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Restoration of von Willebrand factor after transcatheter aortic valve replacement—A possible cause for posttranscatheter aortic valve replacement thrombocytopenia?

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Abstract

Objectives: The aim of the current study was to analyze the clinical and procedural predictors of thrombocytopenia and the relationship between the decrease in platelet count (DPC) and change in vWF function (ΔvWF) after transcatheter aortic valve replacement (TAVR).

Background: TAVR often causes temporary thrombocytopenia. At the same time, TAVR leads to a restoration of von Willebrand factor (vWF) function.

Methods: One hundred and forty-one patients with severe aortic stenosis undergoing TAVR were included in the study. Platelet count and vWF function (vWF:Ac/Ag ratio) were assessed at baseline and 6 h after TAVR. Thrombocytopenia was defined as platelet count <150/nL.

Results: Median platelet count at baseline was 214/nL (interquartile range [IQR]: 176–261) and decreased significantly to 184/nL (IQR: 145–222) 6 h after TAVR. The number of patients with thrombocytopenia increased from 12.8% at baseline to 29.1% after 6 h. DPC 6 h after TAVR showed a significant correlation with ΔvWF ($r = -0.254$, $p = 0.002$). Patients with DPC > 20% had significantly higher ΔvWF (10.9% vs. 6.5%, $p = 0.021$). Obese patients showed a significantly lower DPC (11.8% vs. 19.9%, $p = 0.001$). In multivariate analysis, ΔvWF 6 h after TAVR was the only significant predictor for DPC > 20% ($p = 0.017$).

Conclusions: The restoration of vWF after TAVR is a significant predictor for DPC after TAVR. An increased platelet consumption due to vWF restoration could play a key role in the development of thrombocytopenia after TAVR.

Abbreviations: AVWS, acquired von Willebrand syndrome; BEV, balloon-expandable valve; CM, contrast medium; DPC, decrease in platelet count; EOA, effective orifice area; HMWM, high-molecular-weight von Willebrand multimers; SEV, self-expandable valve; ULVWF, ultra-large vWF multimer; vWF, Von Willbrand factor; ΔvWF, change in vWF:Ac/Ag ratio.

KEYWORDS
aortic valve replacement, platelet consumption, TAVR, thrombocytopenia, von Willebrand factor

1 | INTRODUCTION

Transient postprocedural thrombocytopenia is often observed after transcatheter aortic valve replacement (TAVR).[1,2] However, the cause for the decrease in platelet count (DPC) remains unclear.[3–5] The proposed hypotheses range from impaired platelet production to a potential influence of chemicals used in biological valves.[3,6,7] Furthermore, contrast medium (CM) volume,[8,9] body mass index (BMI)[10,11] and the type of TAVR prosthesis[10,12–15] have been described as potential influencing factors for DPC.

Another important hemostatic parameter, which is influenced by aortic valve replacement, is the von Willebrand factor (vWF). Its function is often impaired in patients with aortic stenosis due to elevated shear stress, but can be restored after aortic valve replacement.[16,17] vWF is essential for primary hemostasis by mediating platelet activation and platelet aggregation.[18,19] Restoration of vWF function could therefore play an important role in platelet activation and DPC after TAVR. To our knowledge this hypothesis was not yet investigated despite the important link between vWF function and platelet activation.

The aim of the current study was to analyze the clinical and procedural predictors of thrombocytopenia and the relationship between the change in vWF function (ΔvWF) and DPC after TAVR.

2 | METHODS

2.1 | Study population

In the investigator initiated single-center study patients presenting with severe aortic stenosis at the University Medical Center Regensburg from May 2017 to October 2018 were prospectively enrolled. The study was approved by the local ethics committee. No external funding was obtained to support the study and all included patients gave informed consent. The local Heart Team evaluated each case carefully for therapy decision. From all patients receiving TAVR 141 patients were included for analysis after exclusion of valve-in-valve procedure, conversion to surgical valve replacement or incomplete laboratory parameters (Figure 1).

2.2 | Blood sampling and laboratory analysis

Blood samples were taken before TAVR and 6 h after the procedure. Platelet count, vWF activity (vWF:Ac), vWF antigen (vWF:Ag), and activity-to-antigen-ratio (vWF:Ac/Ag ratio) were measured for each time point. Thrombocytopenia was defined as platelet count < 150/nl and severe thrombocytopenia as <50/nL. vWF:Ac was measured with the INNOVANCE® vWF Ac system (Siemens Healthcare GmbH), and vWF:Ag was assessed with devices of Siemens Healthcare Diagnostics or SYSMEX (SYSMEX CORPORATION). vWF:Ag and vWF:Ac levels above 600 U/dL, too high to be measured, were determined as 600 U/dL. vWF function was assessed using vWF activity-to-antigen (vWF:Ac/Ag ratio). Patients with vWF:Ac/Ag ratio ≤0.7 were defined to have an acquired von Willebrand syndrome (AVWS). The percentual change 6 h after TAVR was calculated for platelet count (DPC = 100 × [baseline platelet count – 6 h platelet count]/baseline platelet count) and vWF:Ac/Ag ratio (ΔvWF = 100 × [baseline vWF:Ac/Ag ratio – 6 h vWF:Ac/Ag ratio]/baseline vWF:Ac/Ag ratio). In previous publications, different cut-off values at 50% (at nadir),[10] 30% (at nadir),[13] or 20% (after 1 day)[20] were used. To analyze possible causative factors in the present study early DPC was analyzed, accordingly a lower DPC at 20% was chosen as cut off value.

