Platelet function in patients undergoing surgical and transcatheter aortic valve replacement: a comparative study

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ABSTRACT

Background: Intervention-induced platelet hypercoagulability may pose a risk of serious adverse events for patients.

Aims: This study aimed to assess whether surgical and transcatheter aortic valve replacement (SAVR and TAVR) differ in periprocedural platelet activity.

Methods: The total number of 24 patients with a mean age (SD) of 71 (13) years who underwent SAVR (n = 12) or TAVR (n = 12) were recruited for the study. The following parameters were evaluated at 4 time-points: (i) platelet indices: total platelet count (PLT), platelet distribution width (PDW) and mean platelet volume (MPV), (ii) MPV/PLT ratio, (iii) platelet level of lipid peroxidation: malondialdehyde (MDA) content and MDA/PLT ratio. Eventually, percentage variations of PLT, PDW, and MPV in relation to the baseline values were determined.

Results: MPV/PLT ratio increased significantly after procedures in both groups ($P = 0.01$ in TAVI and $P = 0.01$ in SAVR). MDA concentrations were significantly higher when assessed directly post-procedure ($P = 0.04$) as well as 24 hours later ($P = 0.01$) in the SAVR and TAVI groups. The indirect parameter of platelet activity indexed for platelet counts (MDA/PLT) was comparable between both groups before and 48 hours after procedures, but was significantly higher in SAVR patients, particularly after 24 hours after interventions ($P = 0.04$; medians TAVR vs SAVR, respectively).

Conclusions: Standard surgical aortic valve replacement is associated with a more pronounced platelet reaction to intervention-induced injury, as compared to the transcatheter-based procedure. The importance of these laboratory findings requires further investigation focused on early and late clinical outcomes.

Key words: human platelets, lipid peroxidation, surgical aortic valve replacement, transcatheter aortic valve implantation

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INTRODUCTION

Aortic stenosis (AS) is the most common valvular heart disease among elderly patients [1]. Symptomatic severe AS is associated with a survival rate of 50% if untreated [2]. Thus, to improve a patient's prognosis it is crucial to undertake invasive treatment on time. Currently, there are two therapeutic options for patients with severe AS: surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR). SAVR is the treatment of choice in symptomatic patients with severe AS [3]. However, TAVR has lately become less invasive although valuable alternative to manage symptomatic patients at intermediate or high risk of surgical procedure [4, 5]. It has already been proven that TAVR is non-inferior to surgery when performed in experienced centers, with respect to the risk of death or stroke within 5 years of follow-up [6, 7]. The estimation has been made that the number of SAVR procedures is expected to decrease significantly due to the growing number of TAVR procedures [8].

WHAT'S NEW?

Intervention-induced platelet hypercoagulability may pose patients to potentially serious adverse events. This study aimed to assess whether surgical and transcatheter aortic valve replacement (SAVR and TAVR), differ in periprocedural platelet activity caused by iatrogenic injury due to intervention. Demonstrating the significance of parameters regarding platelets number and function such as total platelet count (PLT), platelet distribution width (PDW) and mean platelet volume (MPV), MPV/PLT ratio, platelet level of lipid peroxidation measured by means of its final major product, malondialdehyde (MDA) content and MDA/PLT ratio, and the percentage variation of PLT, PDW and MPV in relation to the baseline values, may be valuable in our understanding the effect of heart procedures on platelet dysfunction. We demonstrated that standard surgical aortic valve replacement is associated with a more pronounced platelet reaction to iatrogenic injury due to intervention, as compared to transcatheter-based technique.

Pathophysiology of AS is an overly complex issue. Impaired fibrinolysis, pronounced calcification, coagulation, and platelet activation abnormalities contribute to the progression due to increased fibrin deposition and inflammation [9–11]. Platelet activity has an impact on the development of atherosclerosis. Platelets contribute to the early stage of vascular pathology, such as endothelial dysfunction and rupture of vulnerable plaque [12]. Platelet activation caused by atherosclerotic plaque rupture or erosion of the endothelium contributes to the formation and progression of the atherothrombotic disease [13]. These processes lead to clinically relevant consequences — adverse cardiovascular events such as myocardial infarction or stroke [14, 15]. The influence of platelet activity on the course of AS has been investigated, but results remain unequivocal [16].

Intervention-induced platelet hypercoagulability may pose patients to potentially serious adverse events. It has already been proven that platelets play a significant role in reparation after injury, wound healing, and organ regeneration [17]. The coagulation cascade is initiated at the injured endothelial surface, where platelets migrate and a fibrin-rich clot is formed. Progressive postinjury thrombocytosis induces a hypercoagulable state associated with an increased risk of thromboembolic complications [18]. Postinjury thrombocytosis seems to be an underestimated factor of a hypercoagulable state causing platelet hyperactivity.

As reported in the previous study, both TAVR and SAVR can induce systemic oxidative stress, although the former is associated with a significantly lower redox imbalance and faster recovery of antioxidant capacity [19]. As established experimentally and through observational studies, increased levels of endo- and exogenous reactive oxygen species are important factors triggering platelet activation [20–22]. It is therefore important to understand whether there is an association between platelet-related oxidative stress and platelet function following TAVR and SAVR procedures. In this regard, malondialdehyde (MDA) in platelets appears to be a feasible marker and a link between oxidative stress and platelet activity, since it is a hallmark of lipid peroxidation, a common outcome of cellular redox imbalance [23]. Moreover, it correlates with platelet aggregation in response to arachidonic acid, epinephrine, and collagen [24], and it is, besides thromboxane A2, a product of prostaglandin H_2 conversion by thromboxane synthase [25, 26].

