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Research Article

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The effect of transcatheter aortic valve implantation on mean platelet volume

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Background/aim: Transcatheter aortic valve implantation (TAVI) is an innovative approach to the treatment of aortic stenosis (AS) as an alternative to surgery in high-risk patients. Mean platelet volume (MPV) is considered an indicator of endothelial dysfunction, platelet function, and activation. In this study, we aimed to investigate MPV changes in patients undergoing TAVI.

Materials and methods: This study included 100 patients diagnosed with symptomatic severe AS and treated with TAVI between July 2011 and August 2013. Hematological parameters of the patients were examined prior to the procedure and 24 h, 1 month, and 6 months after TAVI.

Results: A statistically significant change in patients' MPV was detected after TAVI compared to the baseline situation (P: 0.001). While no statistically significant change was observed on the first day after TAVI, at discharge, compared to the baseline situation, a statistically significant decrease was seen 1 month and 6 months after discharge.

Conclusion: We have demonstrated a decrease in MPV after surgery compared to the value before surgery. We have sought to propound the change in MPV as an indication of endothelial function after TAVI.

Key words: Severe aortic stenosis, transcatheter aortic valve implantation, mean platelet volume

1. Introduction

Degenerative aortic stenosis (AS) is a valvular heart disease that reduces the quality of life in patients with this condition. The disease usually presents with exertional dyspnea, syncope, angina, heart failure, and sudden cardiac death, which mostly seen in elderly patients. It was reported that prevalence of severe AS in the United States is 2% (1). Approximately, 50% of patients die within 2 years of the beginning of symptoms (2). Medical treatment is usually insufficient in this group. Therefore, symptomatic patients should be considered for aortic valve replacement as soon as possible. Surgical aortic valve replacement (sAVR) has been used as a gold standard treatment of severe symptomatic AS for many years. Unfortunately, the risk from surgery is extremely high due to elderliness or co-morbidities and it is found that 30% of patients are not appropriate for surgery (3–5).

Transcatheter aortic valve implantation (TAVI) is a novel treatment option for high-risk patients with severe AS as an alternative to sAVR. It was first performed by Cribier in 2002 (6). TAVI has become a viable method quickly and safely, particularly with the development of percutaneous technology.

It has been suggested that the development of AS is an active process mediated by chronic inflammation rather than aging. This chronic inflammatory process is associated with atherosclerotic risk factors (7). These risk factors are considered to be likely causes of endothelial dysfunction and valve damage (7,8). Increased endothelial permeability, monocyte infiltration, intimal smooth muscle cell proliferation, and platelet aggregation are important components of atherogenesis (9). In recent years, mean platelet volume (MPV) was assessed as an indicator of platelet function and activation (10,11). Increased MPV is considered an indicator of increased risk for cardiovascular disease in the general population. It was found that MPV is also an indicator of atherosclerotic diseases and endothelial dysfunction in several studies (12).

In light of this information, we aimed to research of the impact of TAVI on MPV. We also aimed to show

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whether TAVI has positive effects on the healing aspects of endothelial dysfunction and the effect of endothelial dysfunction in the AS pathogenesis based on the relationship between MPV and endothelial dysfunction.

2. Materials and methods

Between July 2011 and August 2013 one hundred consecutive patients with symptomatic severe AS included in this study were inoperable or high-risk for sAVR. The symptomatic status of patients was determined according to New York Heart Association (NYHA) classification before the TAVI and during the follow-up visits. Patients with aortic valve area (AVA) less than 0.8 cm^2 and/or average transvalvular gradient greater than 40 mmHg, and/or maximal transvalvular blood flow velocity faster than 4.0 m/s were included in the study based on severe AS echocardiographic criteria and current guidelines. The decision regarding TAVI was taken by consensus during the Heart Team meeting. Informed consent was obtained from all patients before the TAVI. Ethical approval was provided from the ethics committee of our hospital before the study.

