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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Prosthesis-patient mismatch and left ventricle systolic strain in patients with severe degenerative aortic stenosis, who are undergoing surgical valve replacement

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Abstract

Background: Prosthesis-patient mismatch (PPM) is an independent predictor of post-operative mortality after aortic valve replacement (AVR), particularly when it is associated with a left ventricle (LV) dysfunction. Two-dimensional speckle-tracking echocardiography (2D-STE) could be useful in assessing LV function in patients with PPM.

Aim: To evaluate the impact of PPM on myocardial multidirectional LV systolic strain in patients who are undergoing AVR for severe degenerative aortic stenosis (AS).

Methods: Sixty-five patients (38 females, 27 males, age: 69.9 ± 9.1 years) with severe degenerative AS and preserved LV ejection fraction were enrolled into the study. Pre- and three-month postoperative 2D-STE was performed to assess LV peak systolic longitudinal strain (LV PSLS), circumferential strain, and LV rotation. The indexed prosthesis effective orifice area (iEOAprosth) was used to define PPM (≤ 0.65 cm^2/m^2), and it was used to distinguish the study groups: PPM (+) (n = 35) and PPM (–) (n = 30).

Results: A significant association of LV PSLS and interaction in the groups [PPM (+) vs. PPM (–)] and intervention (before vs. after AVR; p = 0.019) was observed — the lowest value of LV PSLS was in the PPM (+) group (–14.9 ± 3.5%) after AVR. A significant difference in the mean delta (before/after AVR) values of LV PSLS (0.7 ± 3.1% vs. –1.2 ± 3.6%; p = 0.04) in the PPM (+) vs. the PPM (–) groups was found. LV PSLS correlated with iEOAprosth (r = –0.520, p < 0.001) that was obtained three months after AVR.

Conclusions: The occurrence of PPM in patients undergoing AVR for severe degenerative AS was associated with reduced LV PSLS in a three-month observation.

Key words: prosthesis-patient mismatch, aortic valve replacement, left ventricle, peak systolic longitudinal strain, NT-proBNP

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INTRODUCTION

Aortic valve replacement (AVR) is the second most commonly performed cardiac surgery worldwide after bypass surgery. In 1978 Rahimtoola [1] defined the term prosthesis-patient mismatch (PPM) to describe the situation in which the effective orifice area (EOA) of an inserted prosthetic valve is too small in relation to body size. Prosthesis-patient mismatch is sometimes considered to be an independent predictor of

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post-operative mortality after AVR, particularly when it is associated with an impairment of left ventricular (LV) function [2]. In a study conducted by Ruel et al. [3], patients with PPM and LV systolic dysfunction had more than a two-fold increase in the risk of late death, a five-fold increase in the cumulative incidence of heart failure by three years, and incomplete LV mass regression compared with patients with LV dysfunction and no PPM. However, a large study by Koene et al. [4] recently concluded that PPM is actually not an independent predictor of both early and late mortality after AVR or AVR combined with coronary artery bypass grafting (CABG). Many reports that discuss several aspects of PPM have been published to date, but the definitive clinical impacts of PPM have not yet been clarified [5].

Prosthesis-patient mismatch is most commonly seen in patients with small aortic roots, and this occurs most frequently in the elderly (especially females), who are also more likely to have severe coronary artery disease (CAD) and poorer cardiac function and are therefore already at a higher risk from surgery [6]. With the growing number of older patients with degenerative aortic stenosis (AS), often with a calcified and small aortic root as well as CAD, the issue of PPM is of importance. Implantation of a smaller prosthesis is sometimes a compromise; however, it is known that the occurrence of PPM indicates a worse prognosis. Procedures that can limit the PPM problem, i.e. aortic annuloplasty, should be performed in certain groups of patients [6].

Two-dimensional echocardiography is the standard procedure in the diagnosis, perioperative exam, and postoperative follow-up exam. Two-dimensional speckle-tracking echocardiography (2D-STE) could be useful to detect mild LV dysfunction, and it may help in the evaluation of patients who are scheduled for AVR. Global longitudinal strain (GLS) and basal longitudinal strain when assessed using 2D-STE have been proposed as subtle markers of LV systolic dysfunction that have a potential prognostic value in patients with AS [7]. LV peak systolic longitudinal strain (LV PSLS) quantifies regional and global heart function [8]. In our study we aimed to evaluate the impact of PPM on myocardial multidirectional strain in patients who had been surgically treated for severe degenerative AS. Serum levels of N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) were measured as a reference marker of LV overload.

METHODS

Patient population

Sixty-five consecutive patients (38 females, 27 males, age: 69.9 ± 9.1 years; New York Heart Association [NYHA] class I/II/III: 20/37/8) with severe degenerative AS and preserved LV ejection fraction (LVEF > 50%), who had been surgically treated by AVR, were prospectively enrolled into the study. The trial was conducted in the Silesian Medical Centre in Katowice between 2011 and 2013 in the Departments of Cardiology and Cardiac Surgery. The main inclusion criteria were in line with the current European Society of Cardiology (ESC) guidelines for AVR in AS [9] and included patients with severe AS and any symptoms that are related to AS.