This study aimed to assess whether two available methods of AS treatment differ in periprocedural platelet activity caused by iatrogenic injury due to intervention. To this end, the platelet indices and platelet MDA were compared in patients undergoing TAVR and SAVR during the hospital stay.

METHODS

The total number of 24 patients with a mean age (SD) of 71 (13) years who underwent SAVR (n = 12) or TAVR (n = 12) procedures between May 2016 and March 2017 were recruited for the study. The baseline characteristics of the studied group are summarized in Table 1. Written informed consent was obtained from each patient before participating in the research. The study protocol was approved by the Ethical Committee of the Medical University in Poznan (No. 968/15). All of the studied individuals fulfilled the criteria for high-gradient AS defined according to the current European Societ of Cardiology guidelines [27].

The following parameters were evaluated in all studied patients: (i) platelet indices: total platelet count (PLT), platelet distribution width (PDW) and mean platelet volume (MPV), (ii) MPV/PLT ratio, (iii) platelet level of lipid peroxidation measured by means of its final major product, MDA content and MDA/PLT ratio, and (iv) the percentage variation of PLT, PDW and MPV in relation to the baseline values were also determined [28]. All parameters were measured at 4 time-points: pre-procedure, immediately post-procedure, then 1 and 2 days after the procedure. Subsequently, all values were compared between the two groups at each of the measured time-points: functional parameter (MDA) vs platelet morphological indicators (PLT, MPV, PDW, PLT/MPV). Additionally, the percentage variation of MDA vs PLT values, MDA vs PDW, MDA vs MPV, and MDA vs PLT/MPV ratio, in relation to the baseline values, were calculated.

Malondialdehyde concentration

The content of MDA was measured in isolated platelets. Firstly, the platelet-rich plasma was obtained from the patient's blood samples by centrifugation at 200 g for 12 minutes. Platelet-rich plasma was then transferred to

Table 1. Baseline characteristics of studied patients (n = 24)

Variable	SAVR (n = 12)	TAVR (n = 12)	*P* value
Gender (male), n (%)	7 (58)	6 (50)	0.7
Age, years, mean (SD)	63 (10)	80 (3)	0.001
Height, m, mean (SD)	1.67 (0.11)	1.64 (0.06)	0.43
Weight, kg, mean (SD)	78.8 (13.2)	74.2 (12.3)	0.39
BMI, kg/m^2, mean (SD)	28.2 (3.9)	27.5 (4.7)	0.73
Obesity (BMI >30 kg/m^2), mean (SD)	4 (33)	5 (42)	0.69
Prior medical history			
Arterial hypertension, n (%)	8 (67)	5 (42)	0.24
Atrial fibrillation, n (%)	2 (17)	3 (25)	0.63
PCI, n (%)	3 (25)	5 (42)	0.41
Myocardial infarction, n (%)	0 (0)	3 (25)	0.08
Diabetes mellitus, n (%)	3 (34)	6 (50)	0.43
CABG, n (%)	1 (8)	2 (17)	0.56
COPD, n (%)	1 (8)	2 (17)	0.56
Stroke/TIA, n (%)	0 (0)	2 (17)	0.17

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; TIA, transient ischemic attack

polypropylene tubes, 1/10 vol acid citrate dextrose was added, centrifuged again at 900 g for 15 minutes. Plasma was aspirated and platelets were suspended in 200 µl of distilled water. The platelet MDA level was assessed using the TBARS Assay kit (Cayman Chemicals, Ann Arbor, MI, USA). The platelets were treated with 300 ml of RIPA Buffer (50 mM Tris-HCl, pH 7.4, 1% Triton X-100, 150 mM NaCl, 1% Tergitol type NP-40, 0.5% sodium deoxycholate, 0.1% sodium dodecyl sulfate) to conduct the lysis of cellular components. The butylated hydroxytoluene was added to the RIPA Buffer to prevent artificial lipid peroxidation during platelet lysis. The samples were then centrifuged at 1600 g for 10 minutes and the resulting 100 µl of supernatants were transferred to new tubes. The 800 µl of thiobarbituric acid was added to generate an MDA-thiobarbituric acid adduct. The reaction was conducted at 95°C for 60 minutes, samples were then placed for 10 minutes on an icebath for inhibition and centrifuged at 1600 g for 10 minutes. The absorbance of the final product was measured at 532 nm using a SynergyHTX multi-mode plate reader (BioTek Instruments, Winooski, VT, USA). The MDA content, given as µM, was calculated by comparing the absorbance values to a calibration curve (r^2 = 0.99) prepared using the MDA standard (Cayman Chemicals, Ann Arbor, MI, USA).