Hematological parameters of patients were tested before the procedure, 24 h after the procedure, at the time of discharge, and after 1 and 6 months following the procedure. White blood cell count (WBC, $10^3/mm^3$), hemoglobin (Hg, g/dL), hematocrit value (Htc, %), platelet count ($10^3/mm^3$), and MPV (fL) were examined. Routine physical examinations, echocardiography, laboratory parameters, and functional capacity were evaluated during the follow ups.

2.1. Preparation before TAVI

Aortic valve morphology, aortic annulus, the coronary ostium–annulus distance, the degree of calcification, peripheral arterial suitability, and additional pathologies were assessed for all patients by transthoracic echocardiography, Doppler and 2D images, transesophageal echocardiography, and multislice computed tomography.

2.2. TAVI procedure

Balloon expandable Edwards Sapien and Edwards Sapien XT (Edwards Lifesciences, Irvine, CA, USA) heart valves were implemented in all patients via transfemoral route. The procedures were performed under local anesthesia for 75% of patients and general anesthesia for 25%. During the operation, intravenous heparin was used to achieve an activated clotting time of 250–300 s. A femoral closure device (Prostar XL 10F system, Abbott Vascular, Redwood City, CA, USA, and Proglide, Abbott Vascular Inc.) was used in 85% of patients and surgical closure was applied 15% of patients.

2.3. Laboratory

Tubes containing ethylenediaminetetraacetic acid (EDTA) for automated blood count (15% K3 EDTA 0.054 mL/3 mL blood) were used. In the complete blood count, a Sysmex XE-2100 automated hematology analyzer was used. In our hospital, as a general principle, the blood is drawn with minimal stasis from the antecubital vein into vacuum tubes.

2.4. Statistical analysis

SPSS for Windows 21.0 was used for the assessment by recording study data on a computer. As well as descriptive statistical methods (mean, standard deviation), for the comparison of quantitative data, Student's t test for the comparison of normally distributed parameters between the groups and Wilcoxon's test for the comparison of nonnormally distributed parameters between the groups were used. The paired sample t test was used for intragroup comparison of the parameters. The chi-square test and Fisher's test were used for the comparison of qualitative data. One-way repeated measures analysis of variance (ANOVA) was used for the evaluation of the data obtained at preoperation, postoperation, discharge, first month, and sixth month. Results at 95% confidence interval, $P < 0.05$ significance level were assessed.

3. Results

Approximately 66% of the patients were females and the mean age was 78.2 years. The average valve area and mean gradient were 0.63 ± 0.17 cm^2 and 52.6 ± 13.9 mmHg respectively, according to echocardiography. The patients' mean STS (Society of Thoracic Surgeons) score and mean logistic EuroScore were respectively 7.3 ± 5.2 and 22.4 ± 15.9. According to the SURTAVI risk model, 90% of patients were considered middle and high risk. The operational success rate was 100%. However, second valve implementation was required in a patient due to low positioning and valve embolization to the ascending aorta occurred in another patient. The 23-mm valve was used in 56% of patients, the 26-mm valve in 42% of patients, and the 29-mm valve in 2% of patients. Moreover, 91% of patients were in NYHA class III and IV, 80% of patients had coronary artery disease, 82% of patients had hypertension, 34% of patients had peripheral arterial disease, and 27% of patients had diabetes mellitus. Basal characteristics of the patients and data on TAVI are given in Tables 1 and 2.

After the TAVI, 4 mortalities occurred in hospital because of the following reasons: right ventricular rupture due to rapid pacing in the operation (2 patients), left ventricular rupture due to wire in the left ventricle, and left main coronary artery obstruction caused by calcification on the aortic cusp. Stroke was not observed in any patient. Permanent pacemaker implantation was performed on four patients (4%) due to atrioventricular

Table 1. Baseline characteristics of patients.