Table 1. Size and type of implanted prostheses in the study groups

Type of prosthesis	Group PPM (+)	Group PPM (–)
Mechanical (ATS), n = 24	**14 (58%)**	**10 (42%)**
Size 19	2 (100%)	0 (0%)
Size 21	12 (92%)	1 (8%)
Size 23	0 (0%)	6 (100%)
Size 25	0 (0%)	3 (100%)
Biological	**21 (51%)**	**20 (49%)**
Stented (Mosaic), n = 33	**20 (58%)**	**13 (42%)**
Size 19	4 (100%)	0 (0%)
Size 21	12 (85.7%)	2 (14.3%)
Size 23	4 (36.4%)	7 (63.6%)
Size 25	0 (0%)	2 (100%)
Size 27	0 (0%)	2 (100%)
Stentless (Freestyle), n = 8	**1 (12.5%)**	**7 (87.5%)**
Size 21	1 (50%)	1 (50%)
Size 23	0 (0%)	5 (100%)
Size 27	0 (0%)	1 (100%)

PPM — prosthesis-patient mismatch

The patients' enrolment into the trial was performed one to three months before AVR. Twenty-four (37%) mechanical (ATS, size: 19–25) and 41 (63%) biological prostheses (stented prostheses — Mosaic, size: 19–27; n = 33, 51%; stentless bioprostheses — Freestyle, size: 21–27; n = 8, 12.5%) were implanted without any life-threatening complications (Table 1). Aortic annuloplasty was not performed on our patients.

The study protocol involved the baseline characteristics and a three-month follow-up. Events were defined as rehospitalisation, unstable angina, myocardial infarction, re-percutaneous coronary intervention (PCI), urgent CABG, or death. The indexed prosthesis effective orifice area (iEOAprosth) that was obtained three months after AVR was used to diagnose PPM when ≤ 0.65 cm^2/m^2 and it constituted a discriminating factor for the study groups: PPM (+) (n = 35; 22 female, 13 male; age: 69.9 ± 10 years) and PPM (–) (n = 30; 16 female, 14 male; age: 69.6 ± 8.2 years).

The exclusion criteria included actual indications for coronary revascularisation, segmental wall motion abnormalities, a bad acoustic window (five or more segments that could not be analysed), non-sinus rhythm, a complicated early post-operative period (i.e. cardiogenic shock, hypovolemic shock or a severe infection), a bicuspid aortic valve, moderate/severe mitral regurgitation, acute and chronic inflammatory diseases including myocarditis and endocarditis (in the three preceding months), heart failure in NYHA class IV, dilatation of the aortic root, Marfan syndrome, acute coronary syndromes, atrial fibrillation, recurrent supraventricular and ventricular arrhythmias, acute and chronic kidney disease (glomerular filtration rate [GFR] < 60 mL/min/1.73 m^2), malignancies, autoimmune diseases, immunosuppressive therapy, coexisting psychiatric or neurological disorders, and alcohol or drug abuse.

The study protocol was approved by the local Bioethics Committee. Each patient gave written consent to participate in the study.

Clinical data

The clinical characteristics of the patients in the study included: clinical status (NYHA/Canadian Cardiovascular Society [CCS] class), anthropometric data (body mass and height, waist and hip circumference, body mass index [BMI], waist-to-hip ratio), a physical examination (heart rate, blood pressure), medical history (concomitant diseases, pharmacotherapy used, smoking status) and routine laboratory tests.

Diagnosis of CAD was based on the previous revascularisation history. Coronary angiography, which showed no further indications for PCI or CABG, was performed on all of the patients before AVR.

Laboratory tests

Blood samples (10 mL) were drawn from the peripheral vein from patients in a supine decubitus position in the morning after an overnight fast. Total cholesterol (TC), high- and low-density lipoprotein cholesterol (HDL-C, LDL-C) fractions, triglycerides (TG), and creatinine serum concentrations were measured using routine methods. The GFR was estimated according to the Modification of Diet in Renal Disease study equation.

Serum levels of NT-proBNP (Biomedica, Bratislava, Slovak Republic, intra-assay variability 7%) were measured using an enzyme-linked immunosorbent assay. Individual measurements for each subject were done using a single-use kit in order to avoid inter-assay variability.

Ultrasound assessment

Two-dimensional transthoracic echocardiography (2D TTE) was performed pre- and post-operatively in all patients by an experienced sonographer according to the guidelines of the European Society of Echocardiography [10]. An ultrasound system (GE Vivid 9) equipped with a 3.5–1.75 MHz transthoracic transducer was used for all subjects.