Surgical aortic valve replacement

All operations were performed from full median sternotomy with the use of cardio-pulmonary bypass (CPB) in moderate hypothermia (28°C) and cardioplegic cardiac arrest according to St. Thomas Hospital II formula [29]. CPB was conducted through an arterial cannula introduced to the ascending aorta and a two-staged venous cannula to the right atrium. After the ascending aorta was opened, the aortic valve was completely removed and the aortic prosthesis using 2-0 sutures with Teflon pledges was implanted. After aortotomia was closed with 5-0 monofilament suture and de-airing of the left heart was completed, ascending aorta was de-clamped and reperfusion phase of CPB initiated. Successful weaning from CPB was followed by removal of all cannulas, protamine administration, careful hemostasis, and closure of the chest.

Percutaneous aortic valve implantation

Patients were eligible for TAVR based on the institutional heart team's decision (interventional cardiologist, cardiac surgeon, and echocardiography specialist).

The pre-procedural evaluation included: coronary angiography, transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE); contrast-enhanced computed tomography (CT) with off-line reconstruction to evaluate the aortic valve, and access site (femoral and iliac arteries). The final decision regarding the route of the vascular approach was made based on the results of the CT scan. General anesthesia or deep sedation was used during the procedures. The TTE monitoring was performed and a temporary pacemaker was inserted from the femoral vein for rapid pacing and as a backup in case of iatrogenic atrioventricular block consequences [30].

In patients with the percutaneous femoral approach, two Proglides™ were introduced before insertion of the vascular sheath. The Medtronic CoreValve Evolut R prosthesis was implanted in all cases. Once the prosthesis was correctly positioned, expanded, and deployed, the contrast injection was performed to assess the presence and degree of paravalvular leak. Control angiography of the access site was performed to assess vessel patency and possible bleeding [31].

Data presentation and statistical analysis

First, all continuous variables were checked for normality by means of the Shapiro–Wilk W test. Those meeting the

Table 2. The results of non-parametric tests of multiple comparisons of platelet count

	TAVI			
SAVR	'0'	'1'	'2'	'3'
'0'		0.624	0.239	0.010
'1'	0.022		1.000	0.777
'2'	0.020	1.000		1.000
'3'	0.003	1.000	1.000	

Abbreviations: SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; '0', baseline; '1', immediately post-procedure; 2', 24 hours after procedure; 3', 48 hours after procedure

Table 3. Distribution of mean values and standard deviation (SD) of mean platelet volume (MPV) and platelet distribution width (PDW) depending on sampling time after transcatheter aortic valve implantation (TAVI) and surgical aortic valve replacement (SAVR)

	Sampling time							
	0'		1'		2'		3'	
	MPV, fl	PDW, %	MPV, fl	PDW, %	MPV, fl	PDW, %	MPV, fl	PDW, %
TAVI, mean (SD)	8.83 (0.91)	54.6 (5.4)	8.96 (1.05)	58.8 (5.2)	8.99 (0.86)	59.0 (6.5)	9.27 (0.98)	60.8 (7.0)
SAVR, mean (SD)	8.62 (1.04)	55.1 (5.7)	9.05 (1.17)	60.2 (6.0)	9.31 (1.36)	60.1 (6.6)	9.61 (1.24)	59.7 (6.1)
P value	0.04	0.70	0.30	0.49	0.80	0.48	0.70	0.75

criteria of normal distribution were presented as means with standard deviations and then compared with the use of unpaired Student t-test (between TAVI and SAVR groups) or repeated-measures ANOVA followed by post hoc Tukey HSD test (for time-related changes within groups). Otherwise (i.e., for not normally distributed continuous variables), they were expressed as the medians with interquartile range (IQR: first to third quartile) and then analyzed statistically by non-parametric tests such as Friedman test followed by Dunn's multiple comparisons of ranks. Qualitative variables were compared by means of Yates' corrected χ^2 test. *P*-value <0.05 was considered as statistically significant. Analyses were performed with the use of Statistica 10.0 for the Windows package (StatSoft, Tulsa, OK, USA).

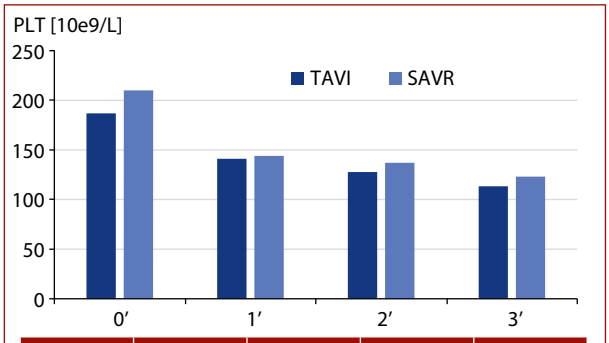
RESULTS

PLT count

In both groups, PLT decreased significantly following procedures (*P* <0.001). However, this drop was more pronounced in the SAVR group (*P* = 0.02 vs TAVI) because in all postoperative analyses (samples '1' to '3') PLT count was markedly lower than before surgery, whereas in the TAVI group only between two points, before procedure vs 48 hours after it (Table 2). Interestingly, the intergroup comparison did not show any statistical significance (Figure 1).

MPV and PDW

In both groups, these platelet parameters did not change during the periprocedural period (MPV, *P* = 0.67 and *P* = 0.26; PDW, *P* = 0.05 and *P* = 0.16; respectively for TAVI and SAVR in ANOVA) (Table 3). Of note, MPV before the procedure was significantly lower in SAVR than in the TAVI group.