Characteristics	N = 100 patients
Male/Female (n)	34/66
Age (years)	78.2 ± 7.2
BMI (kg/m²)	27.9 ± 7.6
NYHA II (n)	7
NYHA III (n)	64
NYHA IV (n)	29
STS score (%)	7.3 ± 5.2
SURTAVI - low risk (n) - mid risk (n) - high risk (n)	 10 32 58
Logistic EuroScore (%)	22.4 ± 15.9
Comorbid conditions	
Coronary artery disease (%) - One vessel (%) - Two vessel (%) - Three vessel (%)	80 30 28 22
Hypertension (%)	82
Diabetes mellitus (%)	27
Hyperlipidemia (%)	45
Smoker (%)	19
COPD (%) - Mild - Moderate - Severe	 46 39 23
Peripheral arterial disease (%)	34
Atrial fibrillation (%)	28

BMI; Body Mass Index, NYHA; New York Heart Association, STS; Society of Thoracic Surgeons, COPD; Chronic Obstructive Pulmonary Disease

Table 2. Echocardiographic variables and procedural features.

Echocardiographic variables	
Maximal gradient (mmHg)	86.3 ± 21.7
Mean gradient (mmHg)	52.6 ± 13.9
AVA (cm²)	0.63 ± 0.17
LVEF (%)	54 ± 14.7
Peak systolic pulmonary artery pressure (mmHg)	47.3 ± 13.3
Aortic regurgitation (n) Low Moderate Severe	 59 3 1
Mitral regurgitation (n) Low Moderate Severe	 60 5 3
Femoral vascular closure (%)	85
Valve diameter mm (n) - 23 - 26 - 29	 56 42 2
Contrast used (cc)	201.5 ± 55.7
Duration of discharge after procedure (days)	7.4 ± 5.4

TEE; transesophageal echocardiography, AVA; aortic valve area, LVEF; Left ventricular ejection fraction

block. When we look at vascular complications, hematoma in one patient and pseudoaneurysm in one patient were observed. Erythrocyte suspension transfusion more than two units was applied to 16% of patients. The average discharge time was 7.4 ± 5.4 days. During the follow up, 2 patients died in the first month and 4 more by 6 months, making a total of 10 mortalities. At discharge after TAVI and during the follow up, statistically significant recovery was observed in valve functions (mean gradient, AVA). Advanced paravalvular aortic regurgitation (AR) developed in one patient. It was also observed that 93% of patients were class 1 and 2 functional capacity according to the NYHA classification.

When we look the effects of TAVI on the hematological parameters, pre-TAVI patients' mean WBC counts were 7.3 ± 4.0 ($10^3/mm^3$), Hg (g/dL) was 12.7 ± 1.3, Hct was 35 ± 6.1 (%), platelet counts were 226.1 ± 137 ($10^3/mm^3$), and MPV was 10.7 ± 0.8 (fL). Post-TAVI at discharge, WBC counts were 8.3 ± 6.4, Hg was 10.3 ± 1.4, Htc was 30.9 ± 4.1, platelet counts were 183.6 ± 98.4, and MPV was 10.5 ± 1.3 (Table 3). In Hg and Hct values of patients, statistically significant changes were observed compared to before TAVI ($P < 0.001$). There was a statistically significant decrease in Hg and Hct values one day after TAVI and at discharge but there was a statistically nonsignificant increase in Hg and Hct values at one month and six months and these values reached the levels they had been before the TAVI.

There were statistically significant changes in patients' platelet counts than before TAVI ($P < 0.001$). However, a statistically significant decrease was seen in platelet counts one day after the operation, at discharge, and at one and six

Table 3. Changing of hematologic parameters with TAVI at follow up.