Left ventricular geometry and function

The standard techniques as described previously [11] were used to assess the LV geometry and function.

Two-dimensional M-mode echocardiography was used to measure the LV dimensions in the left parasternal long-axis view. LV end-diastolic diameter (LVEDD) and end-systolic diameter (LVESD), posterior wall (PW), and septal wall thickness (IVS) were measured at the end-diastole.

Left ventricular mass (LVM) was calculated according to the following formula: $LVM = 1.04 \times [(LVEDD + IVS + PW)^3 - LVEDD^3] - 13.6$ and indexed for body surface area (BSA) to obtain the LVM index (LVMI).

The values of LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) were measured using the Simpson method; LVEF and left ventricular cardiac output (CO) were also obtained.

Additionally, the standard markers of diastolic dysfunction were measured. Left atrial area (LAA) was measured in a four-chamber apical view. Peak early velocity of mitral inflow (E) was obtained using the pulsed-wave Doppler method. Peak early diastolic (E′) mitral annular velocities were measured at the lateral side of the mitral annulus using pulsed wave tissue Doppler imaging. The E/E′ ratio was calculated [11].

Severity of aortic valve stenosis/effective orifice area of the implanted prosthesis

The Doppler echocardiographic indices of AS severity, which included maximal (P_{max}) and mean (P_{mean}) transvalvular pressure gradients, were obtained in all of the patients, using a modified Bernoulli equation, and the EOA was measured using the continuity equation. The LV outflow tract (LVOT) dimension was measured 3–4 times in the parasternal long-axis view in mid-systole, and finally the mean LVOT value was used in the automatically calculated EOA. The same protocol was used to measure the EOA of an implanted prosthesis (EOAprosth). The internal diameter of an implanted prosthesis was also measured in the parasternal long-axis view. The values of the EOA/EOAprosth were indexed for BSA. The iEOAprosth was used to define PPM when ≤ 0.65 cm^2/m^2.

Speckle-tracking echocardiography

Assessment of LV strain and rotation was done using 2D-STE. Standard 2D grey-scale images from the apical two-, three-, and four-chamber views and a parasternal short-axis view at the mid-LV level (papillary muscle) was acquired and transferred to a workstation for further offline analysis. The images were taken at a frame rate of 60–90 Fr/s and were obtained during an end-expiratory breath-hold.

Strain measurements were done offline using EchoPAC version 6.00 (GE Medical Systems, Milwaukee, WI). The LV longitudinal strain was averaged from 17 segment measurements from the apical two-, three-, and four-chamber views. Circumferential strain and LV rotation angles were obtained for six segments on the short-axis plane at the parasternal mid-LV level. The technique for strain measurement required manually outlining the LV endocardial contour, after which the system automatically generated the myocardial contour in an end-systolic frame. The myocardial tracking was verified manually, and if necessary a strain analysis was done by dividing each LV image into six segments per view. The system generated the curves for each LV segment. The LV PSLS was the maximal negative strain value during the ejection phase with the beginning of the QRS complex and the aortic valve close time as the reference points.

Segments with poor visualisation were excluded from further analysis. Patients in whom five or more segments could not be analysed were excluded.

The peak-systolic strain/peak-systolic rotation was measured for all of the strain parameters for all of the analysed segments and averaged to derive the mean value, which was used for the analysis.

Strain measurements were done by one observer. Twenty studies were reanalysed by the same observer, and by another observer in order to assess any intra- and inter-observer variability.

Statistical analysis

Statistical analysis was performed using MedCalc for Windows, version 10.0. All of the text and table results are expressed as means ± standard deviation (SD) or a number (percentage); the median and interquartile ranges are presented in the case of an abnormal distribution. The normal distribution result was analysed using the Kołmogorov-Smirnov test. In the case of an abnormal distribution, a logarithmic transformation was used.

The baseline clinical parameters and the results of ancillary investigations were compared using the two-sample t-tests for normally distributed continuous variables (Student's t-test); where there was an abnormal distribution, the Mann-Whitney U test was used. Categorical variables were compared using the χ^2 test.

To compare the change in 2D-STE values over time, the data were analysed as a repeated measures analysis of variances taking into account PPM, the intervention factor (AVR), and time.

The Spearman rank-order test or Pearson correlations were used to determine the relationship between variables. Multivariate regression of the baseline variables (age, sex, BMI, concomitant diseases, laboratory tests, LVMI, LVEF, CO, LAA, E/E') and iEOAprosth were used to assess the independent predictors of LV PSLS. Additionally, a multivariable logistic regression of all of the baseline variables (variables presented in Tables 1–3) was used to assess the independent predictors of the occurrence of PPM. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Baseline parameters

Data regarding clinical status, anthropometric data, physical examination, medical history (concomitant diseases and smoking status), and routine laboratory tests are presented in Table 2. A significantly increased BMI was found in the PPM (+) group (30.7 ± 4.2 kg/m^2) as compared to the PPM (–) group (28.3 ± 4.1 kg/m^2; p = 0.04).

