Association between calcifications of mitro-aortic continuity and mitral regurgitation in patients undergoing transcatheter aortic valve replacement

Małgorzata Ryś[1], Tomasz Hryniewiecki[1], Adam Witkowski[2], Ilona Michałowska[3], Karina Zatorska[1], Patrycjusz Stokłosa[1], Małgorzata Nieznańska[1], Piotr Szymański[4]

[1]Department of Valvular Heart Disease, National Institute of Cardiology, Warszawa, Poland
[2]Department of Interventional Cardiology and Angiology, National Institute of Cardiology, Warszawa, Poland
[3]Department of Radiology, National Institute of Cardiology, Warszawa, Poland
[4]Center for Non-Invasive Cardiovascular Diagnostic Services, Central Clinical Hospital of MSWiA and Center for Postgraduate Medical Education, Warszawa, Poland

Correspondence to:
Prof. Piotr Szymański, MD, FESC,
Center for Non-Invasive Cardiovascular Diagnostic Services,
Central Clinical Hospital of MSWiA,
Wołoska 137, 02–507 Warszawa, Poland,
phone: +477721830,
e-mail: pszymanski@ptkardio.pl

Kardiol Pol. 2021; 79 (6): 669–675;
DOI: 10.33963/KP.15987

Received:
November 22, 2020

Revision accepted:
April 20, 2021

Published online:
April 29, 2021

ABSTRACT

Background: The presence of mitral annular calcification (MAC) affects prognosis in patients undergoing transcatheter aortic valve implantation (TAVI). MAC frequently coexists with calcifications of mitro-aortic continuity (CMAC).

Aims: We aimed at qualitative and semi-quantitative analysis of calcifications of the mitral complex — MAC and CMAC in multi-slice computed tomography, in order to assess their impact on the occurrence and dynamics of mitral regurgitation (MR) following TAVI.

Methods: The study group consisted of 94 patients (mean [SD] age was 79.9 [8.02] years; 67.1% female). Agatston scale — Calcium Score was used for quantitative analysis. MAC and CMAC were also assessed semi-quantitatively as either non-severe or severe. MR following TAVI was defined as unchanged, improved or worsened by at least one degree.

Results: Patients with MAC (59.6%) had higher mean aortic gradients ($P = 0.02$) and smaller left ventricular diastolic diameter ($P = 0.002$). Patients with CMAC (48.9%) had higher Calcium Score aortic valve ($P = 0.006$). After TAVI MR improved in 17 (18.1%) patients and worsened in 7 (7.5%) patients. In multivariable logistic regression analysis MR worsening was associated with higher CMAC (OR, 1.092; 95% CI, 1.006–1.185; $P = 0.03$), as well as bicuspid aortic valve (OR, 6.348; 95% CI, 1.048–38.436; $P = 0.04$).

Conclusions: CMAC was associated with MR worsening following TAVI. This is of relevance in procedural planning in patients with severe aortic stenosis (AS) and coexisting MR in whom arguments for and against surgical repair of concomitant mitral insufficiency are considered.

Key words: aortic stenosis, calcification of mitro-aortic continuity, mitral annular calcification, mitral regurgitation, transcatheter aortic valve implantation

Kardiol Pol 2021; 79, 6: 669–675

INTRODUCTION

Mitral annular calcification (MAC) occurs as a result of a chronic degenerative process of the fibrous support structure of the mitral valve. MAC is present in approximately 8%–15% of the general population, more often in women [1–3]. MAC commonly coexists with aortic stenosis (AS) [4, 5] and may have similar etiology and pathophysiological mechanism [6, 7]. About one-fifth of patients with mild to moderate AS and half with severe AS have at least some degree of MAC [4, 8]. Half of all patients undergoing transcatheter aortic valve implantation (TAVI) have MAC, and approximately 20% have severe MAC [8–11]. The latter is associated with increased all-cause and cardiovascular mortality and with conduction abnormalities in patients undergoing TAVI [10, 11]. Several studies assessed the role of mitral regurgitation (MR) following TAVI [12, 13], but only few examined the influence of MAC on its changes after TAVI [8, 11, 14, 15]. MAC frequently coexists with calcification of mitro-aortic continuity (CMAC) [16]. The latter may influence the results of TAVI, especially in the case of deeper implantation, protruding to left ventricular outflow tract (LVOT). To the best of our knowledge, the role of CMAC on

WHAT'S NEW?

Aortic valve calcifications in patients with aortic stenosis (AS) undergoing transcatheter aortic valve implantation (TAVI) are frequently accompanied by calcifications of mitro-aortic continuity (CMAC). Their presence is frequently disregarded and not included in the qualitative and semi-quantitative analyses of calcifications of the aortic-mitral complex. We have demonstrated that the presence of CMAC was associated with mitral regurgitation (MR) worsening after TAVI. This is a novel finding, which may be of relevance for procedural planning, in particular in patients with severe AS and coexisting MR in whom arguments for and against surgical repair of concomitant mitral insufficiency are considered, as opposed to isolated aortic valve procedure.

the occurrence and dynamic changes of MR during TAVI procedure has never been examined.