Median with IQR	0'	1'	2'	3'
TAVI	175 (157–231)	141 (117–182)	137 (117–156)	112 (99–137)[a]
SAVR	210 (169–230)	144 (102–164)	137 (98–172)[a]	123 (11–140)[a]
P value	0.600	0.470	0.862	0.624

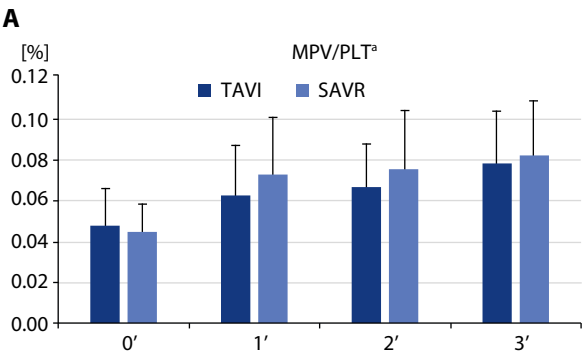
Figure 1. Platelet counts in the periprocedural period.

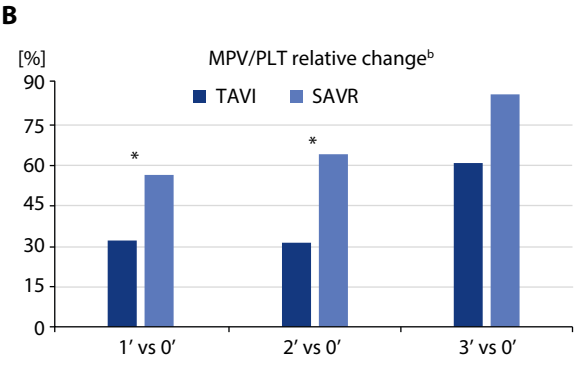
[a]*P* <0.05 after ('1'–'3') vs before procedure ('0') in multiple comparisons of ranks.
Abbreviations: PLT, platelet counts; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

MPV/PLT

MPV/PLT ratio increased significantly after procedures in both groups (*P* = 0.01 in TAVI and *P* = 0.01 in SAVR), although its value did not differ between groups (Figure 2A).

Post-hoc analysis disclosed that marked increase in MPV/PLT ratio between baseline vs both 24 (*P* = 0.04) and 48 hours (*P* = 0.01) after valve implantations in the SAVR group whereas in the TAVI group only between baseline and 48 hours after (*P* = 0.01) the procedures. These findings encouraged us to perform a more detailed analysis of this parameter. In the next step, a relative increase of this ratio was compared between groups and was found to be more pronounced 24 hours after procedures (Figure 2B).





[%]	'1' vs '0'	2' vs '0'	3' vs '0'
TAVI	31.4 (17.2–39.8)	30.5 (20.4–58.1)	60.4 (47.9–81.9)
SAVR	56.2 (42.0–86.6)	63.2 (31.0–94.3)	85.4 (62.8–114.6)
P value	0.09	0.04	0.34

Figure 2. MPV/PLT ratio (**A**) and its relative changes (**B**) after procedures.

Data are presented as the means with standard deviations ([a]) or the medians ([b]). *$P < 0.05$ TAVI vs SAVR.
Abbreviations: MPV, mean platelet volume; others: see Figure 1

MDA and MDA/PLT

Multiple comparisons of ranks test revealed that platelet levels of MDA were significantly higher soon after procedures ($P = 0.046$) and 24 hours ($P = 0.02$) later in the SAVR group than in the TAVI group (Figure 3A).

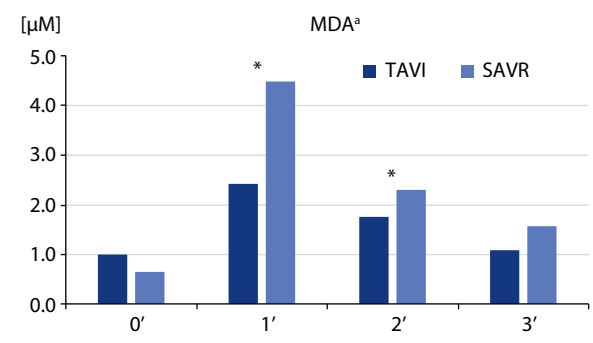
The parameter of single platelet activity (i.e., MDA/PLT) was comparable between groups before and 48 hours after procedures but in the other sampling points its value was significantly higher in SAVR patients (Figure 3B).

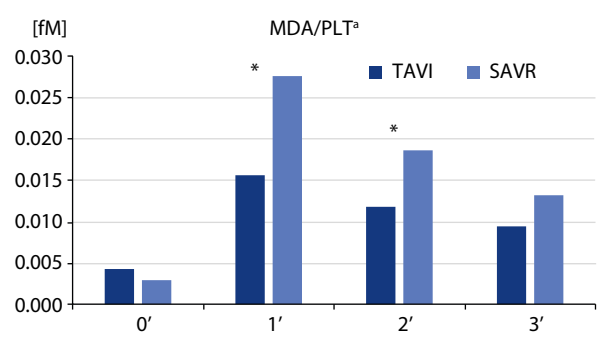
Multiple comparisons of MDA-to-PLT ratios within groups showed differences both in TAVI and SAVR patients. In the SAVR group, significant differences were noted not only after surgery ('1' vs '0'; $P < 0.001$) but also 24 hours later ('2' vs '0'; $P = 0.01$) whereas in TAVI one only soon after procedures ('1' vs '0'; $P = 0.02$).