An evaluation of the echocardiographic indices of LV geometry and function and the severity of AS revealed a significantly smaller diameter of the aortic valve annulus in the PPM (+) group as compared to the PPM (–) group (21.5 ± 1.9 vs. 22.9 ± 2.1 mm; p = 0.013) (Table 3). All of the patients that were examined presented a highly calcified aortic valve.

No differences in the baseline LV 2D-STE indices or the NT-proBNP serum levels were observed in the study groups (Table 4). The mean number of the segments that were analysed was similar in the groups PPM (+) and PPM (–) (13 ± 3 vs. 14 ± 2, respectively).

In a multivariate logistic regression, the aortic valve annulus (OR 0.738, 95% CI 0.580–0.941) and BMI (OR 1.132, 95% CI 1.000–1.281) were the independent factors that determined the occurrence of PPM.

Pharmacotherapy was administrated according to ESC guidelines and was comparable in the study groups**.**

Main outcomes three months after AVR

The clinical outcome was comparable between the study groups; there were no differences in the CCS/NYHA class. No incidence of rehospitalisation, unstable angina, myocardial infarction, re-PCI, urgent CABG, or death was observed.

Prosthesis-patient mismatch was found in 35 (54%) patients. A significantly smaller diameter of the implanted prosthesis (21.7 ± 1.7 vs. 22.9 ± 1.9 mm; p = 0.014) was found in the PPM (+) group; PPM was observed in all of the patients with prostheses with a diameter < 21 mm (n = 6, 100%; size of prosthesis: 19 mm in all patients) and in 29 (49%) patients with prostheses with a diameter ≥ 21 mm (p = 0.026).

Prosthesis-patient mismatch was found with both mechanical (14, 58%) and biological prostheses (21, 51%); it was diagnosed more frequently in stented (20, 58%) vs. stentless bioprostheses (1, 12.5%, p = 0.035). Detailed data on the types and sizes of the implanted prostheses are presented in Table 3.

Comparison of the baseline and three-month results did not reveal any changes in the standard indices of LV geometry and function.

2D-STE indices and NT-proBNP levels

In the ANOVA analysis, a statistically significant association of LV PSLS and the interaction of the group [PPM (+) vs. PPM (–)] and intervention (before vs. after AVR) (p = 0.019) was observed. The lowest values of LV PSLS were found in the PPM (+) group (–14.9 ± 3.5%) three months after AVR. We found no association between LV circumferential strain and LV rotation and the group, the intervention, or the interaction of the group and intervention (Table 1, Fig. 1).

There was an association between the serum NT-proBNP level and the intervention (p = 0.038) and between the interaction of the group and intervention (p = 0.009). A significant decrease in the NT-proBNP concentration was

Table 2. Characteristics of the study groups and controls

	Group PPM (+) (n = 35)	Group PPM (–) (n = 30)	P
Age [years]	69.9 ± 10	69.6± 8.2	0.9
Women/men	22 (63%)/13 (37%)	16 (53%)/14 (47%)	0.7
NYHA class I/II/III	11 (31%)/21(60%)/3(9%)	9 (30%)/16 (53%)/5 (17%)	0.9
CCS class 0/1/2/3	15 (43%)/16 (46%)/2 (6%)/2 (6%)	13 (43%)/15 (50%)/2 (7%)/0 (0%)	0.9
Height [cm]	160 ± 10	164 ± 11	0.9
Weight [kg]	79.9 ± 14.0	77.1 ± 14.2	0.9
Body mass index [kg/m^2]	30.7 ± 4.2	28.3 ± 4.1	0.04
Body surface area [m^2]	1.88 ± 0.21	1.87 ± 0.21	0.9
Waist to hip ratio [cm]	0.98 ± 0.08	0.95 ± 0.06	0.9
Heart rate [bpm]	72.0 ± 9.0	69.3 ± 8.4	0.9
Systolic BP [mm Hg]	124.8 ± 15.9	124.2 ± 17.9	0.9
Diastolic BP [mm Hg]	78.7 ± 8.3	73.5 ± 7.4	0.9
Medical history:			
Coronary artery disease	12 (34%)	13 (43%)	0.7
Hypertension	28 (80%)	25 (83%)	0.8
Diabetes	10 (29%)	10 (33%)	0.7
Current smoking	6 (17%)	4 (13%)	0.7
Smoking history	9 (26%)	7 (23%)	0.7
Routine laboratory tests:			
Triglycerides [mg/dL]	139 ± 46	151 ± 74	0.6
Total cholesterol [mg/dL]	189 ± 49	184 ± 48	0.7
HDL [mg/dL]	49 ± 15	48 ± 16	0.9
LDL [mg/dL]	119 ± 50	117 ± 39	0.9
GFR [mL/min]	88.6 ± 10.2	89.6 ± 8.7	0.9