In the present study we aimed at qualitative and semi-quantitative analysis of calcifications of the mitral complex — MAC and CMAC in multi-slice computed tomography (MSCT) in patients qualified to TAVI, in order to assess their impact on the occurrence and dynamics of MR following aortic valve implantation.

METHODS

Study group

We retrospectively examined 94 consecutive patients with severe AS who underwent TAVI procedure at the Institute of Cardiology in Warsaw, between January 2016 and December 2017. The study protocol was approved by the local Bioethics Committee. All examined patients presented severe symptomatic AS and had been disqualified from surgical aortic valve replacement by an institutional Heart Team. Informed consent for diagnostic and treatment procedures was obtained from all patients.

Before TAVI, all patients underwent routine laboratory testing, transthoracic echocardiography (TTE), coronary angiography, MSCT as well as angio-MSCT of iliac and femoral arteries [17]. Aortic valve anatomy and diameter were evaluated by TTE and MSCT [18]. These studies were used for proper planning of the valve implantation in terms of selection of access route, valve size, and complication risk assessment.

Multi-slice computed tomography

Before TAVI procedure, all patients underwent MSCT with and without contrast. MSCT was performed using a dual-source third generation scanner, Somatom Force (Siemens Healthcare, Forchheim, Germany). CT acquisition parameters were: slice collimation $2 \times 192 \times 0.6$ mm, 384 layers, gantry rotation time 250 ms, tube voltage 80–120 kV, tube current 320–500 mAs (depending on the patient body mass).

A prospective ECG gated non-contrast scan was performed to measure the Calcium Score of the aortic valve and mitral annulus. MAC and CMAC were evaluated in MSCT after contrast administration.

MSCT with contrast was routinely performed in patients before TAVI for evaluation of coronary arteries and access to TAVI (entire aorta and iliofemoral arteries). A bolus of 70 to 100 ml (depending on the patient body mass) of iodinated contrast media (Ultravist 370 Bayer Pharma AG) was administered through an antecubital vein at a rate of 4.0 ml/s.

Quantitative assessment of aortic valve calcifications was done using the Agatston scale — Calcium Score aortic valve [19, 20]. MAC was evaluated quantitatively and semi-quantitatively and CMAC was assessed semi-quantitatively.

MAC was defined as the presence of dense calcium deposits at the base of mitral leaflets at the level of the mitral annulus. The quantitative assessment of calcifications — Calcium Score mitral annulus — was done using the Agatston scale based on the maximum X-ray absorption coefficient measured in Hounsfield units (HU) and the measurement of the calcium deposits size. The absorbing structures were considered to be 130 HU and more.

MAC was assessed in cross-sectional view parallel to the plane of the mitral annulus and rated in the semi-quantitative scale, depending on the degree of annular involvement, in the following way: 0, no calcifications; 1, mild calcifications (less than one-third of the circumference of the annulus involved); 2, moderate calcifications (between one-third and half of the annulus circumference); 3, severe calcifications (more than half of the annulus circumference), according the methodology adopted by others [11, 21].

CMAC was defined as the presence of calcifications localized in the posterior aspect of LVOT — in the continuity between the base of anterior mitral leaflet/mitral annulus and non-coronary aortic cusp. Calcifications localized in the posterior (CMAC) and anterior aspect of LVOT are shown on Figure 1.

CMAC was evaluated semi-quantitatively in sagittal oblique view and assessed along the maximum length of calcification. CMAC was rated depending on the length of calcifications in the largest dimension the following way: 0, no calcifications; 1, mild calcifications (less than 3 mm); 2, moderate calcifications (3–8 mm); 3, severe calcifications (over 8 mm); according the methodology adopted by others [10].

Subsequently, patients were classified in a dichotomous manner as having non-severe or severe MAC and CMAC (grades 0, 1, and 2 versus grade 3). Classification was performed by a single observer, experienced in the

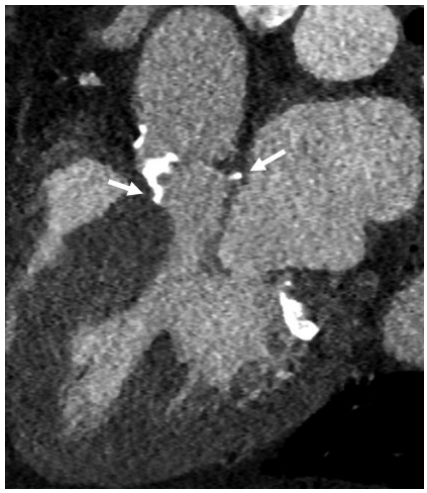

Figure 1. Comparison of calcifications localized in the anterior and posterior aspect of the left ventricular outflow tract in oblique sagittal projection on multislice computed tomography

assessment of pre-TAVR CT scans, blinded to the clinical and other imaging data.

Echocardiography

All patients underwent TTE (Vivid E95, Vivid S70) prior to the procedure, either during the same or preceding hospitalization, as part of diagnostic routine assessment. The follow-up transthoracic echocardiographic examination was routinely performed before discharge following TAVI procedure and up to 30 days after TAVI.

