 (4.6)</td>
<td></td>
</tr>
<tr>
<td>SVT Nautilus</td>
<td>1 (3.8)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td><strong>THV size</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23 mm</td>
<td>1 (3.8)</td>
<td>6 (27.2)</td>
<td></td>
</tr>
<tr>
<td>25 mm</td>
<td>3 (11.5)</td>
<td>1 (4.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>26 mm</td>
<td>4 (15.5)</td>
<td>10 (45.4)</td>
<td></td>
</tr>
<tr>
<td>27 mm</td>
<td>2 (7.7)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>28 mm</td>
<td>0 (0.0)</td>
<td>1 (4.6)</td>
<td></td>
</tr>
<tr>
<td>29 mm</td>
<td>13 (50)</td>
<td>4 (18.2)</td>
<td></td>
</tr>
<tr>
<td>31 mm</td>
<td>2 (7.7)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>34 mm</td>
<td>1 (3.8)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Preprocedural echo</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVA (cm$^2$)</td>
<td>0.74 (0.53 - 0.83)</td>
<td>0.7 (0.57 - 0.8)</td>
<td>0.57</td>
</tr>
<tr>
<td>AVAi (cm$^2$/m$^2$)</td>
<td>0.41 (0.31 - 0.47)</td>
<td>0.39 (0.33 - 0.47)</td>
<td>0.87</td>
</tr>
<tr>
<td><strong>Postprocedural echo</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVA (cm$^2$)</td>
<td>1.86 (1.76-2.0)</td>
<td>1.76 (1.52 - 1.89)</td>
<td>0.04</td>
</tr>
<tr>
<td>AVAi (cm$^2$/m$^2$)</td>
<td>1.04 (0.93 - 1.1)</td>
<td>0.98 (0.94 - 1.07)</td>
<td>0.42</td>
</tr>
</tbody>
</table>

AVA – aortic valve area; AVAi – indexed aortic valve area
Figure 1. Changes parameters following transcatheter aortic valve implantation in patients with functional and non-functional mitral regurgitation: A. left ventricular ejection fraction; B. mitral regurgitation effective orifice area; C. mitral regurgitation volume.
Figure 2. An example illustrating the reduction of functional mitral regurgitation following transcatheter aortic valve implantation.
**Figure 3.** An example illustrating non-functional mitral regurgitation unaffected by transcatheter aortic valve implantation.