Data are presented as the mean ± standard deviation or number (percentage); BP — blood pressure; CCS — Canadian Cardiovascular Society; GFR — glomerular filtration rate; HDL — high-density lipoproteins; LDL — low-density lipoproteins; NYHA — New York Heart Association; PPM — prosthesis-patient mismatch

Table 3. Baseline echocardiographic characteristics of the study groups

	Group PPM (+)	Group PPM (–)	P
LVESV [mL]	47.0 ± 19.1	47.8 ± 17.1	0.9
LVEDV [mL]	115.9 ± 32.6	118.4 ± 39.1	0.9
LVEF [%]	60.5 ± 6.5	60.4 ± 6.4	0.95
Cardiac output [L/min]	4.4 ± 1.2	4.8 ± 1.7	0.9
LVMI [g/m^2]	150.4 ± 32.6	153.9 ± 28.8	0.9
Aortic valve annulus [mm]	21.5 ± 1.9	22.9 ± 2.1	0.013
P_{max} [mm Hg]	95.8 ± 24.7	92.2 ± 24.5	0.9
P_{mean} [mm Hg]	58.6 ± 16.6	54.5 ± 16.0	0.9
Indexed effective orifice area [cm^2/m^2]	0.37 ± 0.08	0.41 ± 0.11	0.3
Left atrial area [cm^2]	22.2 ± 3.5	21.1 ± 2.2	0.5
E/E' index	19.1 ± 5.7	17.9 ± 3.5	0.3

Data are presented as the mean ± standard deviation; LVESV — left ventricular end-systolic volume; LVEDV — left ventricular end-diastolic volume; LVEF — left ventricular ejection fraction; LVMI — left ventricular mass index; P_{max} — maximum gradient across aortic valve; P_{mean} — mean aortic valve gradient; PPM — prosthesis-patient mismatch

Table 4. ANOVA analysis

	Group PPM (+)		Group PPM (–)		P		
	Baseline evaluation	Three-months after AVR	Baseline evaluation	Three-months after AVR	Source of variance		
					G	I	G × I
2D-STE: left ventricle systolic							
Longitudinal [%]	–15.6 ± 3.2	–14.9 ± 3.5	–15.3 ± 3.7	–16.5 ± 3.4	0.4	0.9	**0.019**
Circumferential [%]	–24.3 ± 13.9	–25.7 ± 9.9	–26.3 ± 8.7	–28.3 ± 8.9	0.6	0.4	0.4
Rotation [degrees]	6.5 ± 3.8	7.6 ± 4.6	7.2 ± 3.7	7.8 ± 3.9	0.7	0.3	0.2
NT-proBNP [pg/mL]	1683 ± 1389	1759 ± 1170	2697 ± 5642	1260 ± 2352	0.1	0.04	**0.009**
Median	1413	1626	1177	858			

Data are expressed as the mean ± standard deviation and as medians for abnormally distributed variables; G — group; I — intervention (aortic valve replacement [AVR]); G × I — interaction of the group and intervention; NT-proBNP — N-terminal prohormone of B-type natriuretic peptide; PPM — prosthesis-patient mismatch; 2D-STE — two dimensional speckle-tracking echocardiography

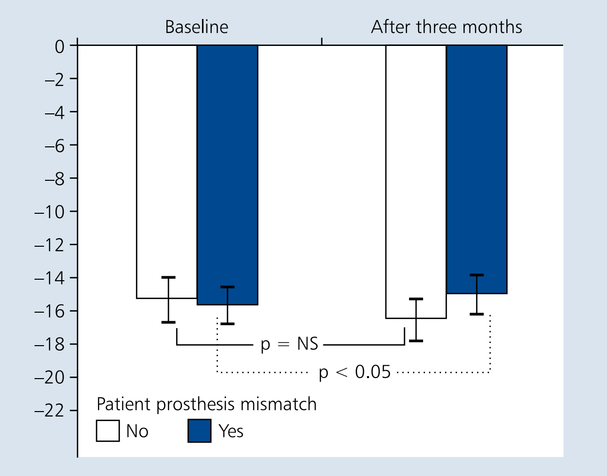

Figure 1. Left ventricle peak systolic longitudinal strain in the groups' baseline and three months after aortic valve replacement

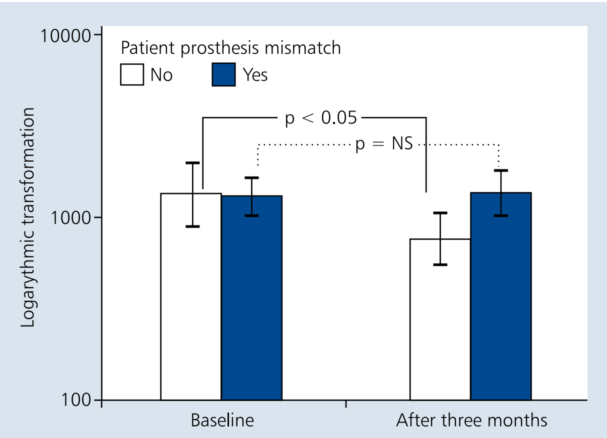

Figure 2. Serum N-terminal prohormone of B-type natriuretic peptide [pg/mL] concentrations in the groups' baseline and three months after aortic valve replacement

observed after AVR and was related to the occurrence of PPM (Table 1, Fig. 2).