MR was evaluated in an integrated manner, according to a current standard, based on color Doppler jet area, vena contracta, proximal isovelocity surface area, effective regurgitant orifice [22, 23], and graded as: 0, no MR; 1, mild MR; 2, moderate MR; 3, severe MR; with significant MR defined as grade ≥2. Changes of MR severity following TAVI were defined as no change, improvement, or worsening by at least one degree.

Statistical analysis

Continuous variables with normal distribution were presented as means with their standard deviations, and in the case of non-normally distributed variables (as confirmed by the Kolmogorov-Smirnov test), in the form of the median and the interquartile range. Categorical variables were expressed as percentages. Patients were divided into groups with severe vs non-severe/absent MAC and CMAC, as previously defined. Comparative analyzes of continuous variables were done using the Student t-test or the Mann-Whitney tests, and of discrete variables using the chi-square test.

In order to evaluate if the degree of calcification of mitral complex affects MR in patients undergoing TAVI, single- and multi-variable logistic regression analyses were used.

A univariate logistic regression analysis was performed to obtain the odds ratio for worsening MR after TAVI.

The following variables were used in univariate models: age, female sex, clinical factors (hypertension, coronary artery disease**,** diabetes mellitus, atrial fibrillation, chronic renal failure, estimated glomerular filtration rate [eGFR]), echocardiographic parameters (left ventricular diastolic diameter, left ventricular systolic diameter, interventricular septal, ejection fraction, LVOT, aortic root, maximum aortic gradient, mean aortic gradient), bicuspid aortic valve (BAV), Calcium Score aortic valve, Calcium Score mitral annulus, CMAC and MAC.

Thereafter, a multivariable logistic regression analysis was performed using the variables with *P*-values <0.10 in the univariate analyses, to examine their independent association with MR worsening after TAVI. Results of the regression model were presented as odds ratios, with 95% confidence intervals. A *P*-value <0.05 was considered statistically significant. All analyses were performed using SAS 9.2.

RESULTS

The study group consisted of 94 patients (63 female [67.1%]), undergoing TAVI. The mean (SD) age of patients was 79.9 (8.02) years. Clinical characteristics and echocardiographic parameters of the studied patients are presented in Table 1. Examples of MAC and CMAC in MSCT are shown in Figure 2 and Figure 3.

Table 1. Baseline characteristics of the study group

Characteristics of patients (n = 94)	
Age, years, mean (SD)	79.86 (8.02)
Female sex, n (%)	63 (67.1)
Hypertension, n (%)	76 (80.8)
Diabetes mellitus, n (%)	34 (36.2)
Coronary artery disease, n (%)	52 (55.3)
Chronic lung disease, n (%)	15 (16.0)
Atrial fibrillation, n (%)	39 (41.5)
NYHA functional class III, n (%)	28 (29.8)
NYHA functional class IV, n (%)	3 (3.2)
eGFR, ml/min, mean (SD)	58.30 (18.67)
BAV, n (%)	23 (25.6)
Pacemaker before TAVI, n (%)	16 (17.2)
LVDD, mm, mean (SD)	48.14 (7.90)
LVDS, mm, mean (SD)	31.11 (9.54)
IVDS, mm, mean (SD)	14.53 (2.42)
EF, %, mean (SD)	55.12 (13.27)
Maximum aortic gradient, mm Hg, mean (SD)	83.58 (22.67)
Mean aortic gradient, mm Hg, mean (SD)	51.13 (14.33)
AVA, cm^2, mean (SD)	0.66 (0.18)
Aortic annulus TTE, mm, mean (SD)	22.99 (2.15)
Aortic root, mm, mean (SD)	31.53 (4.00)
Calcium Score mitral annulus, HU, median (IQR)	161 (0–3016)
Calcium Score aortic valve, HU, median (IQR)	3416 (856.8–8868)

Abbreviations: AVA, aortic valve area; BAV, bicuspid aortic valve; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HU, Hunsfield units; IVDS, interventricular septal; LVDD, left ventricular diastolic diameter; LVDS, left ventricular systolic diameter; NYHA, New York Heart Association; SD, standard deviation; TAVI, transcatheter aortic valve implantation; TTE, transthoracic echocardiography

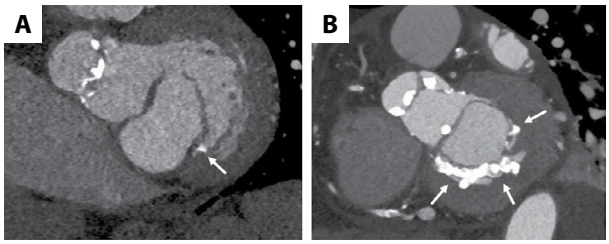

Figure 2. Comparison of reconstruction views showing non-severe mitral annular calcification (**A**) and severe mitral annular calcification (**B**) in sectional view parallel to the mitral annular on multislice computed tomography