Parameters	Pre-TAVI	1 day	Discharge	1 month	6 months	P value
WBC	7.3 ± 4.0	9.4 ± 5.3	8.3 ± 6.4	7.8 ± 8.5	7.4 ± 4.8	0.275
Hg	12.7 ± 1.3	11.3 ± 4.0	10.3 ± 1.4	11.4 ± 1.6	11.9 ± 1.8	<0.001
Hct	35.0 ± 6.1	32.8 ± 6.1	30.9 ± 4.1	34.7 ± 4.9	36.3 ± 4.9	<0.001
Plt	226.1 ± 137.0	203.2 ± 152.6	183.6 ± 98.4	214.4 ± 91.2	217.4 ± 119.6	0.001
MPV	10.7 ± 0.8	10.5 ± 0.8	10.5 ± 1.3	10.3 ± 1.0	10.4 ± 1.0	0.007

WBC: White blood cells, Hg: hemoglobin, Hct: hematocrit, Plt: Platelet, MPV: Mean platelet volume

months after the TAVI, in comparison to platelet counts before the procedure. Statistically significant changes in MPV were also observed after the operation (P = 0.001). No statistically significant changes were observed on the first day or at discharge (short-term) in comparison with preoperational conditions, whereas at one month and six months (midterm) a statistically significant decline was observed (Figure).

4. Discussion

In this study we observed a patient population who had symptomatic severe AS with high risk for surgery and performed TAVI. We then compared pre-TAVI and post-TAVI MPV, which is an indicator of platelet activation and endothelial dysfunction. We showed that the decrease in MPV after TAVI is significant in the midterm in spite of a minor decrease in the short term, as evidence that AS etiopathogenesis can be a generalized endothelial dysfunction and post-TAVI endothelial dysfunction and platelet activation can be cured.

Platelets play a key role in the development of atherosclerosis and its acute complications. Platelet size is an important factor for physical and chemical functions of platelets. It is generally accepted that large platelets are metabolically and enzymatically more active. Large platelets contain more alpha granules and platelet-derived substances and they are inclined to adhesion and aggregation. Platelet size is also related to platelet activation indicators such as increase in intracellular calcium levels, synthesis of thromboxane A2, serotonin