DISCUSSION

Certain laboratory tests are done routinely in everyday clinical practice. The present study aimed to find out whether any of the available platelet-related indices such as PLT, MPV, PDW have importance in perioperative care in patients after TAVI and SAVR.

The decrease in PLT after procedures was observed in both studied groups. Platelet count was significantly lower in patients after SAVR at each time point after the operation. It is worth mentioning that none of the investigated patients had severe thrombocytopenia that would require blood or platelet transfusion following the procedure. Reasons behind the decrease in PLT after SAVR have been studied before. Aortic valve replacement operation was carried out using cardio-pulmonary bypass in moderate hypothermia (28°C). According to previously published data, hemodilution and destructive effect of CPB often cause secondary thrombocytopenia [32]. Moreover,





[μM]	0′	1′	2′	3′
TAVI	1.00 (0.67–1.25)	2.41 (1.92–2.79)	1.72 (1.17–1.88)	1.10 (0.93–1.51)
SAVR	0.63 (0.52–1.59)	4.48 (1.87–5.11)	2.27 (2.03–2.78)	1.54 (1.11–2.14)
P value	0.57	0.046	0.02	0.28

[fM]	0′	1′	2′	3′
TAVI	0.004 (0.003–0.007)	0.016 (0.011–0.020)	0.012 (0.008–0.015)	0.009 (0.007–0.013)
SAVR	0.003 (0.002–0.006)	0.027 (0.019–0.047)	0.019 (0.014–0.027)	0.013 (0.010–0.018)
P value	0.31	0.048	0.045	0.24

Figure 3. Total malondialdehyde (MDA) concentration (**A**) and its content in a single platelet (**B**).

[a]Non-parametric continuous variables are presented as medians. *$P < 0.05$ TAVI vs SAVR.
Abbreviations: see Figure 1

preoperative use of antiplatelet agents and hypothermia aggravate thrombocyte dysfunction [33].

Platelet count drop has already been observed after SAVR but also following percutaneous interventions. It has been postulated that it is due to the use of low-osmolar contrast agents and unfractionated heparin administration during the procedure [34–36]. The decrease in PLT is also a consequence of blood loss during (although minimally but still invasive) intervention. Unsurprisingly, classical aortic valve replacement generates more pronounced blood loss than TAVI, which is a transcatheter procedure. However, in the present study, the PLT was significantly lower 48 hours after TAVI in comparison to baseline. There is evidence that patients who have a decrease in PLT following transcatheter aortic valve implantation are at increased risk of adverse events [37]. However, the exact mechanisms for the condition and its consequences require further investigation.

Other possible reasons for PLT decrease include damage to the endothelium caused by prosthesis implantation and tissue injury. Moreover, shear stress modifications may play an important role in the platelet activation [38].

Large size platelets have increased metabolic and enzymatic activity profile and high prothrombotic potential [39]. It has been proven that increased MPV has an impact on myocardial infarction and cardiovascular death occurrence and thus is associated with worse outcome [40]. There is an inverse relationship between PLT and MPV observed in the physiological and pathophysiological state. The goal is to maintain hemostatic balance by the sustenance of constant platelet mass. The inflammatory process with enhanced thrombopoiesis is a clear example of this mechanism. The number of circulating platelets increases and many reactive large-sized platelets flow to the inflammatory site [41].

However, in the present study, no significant correlation with MPV levels was observed among investigated patients. Only a trend towards an increase of MPV after invasive procedures was noted, probably due to the low number of subjects included in this study.

Further study on a large group of patients is necessary to reveal whether any platelet-related laboratory test could serve as prediction markers and would be useful in the perioperative assessment of patients after SAVR or TAVI. Demonstrating the significance of parameters regarding platelet number and function may be valuable in understanding the effect of heart procedures on platelet dysfunction.

The aim of our study was also to use the levels of MDA in platelets in the assessment of oxidative stress. The present study has indicated that TAVR induced significantly lower redox imbalance as the platelet MDA content, the marker of lipid peroxidation, was lower than that in patients undergoing SAVR. These findings have important implications — they support the observations of previous research in which oxidative stress was measured using several different oxidative-stress biomarkers in the patient's serum [42]. Clearly, redox imbalance is less pronounced in the case of TAVI compared to SAVR, in which serum MDA levels increase significantly right after the surgical procedure [43]. Lower MDA in platelets not only highlights less cellular injury but also relates to how the MDA can affect platelet reactivity. Previous research has indicated the detrimental activation of platelets in some patients after SAVR [44]. Although platelet reactivity can be due to numerous factors and can be triggered via various pathways, reactive oxygen species are known to play their role as important mediators. For example, hydrogen peroxide supports platelet activation depending on arachidonic acid and collagen and triggers tyrosine phosphorylation of β3 [45, 46]. In turn, superoxide anion can enhance platelet activation by ADP, arachidonic acid, collagen, and thrombin, but also through scavenging endothelium- or platelet-derived nitric oxide [47, 48]. Therefore, reactive oxygen species can both induce oxidative stress in platelets and trigger their activation. Furthermore, MDA can be produced enzymatically by the thromboxane synthase in amounts equimolar to thromboxane A2 [49]. This further indicates that increased intraplatelet MDA content, more profoundly seen in patients undergoing SAVR, may also relate to the modification of thrombocyte function. Importantly, other studies suggest that suppression of platelet MDA levels can normalize arachidonate- and collagen-induced aggregation [50]. In SAVR patients, the post-procedural increase in this marker was higher than in TAVR, but a decreasing trend towards the baseline level was seen within 48 hours. This indicates that the potential effects of MDA on platelet activity were most likely ameliorated.