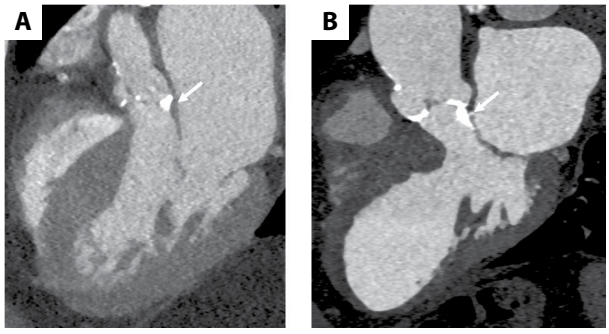

Figure 3. Comparison of reconstruction views showing non-severe calcifications of mitro-aortic continuity (**A**) and severe calcifications of mitro-aortic continuity (**B**) in sagittal oblique view on multislice computed tomography

MAC

Median and the interquartile range of Calcium Score mitral annulus was 161 (0–3016) HU. Fifty six (59.6%) out of 94 patients had MAC. Mild MAC was present in 25 patients (26.7%), moderate MAC in 10 patients (10.6%), and severe MAC in 21 patients (22.3%).

MAC was more prevalent in females (82.1% vs 44.7%; P <0.001) compared to patients without MAC. Patients with MAC had higher mean aortic gradients (mean [SD] 54.07 [13.62] mm Hg vs 46.79 [14.42] mm Hg; P = 0.02) and smaller left ventricular diastolic diameter (mean [SD] 46.09 [6.86] mm vs 51.19 [8.42] mm; P = 0.002) and trend to older patients (mean [SD] 81.09 [7.56] years vs 78.05 [8.42] years; P = 0.07) compared to patients without MAC. Comparison of selected variables in patients with no/non-severe MAC versus severe MAC is presented in Table 2.

CMAC

Almost half of the patients (46 [48.9%]) had CMAC. Mild CMAC was present in 21 patients (22.3%), moderate CMAC in 13 patients (13.8%), and severe CMAC in 12 patients (12.8%). Patients with CMAC had higher Calcium Score aortic valve (mean [SD] 3773.67 [1734.02] HU vs 2875.1 [1352.76] HU; P = 0.006) and a trend to smaller aortic valve area (AVA) (mean [SD] 0.59 [0.16] cm^2 vs 0.66 [0.20] cm^2; P = 0.05) compared to patients without CMAC.

Table 2. Baseline characteristic of patients with and without severe mitral annular calcification, as well as with and without severe calcification of mitro-aortic continuity (n = 94)

	Non severe MAC (n = 73)	Severe MAC (n = 21)	*P*-value	Non severe CMAC (n = 82)	Severe CMAC (n = 12)	*P*-value
Age, years, mean (SD)	78.79 (8.01)	83.57 (7.00)	0.01	80.32 (7.65)	76.75 (9.99)	0.15
Female sex, n (%)	46 (63.0)	17 (80.9)	0.12	52 (63.4)	11 (91.7)	0.09
Hypertension, n (%)	58 (79.4)	18 (85.7)	0.75	66 (80.5)	10 (83.3)	1.00
Coronary artery disease, n (%)	39 (53.4)	13 (61.9)	0.49	48 (58.5)	4 (33.3)	0.10
Diabetes mellitus, n (%)	29 (39.7)	5 (23.8)	0.18	30 (36.6)	4 (33.3)	1.00
Atrial fibrillation, n (%)	33 (54.8)	6 (28.6)	0.17	35 (42.7)	4 (33.3)	0.76
Chronic lung disease, n (%)	13 (17.8)	2 (9.5)	0.51	14 (17.1)	1 (8.3)	0.68
eGFR, ml/min, mean (SD)	57.57 (19.12)	60.84 (17.22)	0.48	58.73 (18.62)	55.4 (19.59)	0.57
BAV, n (%)	21 (30.0)	2 (10.0)	0.07	16 (20.2)	7 (63.6)	0.005
LVDD, mm, mean (SD)	49.35 (8.05)	44.05 (5.82)	0.006	48.41 (8.06)	46.18 (6.57)	0.38
LVDS, mm, mean (SD)	32.25 (10.17)	26.57 (4.50)	0.04	30.79 (9.73)	36.5 (2.12)	0.42
IVDS, mm, mean (SD)	14.17 (2.07)	15.80 (3.12)	0.04	14.51 (2.31)	14.64 (3.23)	0.87
EF, %, mean (SD)	53.75 (14.20)	59.76 (8.14)	0.02	55.35 (13.70)	53.45 (9.81)	0.66
LVOT, mm, mean (SD)	21.54 (2.08)	20.25 (1.48)	0.01	21.43 (2.06)	20.17 (1.40)	0.01
Aortic annulus TTE, mm, mean (SD)	23.20 (2.25)	22.00 (1.45)	0.006	23.09 (2.21)	21.92 (1.38)	0.02
Aortic root, mm, mean (SD)	31.79 (3.88)	30.63 (4.41)	0.27	31.47 (3.87)	32.00 (5.10)	0.69
AVA, cm^2, mean (SD)	0.80 (0.15)	0.66 (0.05)	0.01	0.78 (0.14)	0.63 (0.04)	0.008
Maximum aortic gradient, mm Hg, mean (SD)	82.48 (22.42)	87.38 (23.68)	0.39	83.52 (23.78)	83.96 (13.49)	0.92
Mean aortic gradient, mm Hg, mean (SD)	50.42 (14.09)	53.60 (15.24)	0.37	50.86 (14.97)	52.97 (9.11)	0.64
RVSP, mm Hg, mean (SD)	47.15 (14.73)	40.92 (8.81)	0.06	46.80 (14.03)	39.43 (12.80)	0.19
Pulmonary hypertension, n (%)	33 (45.2)	8 (38.1)	0.56	38 (47.8)	3 (25.0)	0.16
Calcium Score mitral annulus, HU, median (IQR)	0 (0–460.7)	5661 (4008–7598)	<0.0001	139.4 (0–2324)	689.7 (149–4040)	0.18
Calcium Score aortic valve, HU, mean (SD)/median (IQR)	3330.5 (1518.4)	3260.4 (1926.3)	0.86	3113 (1982–4000)	3960 (3371–4474)	0.02