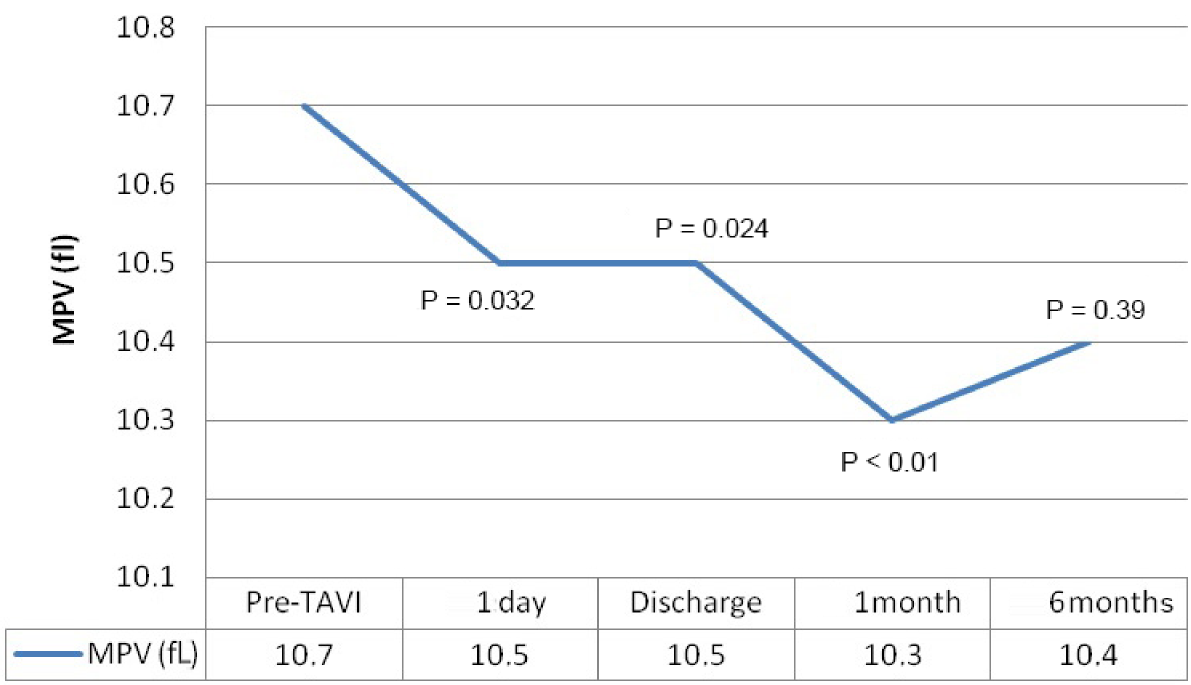

Figure. Changing of MPV after TAVI.

and β thromboglobulin release, and adhesion molecules' expression. Increased MPV indicates larger platelet volume, an indicator of platelet activations and functions that is assumed as increased risk of cardiovascular disease (9,10). Endothelial dysfunction can be summarized as impairment of vasomotor, coagulation, fibrinolysis functions of the vessel; change in local immunity functions; and impairment of endothelial functions characterized by increase in vascular proliferation. Endothelial dysfunction plays a substantially important role in peripheral and coronary atherosclerosis pathogenesis (13). Studies have shown that one of the indicators of endothelial dysfunction is MPV (14).

Previous studies have shown that platelet activation increased due to shear stress induced by turbulence flow in stenotic valve in AS patients. Dimitrov et al. showed that increases in thrombin and platelet activation indicators in AS patients are independent of coronary and carotid atherosclerosis (15). Sucu et al. observed increases in platelet activation indicators including MPV and PDW in patients with aortosclerosis (16). Varol et al. showed that MPV increased in AS patients independently of miscellaneous risk factors (17). Bilen et al. found that MPV increases in patients with bicuspid aortic valves (18). Varol et al. showed increases in MPV in patients with mitral stenosis in sinus rhythm in comparison with their control group (19). Erdogan et al. showed significant decreases in MPV at one month postoperation in comparison with the preoperative period in patients who underwent balloon valvuloplasty due to rheumatismal mitral stenosis (20).

The incidence of chronic kidney failure increases in elderly patients with severe aortic stenosis. Previous studies have shown that MPV is increased in chronic kidney failure patients and it is also associated with mortality. Keles et al. found that 51.4% of patients with severe aortic stenosis treated with TAVR have chronic kidney failure and the glomerular filtration rate is better following the TAVR procedure (21).

Gul et al. observed 33 patients for 4 months; they experienced a progressive decrease in MPV after TAVI (22). Magri et al. showed preoperative low MPV is associated with increased vascular complications after transfemoral TAVI and life-threatening bleeding (23). In our study we found 10.7 ± 0.8 fL average values for MPV in patients before the operation. During follow up, there was no statistically significant change in patients' MPV at 1 day postoperation or at discharge (short term) in comparison with preoperation. Regarding preoperation MPV, at 1 and 6 months postoperation (midterm) a statistically significant decrease was observed. In the literature there is no extensive study conducted in the long term dealing with the effects of TAVI on MPV. In addition, according to our study, a statistically significant decrease in platelet counts of patients was observed 1 day after TAVI in comparison with preoperational levels. However, platelet levels were found to increase at discharge and 1 and 6 months postoperation compared to preoperative levels. Changes in platelet, Hg, and Hct levels are considered to be associated with blood loss and hypervolume.

In conclusion, in developed societies, incidence of severe AS increases continuously together with average life expectancy. The rate of TAVI application in patients who have high risks of sAVR rises gradually. In this study we have demonstrated the effect of TAVI on MPV. We propound that there is a decrease in MPV compared with its preoperative value after TAVI. This result can be interpreted to indicate that post-TAVI endothelial functions may be restored and platelet activation may decrease. Large population and randomized studies on significance of post-TAVI change in MPV and its possible effects on mortality are needed.

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