Limitations

The limitations of the present study should also be highlighted. Firstly, the research encompassed a small sample size. It is an effect of the complex protocol including the performance of surgical procedures requiring many preparations, precise timing of blood sample collection at 4 accurate time-points and a proper sample transfer to the experimental laboratory for determination of MDA levels. Furthermore, there is a need to emphasize a significant difference in the age of patients in both studied groups (TAVI vs SAVR; mean 80 years vs 63 years, respectively). It is a consequence of the qualification process by the heart team according to European Society of Cardiology guidelines on the management of patients with severe symptomatic AS. TAVR is a method preferred in elderly and high-risk patients. The findings of the present study cannot be used to modify the antiplatelet therapy, although they lay a foundation for further investigations encompassing larger groups and additional platelet-related parameters.

CONCLUSIONS

Standard surgical aortic valve replacement is associated with a more pronounced platelet reaction to intervention-induced injury, as compared to the transcathe-

ter-based technique. The importance of these laboratory findings warrants further investigation focused on early, as well as late, clinical outcomes. Whether these findings are of any significance in terms of selecting the appropriate antiplatelet therapy after SAVR and TAVI requires further investigations.

Article information

Conflict of interest: None declared.

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REFERENCES

1. Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: a population-based study. Lancet. 2006; 368(9540): 1005–1011, doi: 10.1016/S0140-6736(06)69208-8, indexed in Pubmed: 16980116.
2. Iung B, Vahanian A. Epidemiology of valvular heart disease in the adult. Nat Rev Cardiol. 2011; 8(3): 162–172, doi: 10.1038/nrcardio.2010.202, indexed in Pubmed: 21263455.
3. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017; 135(25): e1159–e1195, doi: 10.1161/CIR.0000000000000503 , indexed in Pubmed: 28298458.
4. Cribier A, Eltchaninoff H, Tron C, et al. Treatment of calcific aortic stenosis with the percutaneous heart valve: mid-term follow-up from the initial feasibility studies: the French experience. J Am Coll Cardiol. 2006; 47(6): 1214–1223, doi: 10.1016/j.jacc.2006.01.049, indexed in Pubmed: 16545654.
5. Gocoł R, Malinowski M, Bis J, et al. Long-term outcomes of aortic valve repair in over 500 consecutive patients: a single-center experience. Kardiol Pol. 2020; 78(9): 861–868, doi: 10.33963/KP.15406, indexed in Pubmed: 32486628.
6. Mack MJ, Leon MB, Smith CR, et al. 5-Year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomized controlled trial. Lancet. 2015; 385(9986): 2477–2484, doi: 10.1016/S0140-6736(15)60308-7, indexed in Pubmed: 25788234.
7. Sorysz D, Dziewierz A, Bagieński M, et al. Early results of the ongoing Polish Registry of Valve Thrombosis after Transcatheter Aortic Valve Implantation (ZAKPOLTAVI). Kardiol Pol. 2020; 78(7-8): 681–687, doi: 10.33963/KP.15426, indexed in Pubmed: 32543799.
8. Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the All-Comers NOTION Randomized Clinical Trial. J Am Coll Cardiol. 2015; 65(20): 2184–2194, doi: 10.1016/j.jacc.2015.03.014, indexed in Pubmed: 25787196.
9. Natorska J, Wypasek E, Grudzień G, et al. Impaired fibrinolysis is associated with the severity of aortic stenosis in humans. J Thromb Haemost. 2013; 11(4): 733–740, doi: 10.1111/jth.12122, indexed in Pubmed: 23289423.
10. Lee SH, Choi JH. Involvement of inflammatory responses in the early development of calcific aortic valve disease: lessons from statin therapy. Anim Cells Syst (Seoul). 2018; 22(6): 390–399, doi: 10.1080/19768354.2018.1528175, indexed in Pubmed: 30533261.
11. Panigrahi S, Ma Yi, Hong Li, et al. Engagement of platelet toll-like receptor 9 by novel endogenous ligands promotes platelet hyperreactivity and thrombosis. Circ Res. 2013; 112(1): 103–112, doi: 10.1161/CIRCRESAHA.112.274241, indexed in Pubmed: 23071157.