Abbreviations: AVA, aortic valve area; BAV, bicuspid aortic valve; CMAC, mitro-aortic continuity; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HU, Hunsfield units; IVDS, interventricular septal; LVDD, left ventricular diastolic diameter; LVDS, left ventricular systolic diameter; LVOT, left ventricular outflow tract; MAC, mitral annular calcification; RVSP, right ventricular systolic pressure; SD, standard deviation; TTE, transthoracic echocardiography

Comparison of selected variables in patients with no/non-severe CMAC versus severe CMAC is presented in Table 2.

Association between MAC/CMAC and mitral regurgitation following TAVI

Before TAVI 64.9% of patients had mild or no MR (grades 1 or 0) and 35.1% of the patients had more than mild MR (grades 2 or 3). After TAVI 77.6% of patients had mild or no MR (grades 1 or 0). Patients with higher degrees of MR before TAVI had lower ejection fraction (EF) (mean [SD] 49% [15.12%] vs 58.38% [10.96%]; $P = 0.003$) as well as more frequent pulmonary hypertension (60.6% vs 34.3%; $P = 0.01$).

Calcium Score mitral annulus ($P = 0.34$), Calcium Score aortic valve ($P = 0.59$), MAC ($P = 0.15$) and CMAC ($P = 0.70$) were similar in patients with and without significant MR at baseline. MR improved by at least one grade following TAVI in 17 (18.1%) patients and worsened by at least one grade in 7 (7.5%).

Patients in whom MR improved after TAVI had diabetes mellitus more frequently (58.8% vs 31.2%; $P = 0.03$) and had a trend to lower baseline EF (mean [SD] 49.71% [12.92%] vs 56.35% [13.13%]; $P = 0.06$). Patients in whom MR worsened after TAVI more frequently had BAV (71.4% vs 21.7%; $P = 0.01$) and CMAC ($P = 0.03$).

The results of univariate logistic regression analysis of factors influencing MR worsening following TAVI are presented in Table 3. In multivariable logistic regression analysis, MR worsening was associated with higher CMAC (OR, 1.092; 95% CI, 1.006–1.185; $P = 0.03$), as well as the presence of BAV (OR, 6.348; 95% CI, 1.048–38.436; $P = 0.04$).

Table 3. Univariable logistic regression analysis: factors independently associated with MR worsening after TAVI

Variables	Univariable logistic regression analysis	
	OR (95% CI)	*P*-value
Age, years	0.96 (0.88–1.05)	0.41
Female sex	1.58 (0.33–7.54)	0.68
Hypertension	0.56 (0.10–3.17)	0.62
Coronary artery disease	0.58 (0.12–2.76)	0.69
Diabetes mellitus	1.35 (0.28–6.45)	0.70
Atrial fibrillation	1.98 (0.42–9.34)	0.44
eGFR, ml/min	0.99 (0.95–1.03)	0.71
BAV	9.03 (1.64–50.46)	0.01
LVDD, mm	1.03 (0.94–1.13)	0.52
LVDS, mm	0.97 (0.83–1.12)	0.65
IVDS, mm	1.12 (0.82–1.52)	0.49
EF, %	0.99 (0.93–1.04)	0.64
LVOT, mm	0.89 (0.60–1.34)	0.59
Aortic annulus TTE, mm	1.08 (0.77–1.52)	0.65
Aortic root, mm	1.148 (0.966–1.363)	0.11
Maximum aortic gradient, mm Hg	1.01 (0.98–1.05)	0.54
Mean aortic gradient, mm Hg	1.02 (0.96–1.08)	0.49
Calcium Score mitral annulus, HU	0.94 (0.76–1.16)	0.55
Calcium Score aortic valve, HU	2.47 (0.46–13.27)	0.29
CMAC ≥2, 3[a]	1.10 (1.02–1.19)	0.01
MAC ≥2[a]	0.56 (0.06–4.92)	1.00

[a]Grades of calcifications: 1, mild; 2, moderate; 3, severe.