A comparison of the delta values of the variables (before AVR/three months after AVR) revealed significant differences in the mean delta values of the EOA ($p < 0.001$) and NT-proBNP ($p < 0.001$) as well as LV PSLS ($p = 0.04$) in the PPM (+) vs. PPM (–) groups (Table 5).

Regression analysis

Correlations between the EOA, 2D-STE indices, and NT-proBNP levels that were obtained at baseline and three months after AVR are presented in Table 6 — LV PSLS correlated with both iEOA ($r = –0.260$; $p = 0.035$) and with iEOAprosth ($r = –0.520$; $p < 0.001$) (Fig. 3). The LV PSLS values correlated with the serum NT-proBNP levels at both the baseline ($r = –0.513$; $p < 0.001$) and three months after AVR ($r = –0.451$; $p < 0.001$) (Fig. 4). Multivariate regression analysis did not reveal independent factors that determined the LV PSLS strain three months after AVR.

The delta values of LV PSLS correlated with the delta values of the NT-proBNP levels ($r = 0.247$; $p = 0.049$).

The inter- and intra-observer variabilities were 7% and 5% for the longitudinal strain, 8% and 7% for the circumferential strain and 9% and 7% for the rotation measurements, respectively.

DISCUSSION

In the presented study we analysed the impact of PPM on myocardial multidirectional LV systolic strain in patients who were undergoing surgical AVR for severe degenerative AS. We confirmed the subclinical importance of PPM in a three-month follow-up of AVR patients. The PPM influenced the sensitive markers of LV function and overload — both LV PSLS and NT-proBNP levels. Abnormalities in LV deformation persisted three months after AVR, especially in PPM (+) patients.

The measurement of myocardial deformation by 2D-STE is a relatively new technique that can identify subclinical

Table 5. Comparison of the delta 2D-STE indices and the delta N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) levels (baseline vs. three months after aortic valve replacement)

	Group PPM (+)		Group PPM (–)		Difference	95% CI of difference	P
	Mean	SD	Mean	SD			
Delta of effective orifice area	0.63	0.13	1.1	0.36	0.47	0.31–0.63	< 0.001
Delta of 2D-STE indices							
Longitudinal [%]	0.7	3.1	–1.2	3.6	1.9	0.8–3.2	0.04
Circumferential [%]	–1.5	9.2	–2.0	8.1	0.5	0.1–1.1	0.9
Rotation [degrees]	1.0	3.7	0.6	3.2	0.4	0.2–1.2	0.8
	Median	25–75 Q	Median	25–75 Q			
Delta NT-proBNP [pg/mL]	72	–533–719	–657	–1340–218	–	–	< 0.001

2D-STE — two-dimensional speckle-tracking echocardiography; PPM — prosthesis-patient mismatch; CI — confidence interval; SD — standard deviation

Table 6. Correlations between the iEOA, iEOAprosth, 2D-STE indices, and N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) levels obtained at baseline and three months after AVR ($p < 0.05$)

	LV longitudinal strain	LV circumferential strain	LV rotation	NT-proBNP
Baseline: iEOA	r = –0.260	NS	NS	r = –0.513
Three-months after AVR: iEOAprosth	r = –0.520	NS	NS	r = –0.451

2D-STE — two-dimensional speckle-tracking echocardiography; AVR — aortic valve replacement; iEOA — indexed effective orifice area; iEOAprosth — indexed effective prosthesis orifice area; LV — left ventricle

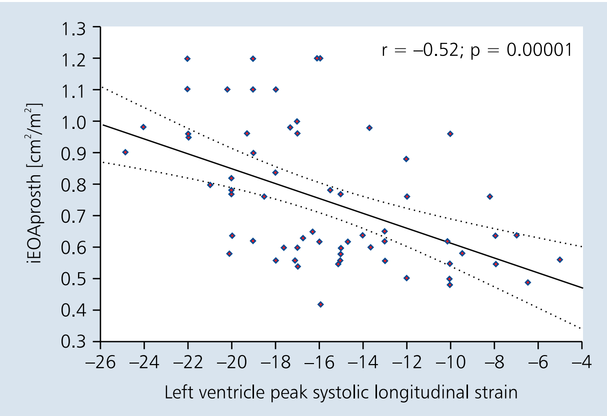

Figure 3. Relationship between left ventricle peak systolic longitudinal strain and indexed effective prosthesis orifice area (iEOAprosth) obtained three months after aortic valve replacement