12. Michelson AD, Barnard MR, Krueger LA, et al. Circulating monocyte-platelet aggregates are a more sensitive marker of in vivo platelet activation than platelet surface P-selectin: studies in baboons, human coronary intervention, and human acute myocardial infarction. Circulation. 2001; 104(13): 1533–1537, doi: 10.1161/hc3801.095588, indexed in Pubmed: 11571248.
13. Jennings LK. Mechanisms of platelet activation: need for new strategies to protect against platelet-mediated atherothrombosis. Thromb Haemost. 2009; 102(2): 248–257, doi: 10.1160/TH09-03-0192, indexed in Pubmed: 19652875.
14. Gawaz M. Role of platelets in coronary thrombosis and reperfusion of ischemic myocardium. Cardiovasc Res. 2004; 61(3): 498–511, doi: 10.1016/j.cardiores.2003.11.036, indexed in Pubmed: 14962480.
15. Komosa A, Siller-Matula JM, Lesiak M, et al. Association between high on-treatment platelet reactivity and occurrence of cerebral ischemic events in patients undergoing percutaneous coronary intervention. Thromb Res. 2016; 138: 49–54, doi: 10.1016/j.thromres.2015.12.021, indexed in Pubmed: 26826508.
16. Prohaska W, Zittermann A, Lüth JU, et al. Prevalent platelet dysfunction in patients with aortic valve disease. J Heart Valve Dis. 2008; 17(5): 542–547, indexed in Pubmed: 18980088.
17. Lesurtel M, Graf R, Aleil B, et al. Platelet-derived serotonin mediates liver regeneration. Science. 2006; 312(5770): 104–107, doi: 10.1126/science.1123842, indexed in Pubmed: 16601191.
18. Kashuk JL, Moore EE, Johnson JL, et al. Progressive postinjury thrombocytosis is associated with thromboembolic complications. Surgery. 2010; 148(4): 667–674, doi: 10.1016/j.surg.2010.07.013, indexed in Pubmed: 20719351.
19. Heldmaier K, Stoppe C, Goetzenich A, et al. Oxidation-reduction potential in patients undergoing transcatheter or surgical aortic valve replacement. Biomed Res Int. 2018; 2018: 8469383, doi: 10.1155/2018/8469383, indexed in Pubmed: 30539023.
20. Ferroni P, Vazzana N, Riondino S, et al. Platelet function in health and disease: from molecular mechanisms, redox considerations to novel therapeutic opportunities. Antioxid Redox Signal. 2012; 17(10): 1447–1485, doi: 10.1089/ars.2011.4324, indexed in Pubmed: 22458931.
21. Vara D, Pula G. Reactive oxygen species: physiological roles in the regulation of vascular cells. Curr Mol Med. 2014; 14(9): 1103–1125, doi: 10.2174/1566524014666140603114010, indexed in Pubmed: 24894168.
22. Papaharalambus CA, Griendling KK. Basic mechanisms of oxidative stress and reactive oxygen species in cardiovascular injury. Trends Cardiovasc Med. 2007; 17(2): 48–54, doi: 10.1016/j.tcm.2006.11.005, indexed in Pubmed: 17292046.
23. Ayala A, Muñoz MF, Argüelles S. Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. Oxid Med Cell Longev. 2014; 2014: 360438, doi: 10.1155/2014/360438, indexed in Pubmed: 24999379.
24. Weiss HJ, Lages B. Platelet malondialdehyde production and aggregation responses induced by arachidonate, prostaglandin-G2, collagen, and epinephrine in 12 patients with storage pool deficiency. Blood. 1981; 58(1): 27–33, indexed in Pubmed: 6786394.
25. Hecker M, Haurand M, Ullrich V, et al. Products, kinetics, and substrate specificity of homogeneous thromboxane synthase from human platelets: development of a novel enzyme assay. Arch Biochem Biophys. 1987; 254(1): 124–135, doi: 10.1016/0003-9861(87)90088-9, indexed in Pubmed: 3579292.
26. Zagol-Ikapite I, Sosa IR, Oram D, et al. Modification of platelet proteins by malondialdehyde: prevention by dicarbonyl scavengers. J Lipid Res. 2015; 56(11): 2196–2205, doi: 10.1194/jlr.P063271, indexed in Pubmed: 26378094.
27. Falk V, Baumgartner H, Bax JJ, et al. ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017; 38(36): 2739–2791, doi: 10.1093/eurheartj/ehx391, indexed in Pubmed: 28886619.
28. Komosa A, Rzymski P, Perek B, et al. Platelets redox balance assessment: Current evidence and methodological considerations. Vascul Pharmacol. 2017; 93-95: 6–13, doi: 10.1016/j.vph.2017.06.002, indexed in Pubmed: 28684282.