Abbreviations: BAV, bicuspid aortic valve; CI, confidence interval; CMAC, mitro-aortic continuity; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HU, Hunsfield units; IVDS, interventricular septal; LVDD, left ventricular diastolic diameter; LVDS, left ventricular systolic diameter; LVOT, left ventricular outflow tract; MAC, mitral annular calcification; OR, odds ratio; TTE, transthoracic echocardiography

DISCUSSION

MAC and CMAC are frequent in severe aortic valve stenosis. In our study, MAC and CMAC were present in approximately half of the patients undergoing TAVI. In our series, MR severity changed following TAVI, as also described by others [8, 11–13, 24, 25].

Female sex, higher transvalvular gradient, and older age were more frequently present in patients with MAC, which is consistent with previous reports [4, 26]. Anatomic features, important from diagnostic and procedural point of view, such as narrower aortic annulus and LVOT and thicker interventricular septum, were associated with severe MAC. Conversely, other conditions frequently reported as risk factors for MAC (e.g, hypertension, diabetes mellitus, advanced kidney disease, atrial fibrillation) were not independent predictors in our population, perhaps due to smaller numbers and preselection of patients with AS [2, 27]. Only few studies examined the influence of MAC on the degree of MR after TAVI, with discordant results [8, 11, 14, 15]. In some series MAC was associated with worsening of MR [8, 14, 15]. Other authors did not report such relationship [11]. We did not observe differences in the degree of MR after TAVI in patients with and without MAC; however, the number of patients in whom the MR worsened was small.

In contrast to the relatively well defined role of MAC in patients with AS, including those undergoing TAVI, little is known about the potential role of CMAC in these patients. We demonstrated a correlation between CMAC and higher Calcium Score aortic valve, thicker ventricular septum, narrower aortic annular and LVOT diameters, smaller AVA, as well as female sex. These are important endpoints, relevant both to the diagnosis of severe AS, and to procedural issues, such as valve sizing, as well as prognosis [28]. A closer look at CMAC in larger datasets is necessary in order to better establish its influence on the procedure and its long term results.

The presence or absence of CMAC in patients with MAC may offer explanation to the discordant results of the studies examining the influence of MAC on the degree of MR after TAVI. Previous studies did not clearly distinguish between MAC and CMAC. In our study however, in contrast to MAC, the presence of CMAC was an independent predictor of worsened MR. To the best of our knowledge, this study is the first in which the role of CMAC in MR development was assessed. This is an important and novel finding, that may have implications in clinical practice. CMAC influences both LVOT geometry and mitral valve function. Theoretically, the presence of CMAC, working as a rigid scaffold, may limit potentially favorable reverse remodeling of mitral valve apparatus related to improved left ventricular function following TAVI.

The presence of CMAC may also influence prosthetic valve positioning and expansion, indirectly affecting also anterior mitral valve leaflet movement restriction. This is probably especially relevant in case of self-expandable valves protruding to a greater extend to LVOT, as valve implantation depth is related to the presence of MR [29].

In our series, lower LV ejection fraction predicted MR improvement. This was also observed by others [15, 30, 31]. Apart from reduced retrograde transmitral gradient, improvement of MR in patients with lower EF (also within normal limits) may be partially explained by the removal of afterload mismatch following TAVI [32], as acute improvement in MR reported following TAVR was related to immediate post-procedural changes in left ventricular hemodynamics and improved mitral leaflet tethering, resulting from reduced afterload [33]. In our patients, as in the other series, MR worsened following TAVI only in a minority of patients [34–37].

Study limitations

The main limitation of the present study is that it represents a retrospective, single-center experience. The relatively small population, allowed only for hypothesis generating results.

CONCLUSIONS

The study demonstrated that CMAC was prevalent in patients undergoing TAVI and associated with MR worsening. This is a novel finding, which may be of relevance for procedural planning and prevention of implantation failure. Its presence is of particular importance in patients with severe AS and coexisting MR in whom arguments for and against surgical repair of concomitant mitral insufficiency are considered, as opposed to isolated aortic valve procedure. Severe CMAC may be an additional argument to consider bivalvular cardiac surgery in patients with equivocal MR accompanying AS, rather than isolated percutaneous aortic procedure.

Article information

Conflict of interest: None declared.

How to cite: Ryś M, Hryniewiecki T, Witkowski A, et al. Association between calcification of mitro-aortic continuity and mitral regurgitation in patients undergoing transcatherer aortic valve replacement. Kardiol Pol. 2021; 79(6): 669–675, doi: 10.33963/KP.15987.