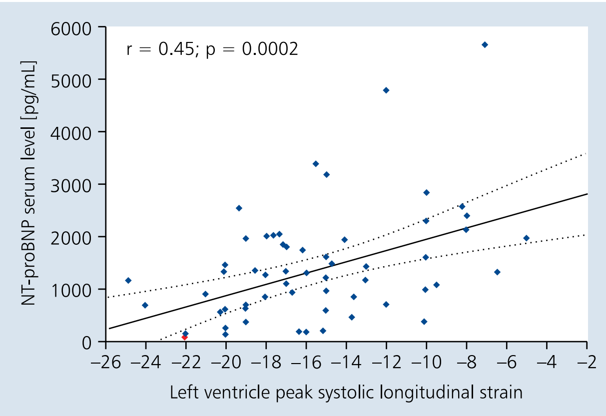

Figure 4. Relationship between left ventricle peak systolic longitudinal strain and N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) levels obtained three months after aortic valve replacement

changes in the LV contractile function [12]. Recent data suggest that evaluation of 2D-STE could be a sensitive tool for myocardial function assessment [13]. It is a well-known fact that GLS is often reduced in AS despite a normal LVEF. Dahl et al. [14] demonstrated that in patients with symptomatic severe AS undergoing AVR reduced GLS provided important prognostic information beyond the standard risk factors. On the other hand, LV loading conditions change acutely after AVR with a dramatic decrease in LV pressure overload [15]. It has been shown that changes in LV myocardial strain and strain-rate are related more to changes in LV afterload rather than LVM reduction after AVR [16].

In our study we showed that the values of longitudinal strain were reduced in patients with PPM but have a tendency to increase in patients without PPM after AVR. The values of LV PSLS that were obtained three months after AVR correlated with iEOAprosth. Because we analysed an early period after valve replacement, 2D-STE was used to identify subtle LV changes that might appear just after surgery. One might suspect that we would also see differences in the standard markers of LV remodelling such as LVMI or LVEF in the long term, especially since it is well-established that a regression of LV hypertrophy after AVR constitutes a prolonged process that is observed some months after surgery [17].

It is known that among the many strain parameters longitudinal strain is the most sensitive for detecting early changes in function. In our study we did not observe any differences in rotation and circumferential strain. This might be explained by the fact that longitudinal deformations are managed primarily by subendocardial fibres, which are most susceptible to any adverse consequences of pathologies because of their location. Moreover, rotation and circumferential strain are unaffected in the first stage of pathogenesis.

Our observations of LV PSLS were confirmed by concordant changes in the NT-proBNP serum levels. Moreover, a comparison of the delta values of the variables (before/three months after AVR) revealed significant differences in the mean delta values of both LV PSLS and NT-proBNP between the PPM (+) and PPM (–) groups.

NT-proBNP is a marker of systolic and diastolic dysfunction and a strong predictor of mortality in heart failure patients [18, 19]. Markers of LV overload such as NT-proBNP have already been shown to decrease after successful AVR [20]. NT-proBNP is a good indicator of LV wall stress. It has also been proven that BNP levels might correlate with the degree of native valvular stenosis; however, this has been questioned in a recent COFRASA-GENERAC study [21]. Moreover, Ben-Dor et al. [22] claim that the BNP level does not appear to be significantly associated with the degree of the severity of AS but actually reflects heart failure status. Recently, a published study by Melina et al. [20] showed that NT-proBNP levels were independently related to PPM late after isolated AVR in patients with preserved LV function, which is in accordance with our study.

Prosthesis-patient mismatch was a relatively frequent phenomenon in our group. It was observed in almost 50% of the patients after AVR. In previous studies mismatch was also a common phenomenon when using a relatively conservative definition (i.e. iEOAprosth ≤ 0.85 cm^2/m^2) and was observed in 20–70% of cases, whereas the prevalence of severe PPM ranged from 2% to 10% [23].

Probably, the high frequency of patients with a relatively small aortic valve annulus as well as the types and sizes of the implanted prostheses might be the causative agents of the high rate of PPM. Unfortunately, aortic annuloplasty had not been performed in our population.

Regardless of the fact that the problem of PPM is well known, a prospective observation of patients after AVR, who were implanted, had not been performed in our centre. Our study was the first one that was dedicated to this issue, and our analysis of the data made us conscious of the problem. As a result of our data, some of prostheses have been removed and more frequent aortic annuloplasty has been implemented in the Department of Cardiac Surgery.

In this three-month observation, PPM did not correspond with a patient's clinical status; however, we may suspect its long-term implications.