29. Perek B, Casadei V, Puślecki M, et al. Clinical presentation, surgical management, and outcomes of patients treated for aortic stenosis and coronary artery disease. Does age matter? Kardiol Pol. 2018; 76(3): 655–661, doi: 10.5603/KP.2018.0005, indexed in Pubmed: 29313564.
30. Olasinska-Wisniewska A, Grygier M, Lesiak M, et al. Short- and mid-term outcome of transcatheter aortic valve implantation in patients with advanced age. Cardiol J. 2017; 24(4): 358–363, doi: 10.5603/CJ.a2016.0093, indexed in Pubmed: 27747858.
31. Olasińska-Wiśniewska A, Grygier M, Lesiak M, et al. Femoral artery anatomy-tailored approach in transcatheter aortic valve implantation. Postepy Kardiol Interwencyjnej. 2017; 13(2): 150–156, doi: 10.5114/pwki.2017.68050, indexed in Pubmed: 28798786.
32. Martin JF, Daniel TD, Trowbridge EA. Acute and chronic changes in platelet volume and count after cardiopulmonary bypass induced thrombocytopenia in man. Thromb Haemost. 1987; 57(1): 55–58, indexed in Pubmed: 3590081.
33. Bojar RM. Manual of Perioperative Care in Adult Cardiac Surgery. John Wiley & Sons 2011: 281–312.
34. Bata P, Tarnoki AD, Tarnoki DL, et al. Acute severe thrombocytopenia following non-ionic low-osmolarity intravenous contrast medium injection. Korean J Radiol. 2012; 13(4): 505–509, doi: 10.3348/kjr.2012.13.4.505, indexed in Pubmed: 22778575.
35. Mitrosz M, Kazimierczyk R, Sobkowicz B, et al. The causes of thrombocytopenia after transcatheter aortic valve implantation. Thromb Res. 2017; 156: 39–44, doi: 10.1016/j.thromres.2017.05.020, indexed in Pubmed: 28582640.
36. Siller-Matula JM, Mamas MA. Prediction for Contrast Volume in Transcatheter Aortic Valve Replacement - Important but Modifiable? Cardiology. 2020; 145(9): 611–614, doi: 10.1159/000508281, indexed in Pubmed: 32506061.
37. Gallet R, Seemann A, Yamamoto M, et al. Effect of transcatheter (via femoral artery) aortic valve implantation on the platelet count and its consequences. Am J Cardiol. 2013; 111(11): 1619–1624, doi: 10.1016/j.amjcard.2013.01.332, indexed in Pubmed: 23523059.
38. Consolo F, Sheriff J, Gorla S, et al. High frequency components of hemodynamic shear stress profiles are a major determinant of shear-mediated platelet activation in therapeutic blood recirculating devices. Sci Rep. 2017; 7(1): 4994, doi: 10.1038/s41598-017-05130-5, indexed in Pubmed: 28694489.
39. Gasparyan AY, Ayvazyan L, Mikhailidis DP, et al. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des. 2011; 17(1): 47–58, doi: 10.2174/138161211795049804, indexed in Pubmed: 21247392.
40. Chu H, Chen WL, Huang CC, et al. Diagnostic performance of mean platelet volume for patients with acute coronary syndrome visiting an emergency department with acute chest pain: the Chinese scenario. Emerg Med J. 2011; 28(7): 569–574, doi: 10.1136/emj.2010.093096, indexed in Pubmed: 20650916.
41. Thompson CB, Jakubowski JA. The pathophysiology and clinical relevance of platelet heterogeneity. Blood. 1988; 72(1): 1–8, indexed in Pubmed: 3291975.
42. Komosa A, Perek B, Rzymski P, et al. Transcatheter aortic valve replacement is associated with less oxidative stress and faster recovery of antioxidant capacity than surgical aortic valve replacement. J Clin Med. 2019; 8(9), doi: 10.3390/jcm8091364, indexed in Pubmed: 31480644.
43. Heldmaier K, Stoppe C, Goetzenich A, et al. Oxidation-reduction potential in patients undergoing transcatheter or surgical aortic valve replacement. Biomed Res Int. 2018; 2018: 8469383, doi: 10.1155/2018/8469383, indexed in Pubmed: 30539023.
44. Uhle F, Castrup C, Necaev AM, et al. Inflammation and its consequences after surgical versus transcatheter aortic valve replacement. Artif Organs. 2018; 42(2): E1–E12, doi: 10.1111/aor.13051, indexed in Pubmed: 29226341.
45. Pratico D, Iuliano L, Pulcinelli FM, et al. Hydrogen peroxide triggers activation of human platelets selectively exposed to nonaggregating concentrations of arachidonic acid and collagen. J Lab Clin Med. 1992; 119(4): 364–370, indexed in Pubmed: 1583386.
46. Irani K, Pham Y, Coleman LD, et al. Priming of platelet alphaIIbbeta3 by oxidants is associated with tyrosine phosphorylation of beta3. Arterioscler Thromb Vasc Biol. 1998; 18(11): 1698–1706, doi: 10.1161/01.atv.18.11.1698, indexed in Pubmed: 9812907.
47. Yamagishi SI, Edelstein D, Du XL, et al. Hyperglycemia potentiates collagen-induced platelet activation through mitochondrial superoxide overproduction. Diabetes. 2001; 50(6): 1491–1494, doi: 10.2337/diabetes.50.6.1491, indexed in Pubmed: 11375352.
48. Krötz F, Sohn HY, Gloe T, et al. NAD(P)H oxidase-dependent platelet superoxide anion release increases platelet recruitment. Blood. 2002; 100(3): 917–924, doi: 10.1182/blood.v100.3.917, indexed in Pubmed: 12130503.
49. Hecker M, Haurand M, Ullrich V, et al. Products, kinetics, and substrate specificity of homogeneous thromboxane synthase from human platelets: development of a novel enzyme assay. Arch Biochem Biophys. 1987; 254(1): 124–135, doi: 10.1016/0003-9861(87)90088-9, indexed in Pubmed: 3579292.
50. Hovinga JK, Felix R, Furlan M, et al. Malondialdehyde formation by blood platelets: a diagnostic test to assess acetylsalicylic acid induced thrombocytopathy? Thromb Res. 1990; 59(1): 89–95, doi: 10.1016/0049-3848(90)90274-g, indexed in Pubmed: 2399531.