REFERENCES

1. Korn D, Desanctis RW, Sell S. Massive calcification of the mitral annulus. A clinicopathological study of fourteen cases. N Engl J Med. 1962; 267: 900–909, doi: 10.1056/NEJM196211012671802, indexed in Pubmed: 14034804.
2. Nestico PF, Depace NL, Morganroth J, et al. Mitral annular calcification: clinical, pathophysiology, and echocardiographic review. Am Heart J. 1984; 107(5 Pt 1): 989–996, doi: 10.1016/0002-8703(84)90840-8, indexed in Pubmed: 6372421.
3. Michałowska I, Szymański P, Kwiatek P, et al. Caseous calcification of the mitral annulus - the complementary role of computed tomography and transthoracic echocardiogram. Pol J Radiol. 2018; 83: e621–e626, doi: 10.5114/pjr.2018.81148, indexed in Pubmed: 30800201.
4. Takami Y, Tajima K. Mitral annular calcification in patients undergoing aortic valve replacement for aortic valve stenosis. Heart Vessels. 2016; 31(2): 183–188, doi: 10.1007/s00380-014-0585-5, indexed in Pubmed: 25252778.
5. Mejean S, Bouvier E, Bataille V, et al. Mitral annular calcium and mitral stenosis determined by multidetector computed tomography in patients referred for aortic stenosis. Am J Cardiol. 2016; 118(8): 1251–1257, doi: 10.1016/j.amjcard.2016.07.044, indexed in Pubmed: 27567138.
6. Abramowitz Y, Jilaihawi H, Chakravarty T, et al. Mitral annulus calcification. J Am Coll Cardiol. 2015; 66(17): 1934–1941, doi: 10.1016/j.jacc.2015.08.872, indexed in Pubmed: 26493666.
7. Johnson RC, Leopold JA, Loscalzo J. Vascular calcification: pathobiological mechanisms and clinical implications. Circ Res. 2006; 99(10): 1044–1059, doi: 10.1161/01.RES.0000249379.55535.21, indexed in Pubmed: 17095733.
8. Cortés C, Amat-Santos I, Nombela-Franco L, et al. Mitral regurgitation after transcatheter aortic valve replacement. JACC: Cardiovasc Interv. 2016; 9(15): 1603–1614, doi: 10.1016/j.jcin.2016.05.025, indexed in Pubmed: 27491611.
9. 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; 29(12): 1542–1547, doi: 10.1093/eurheartj/ehn172, indexed in Pubmed: 18443031.
10. Ancona MB, Giannini F, Mangieri A, et al. Impact of mitral annular calcium on outcomes after transcatheter aortic valve implantation. Am J Cardiol. 2017; 120(12): 2233–2240, doi: 10.1016/j.amjcard.2017.09.006, indexed in Pubmed: 29106835.
11. Abramowitz Y, Kazuno Y, Chakravarty T, et al. Concomitant mitral annular calcification and severe aortic stenosis: prevalence, characteristics and outcome following transcatheter aortic valve replacement. Eur Heart J. 2017; 38(16): 1194–1203, doi: 10.1093/eurheartj/ehw594, indexed in Pubmed: 28039339.
12. Giordana F, Capriolo M, Frea S, et al. Impact of TAVI on mitral regurgitation: a prospective echocardiographic study. Echocardiography. 2013; 30(3): 250–257, doi: 10.1111/echo.12050, indexed in Pubmed: 23190425.
13. Szymański P, Hryniewiecki T, Dąbrowski M, et al. Mitral and aortic regurgitation following transcatheter aortic valve replacement. Heart. 2016; 102(9): 701–706, doi: 10.1136/heartjnl-2015-308842, indexed in Pubmed: 26908096.
14. Durst R, Avelar E, McCarty D, et al. Outcome and improvement predictors of mitral regurgitation after transcatheter aortic valve implantation. J Heart Valve Dis. 2011; 20(3): 272–281, indexed in Pubmed: 21714416.
15. Chiche O, Rodés-Cabau J, Campelo-Parada F, et al. Significant mitral regurgitation in patients undergoing TAVR: mechanisms and imaging variables associated with improvement. Echocardiography. 2019; 36(4): 722–731, doi: 10.1111/echo.14303, indexed in Pubmed: 30834579.
16. Saremi F, Sánchez-Quintana D, Mori S, et al. Fibrous skeleton of the heart: anatomic overview and evaluation of pathologic conditions with CT and MR imaging. Radiographics. 2017; 37(5): 1330–1351, doi: 10.1148/rg.2017170004, indexed in Pubmed: 28820653.
17. Parma R, Zembala MO, Dąbrowski M, et al. Transcatheter aortic valve implantation. Expert Consensus of the Association of Cardiovascular Interventions of the Polish Cardiac Society and the Polish Society of Cardio-Thoracic Surgeons, approved by the Board of the Polish Cardiac Society…. Kardiol Pol. 2017; 75(9): 937–964, doi: 10.5603/KP.2017.0175, indexed in Pubmed: 28895996.
18. Stokłosa P, Michałowska I, Duchnowski P, et al. Predictors of aortic stenosis severity reclassification using an imaging data fusion method in patients referred for transcatheter aortic valve implantation. Kardiol Pol. 2018; 76(12): 1725–1732, doi: 10.5603/KP.a2018.0195, indexed in Pubmed: 30211435.