In our population the patients with severe degenerative AS and preserved LVEF, who were predisposed to PPM, were characterised by a smaller aortic valve annulus and increased BMI. Both a small aortic valve diameter and obesity are well-documented risk factors for PPM [24].

Taggart [6] states that PPM is most common in patients with small aortic roots and this occurs most frequently in the elderly (especially females), who are also more likely to have severe CAD and poorer cardiac function, and are therefore already at a higher risk from surgery. The nominal size of a prosthesis as determined by BSA may *a priori* predict PPM. Procedures that can minimise the PPM problem, i.e. aortic annuloplasty, should be performed in these groups of patients [6].

In the study PPM was observed with both mechanical and biological prostheses; it was diagnosed more frequently in stented vs. stentless bioprostheses, which is well-recognised in the data [25]. Pharmacotherapy was standard and was carried out according to ESC guidelines, and it did not differ between the two groups.

Limitations of the study

A limitation of the study was the relatively small number of enrolled patients. Multivariate regression analysis did not reveal independent factors that determined the LV PSLS strain three months after AVR. However, we presented some other findings that allowed us to conclude that PPM was associated with reduced LV PSLS (ANOVA, regression analysis).

Until now the only parameter that has proven to be consistently and realistically useful to define PPM is the iEOAprosth [26], which was obtained using echocardiography. Any limitations related to the potential echocardiographic mistakes were minimised because all of the examinations were performed by one experienced sonographer. Blood pressure and pulse values were comparable in both of the groups; therefore, any limitation of potential differences in the parameters during the examinations that might affect the severity of AS can be ignored.

We did not use parameters such as twist and untwist in the study because those parameters require a longer echocardiographic study and seemed to be inaccurate for the aim of our trial.

We analysed an early (three-month) period after AVR. Long-term observation and a more accurate definition of PPM are necessary in order to identify the real clinical significance of this problem.

CONCLUSIONS

The occurrence of PPM in patients who are undergoing AVR for severe degenerative AS is important for the improvement of early LV function. PPM is associated with reduced LV PSLS in three-month observation, which corresponds with the NT-proBNP level as a marker of LV overload. It suggests that all of the techniques that may allow PPM to be omitted are of high value in subjects undergoing AVR.

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Conflict of interest: *none declared*

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Zjawisko niedopasowania zastawki a odkształcenie skurczowe lewej komory u pacjentów z ciężką degeneracyjną stenozą aortalną po chirurgicznym zabiegu wymiany

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Streszczenie

Wstęp: Zjawisko niedopasowania zastawki (PPM) jest niezależnym czynnikiem śmiertelności po zabiegu wymiany zastawki aortalnej (AVR), zwłaszcza w przypadkach upośledzenia funkcji skurczowej lewej komory (LV). Technika dwuwymiarowa śledzenia markerów akustycznych (2D-STE) może być pomocna w ocenie funkcji LV u pacjentów z PPM.

Cel: Celem pracy była ocena wpływu PPM na parametry odkształcenia skurczowego LV u pacjentów poddanych zabiegowi AVR z powodu ciężkiej degeneracyjnej stenozy aortalnej (AS).

Metody: Do badania włączono 65 osób (38 kobiet i 27 mężczyzn w wieku 69,9 ± 9,1 roku) z ciężką degeneracyjną AS i zachowaną frakcją wyrzutową LV. W 2D-STE wykonanym przed oraz 3 miesiące po AVR oceniano szczytowe skurczowe odkształcenie podłużne (LV PSLS), okrężne i rotację LV. Indeksowane efektywne pole ujścia protezy aortalnej (iEOAprosth) definiowało PPM (≤ 0,65 cm^2/m^2) i stanowiło kryterium podziału na grupy: PPM (+) (n = 35) oraz PPM (–) (n = 30).

Wyniki: Wykazano istotny związek między LV PSLS a przynależnością do grupy [PPM (+) *vs*. PPM (–)] i przeprowadzonym zabiegiem (przed i po AVR; p = 0.019 — najmniejszą wartość LV PSLS stwierdzono w grupie PPM (+) (–14,9 ± 3,5%) 3 miesiące po zabiegu AVR. Porównanie wartości delta (przed i po AVR) w grupach PPM (+) i PPM (–) wykazało znamienne różnice w wartościach średnich LV PSLS (0,7 ± 3,1% vs. –1,2 ± 3,6%; p = 0,04) Stwierdzono istotną korelację między LV PSLS a iEOAprosth (r = –0,520; p < 0,001) po 3 miesiącach od AVR.

Wnioski: Obecność PPM u pacjentów po chirurgicznym zabiegu AVR z powodu degeneracyjnej AS wiąże się z upośledzeniem LV PSLS w 3-miesięcznej obserwacji.

Słowa kluczowe: zjawisko niedopasowania zastawki, wymiana zastawki aortalnej, lewa komora, szczytowe skurczowe odkształcenie podłużne, NT-końcowy natriuretyczny peptyd typu B

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