19. Pawade T, Clavel MA, Tribouilloy C, et al. Computed tomography aortic valve calcium scoring in patients with aortic stenosis. Circ Cardiovasc Imaging. 2018; 11(3): e007146, doi: 10.1161/CIRCIMAGING.117.007146, indexed in Pubmed: 29555836.
20. Paulsen NH, Carlsen BB, Dahl JS, et al. Association between aortic valve calcification measured on non-contrast computed tomography and aortic valve stenosis in the general population. J Cardiovasc Comput Tomogr. 2016; 10(4): 309–315, doi: 10.1016/j.jcct.2016.05.001, indexed in Pubmed: 27247181.
21. Carpentier AF, Pellerin M, Fuzellier JF, et al. Extensive calcification of the mitral valve anulus: pathology and surgical management. J Thorac Cardiovasc Surg. 1996; 111(4): 718–730, doi: 10.1016/s0022-5223(96)70332-x, indexed in Pubmed: 8614132.
22. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2012; 33(19): 2451–2496, doi: https://doi.org/10.1093/eurheartj/ehs109.
23. Zoghbi WA, Adams D, Bonow RO, et al. Recommendations for noninvasive evaluation of native valvular regurgitation a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascula Magnetic Resonance. J Am Soc Echocardiogr. 2017; 30(4): 303–371, doi: 10.1016/j.echo.2017.01.007, indexed in Pubmed: 28314623.
24. Sahinarslan A, Vecchio F, MacCarthy P, et al. Dynamics of concomitant functional mitral regurgitation in patients with aortic stenosis undergoing TAVI. Acta Cardiol Sin. 2016; 32(4): 477–484, doi: 10.6515/acs20150629c, indexed in Pubmed: 27471361.
25. Vollenbroich R, Stortecky S, Praz F, et al. The impact of functional vs degenerative mitral regurgitation on clinical outcomes among patients undergoing transcatheter aortic valve implantation. Am Heart J. 2017; 184: 71–80, doi: 10.1016/j.ahj.2016.10.015, indexed in Pubmed: 27892889.
26. Adler Y, Fink N, Spector D, et al. Mitral annulus calcification — a window to diffuse atherosclerosis of the vascular system. Atherosclerosis. 2001; 155(1): 1–8, doi: 10.1016/s0021-9150(00)00737-1, indexed in Pubmed: 11223420.
27. Kanjanauthai S, Nasir K, Katz R, et al. Relationships of mitral annular calcification to cardiovascular risk factors: the Multi-Ethnic Study of Atherosclerosis (MESA). Atherosclerosis. 2010; 213(2): 558–562, doi: 10.1016/j.atherosclerosis.2010.08.072, indexed in Pubmed: 20926076.
28. Achenbach S, Delgado V, Hausleiter J, et al. SCCT expert consensus document on computed tomography imaging before transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR). J Cardiovasc Comput Tomogr. 2012; 6(6): 366–380, doi: 10.1016/j.jcct.2012.11.002, indexed in Pubmed: 23217460.
29. 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(4): 638–644, doi: 10.1002/ccd.23045, indexed in Pubmed: 21805556.
30. Hekimian G, Detaint D, Messika-Zeitoun D, et al. Mitral regurgitation in patients referred for transcatheter aortic valve implantation using the Edwards Sapien prosthesis: mechanisms and early postprocedural changes. J Am Soc Echocardiogr. 2012; 25(2): 160–165, doi: 10.1016/j.echo.2011.10.001, indexed in Pubmed: 22071307.
31. Tzikas A, Piazza N, van Dalen BM, et al. Changes in mitral regurgitation after transcatheter aortic valve implantation. Catheter Cardiovasc Interv. 2010; 75(1): 43–49, doi: 10.1002/ccd.22197, indexed in Pubmed: 19739261.
32. Ross J. Afterload mismatch in aortic and mitral valve disease: Implications for surgical therapy. J Am Coll Cardiol. 1985; 5(4): 811–826, doi: 10.1016/s0735-1097(85)80418-6, indexed in Pubmed: 3882814.
33. Shibayama K, Harada K, Berdejo J, et al. Effect of transcatheter aortic valve replacement on the mitral valve apparatus and mitral regurgitation: real-time three-dimensional transesophageal echocardiography study. Circ Cardiovasc Imaging. 2014; 7(2): 344–351, doi: 10.1161/CIRCIMAGING.113.000942, indexed in Pubmed: 24474596.
34. Toggweiler S, Boone RH, Rodés-Cabau J, et al. Transcatheter aortic valve replacement: outcomes of patients with moderate or severe mitral regurgitation. J Am Coll Cardiol. 2012; 59(23): 2068–2074, doi: 10.1016/j.jacc.2012.02.020, indexed in Pubmed: 22483326.
35. O'Sullivan CJ, Tüller D, Zbinden R, et al. Impact of mitral regurgitation on clinical outcomes after transcatheter aortic valve implantation. Interv Cardiol. 2016; 11(1): 54–58, doi: 10.15420/icr.2016:11:1, indexed in Pubmed: 29588707.
36. Costantino MF, Dores E, Innelli P, et al. The beneficial effects of TAVI in mitral insufficiency. Cardiovasc Ultrasound. 2015; 13: 49, doi: 10.1186/s12947-015-0040-5, indexed in Pubmed: 26714887.
37. Scisło P, Grodecki K, Rymuza B, et al. Impact of transcatheter aortic valve implantation on coexistent mitral regurgitation parameters. Kardiol Pol. 2021; 79(2): 179–184, doi: 10.33963/KP.15680, indexed in Pubmed: 33198449.