2.3 | TAVR procedure and device success

Before TAVR the following aortic valve characteristics were assessed with transthoracic echocardiography (TTE): mean transvalvular gradient (Pmean), stroke volume index (SVI), ejection fraction (EF) and effective orifice area (EOA). The procedure was conducted in a hybrid operating room. Patients with contra-indication for a transfemoral approach were treated by transapical (6.4%) or subclavian access (1.4%). Pmean after

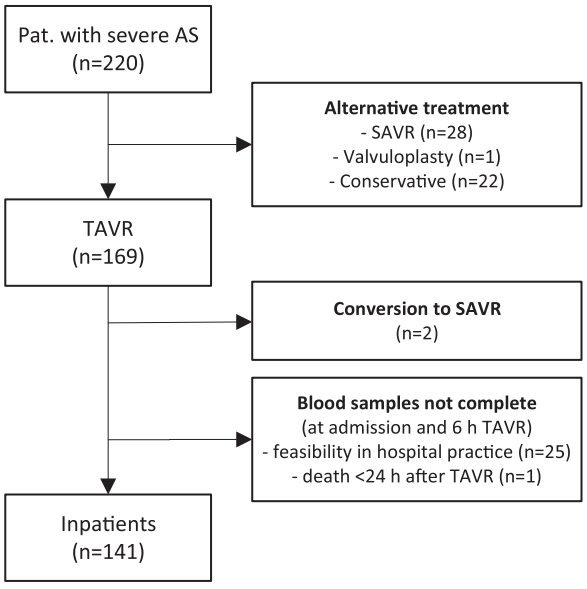


FIGURE 1 Flowchart patients.

TAVR was not measured in three patients. Major vascular complications, bleeding events and significant paravalvular leak (PVL ≥ II°) were assessed according to VARC-2 criteria.[21] The standard procedure for periprocedural antiplatelet therapy was ASS 100 mg before TAVR, after the procedure Clopidogrel 75 mg was added and dual antiplatelet therapy was continued for 3 months. In patients with atrial fibrillation oral anticoagulation was paused for the procedure and an antiplatelet agent was added for 3 months. There was no Clopidogrel loading dose applied.

3 | STATISTICS

Median with interquartile range (IQR) was used for the description of nonnormally distributed data. Correlations between two variables were calculated with Spearman's rank correlation coefficient. Mann–Whitney-*U* test was used to test nonnormally distributed, independent variables, with categorical variables χ^2 test was used. Related variables were analyzed using Wilcoxon signed rank test. To compare the potential influencing factors BMI, CM volume, valve type, and ΔvWF on DPC after TAVR, binary logistic regression analysis was conducted. For all analyses, commercially available statistical software was used (IBM SPSS Statistics 29, SPSS Inc).

4 | RESULTS

4.1 | Study population and baseline parameters

Baseline characteristics are presented in Table 1. The median age of the study population was 82 years (IQR: 78–85) and 55.3% were male. Between patients with DPC > 20% 6 h after TAVR ($n = 56$) and others, there was no significant difference in demographic data, medication, or comorbidities except for treatment with digitalis and the number of obese patients (BMI ≥ 30 kg/m^2). Five patients in the DPC > 20% group were obese (8.9%), compared to 26 patients (30.6%) in the other group ($p = 0.002$). Mean transvalvular gradient before TAVR was higher in patients with DPC > 20% ($p = 0.039$). SVI, EF, and EOA did not differ significantly between groups (p = n.s.). Concerning procedural parameters including valve type, access site, bleeding complications, PVL and mean transprosthetic gradient, there was no significant difference between groups (p = n.s., Table 1).

At hospital admission median platelet count was 214/n: (IQR: 176–261) and 18 (12.8%) patients suffered from thrombocytopenia (platelet count < 150 nL). There were no significant differences in baseline vWF parameters between patients with DPC >20% and ≤20% (each p = n.s., Table 2).

4.2 | Platelet count after TAVR

Within 6 h after TAVR platelet count decreased significantly to 184/nL (IQR; 145–222, $p < 0.001$, Figure 2). Median DPC was 17.8% (IQR: 8.5–25.7) 6 h after TAVR. The number of patients with thrombocytopenia increased from 18 (12.8%) patients at baseline to 41 (29.1%) patients 6 h after TAVR.

4.3 | vWF function

At the same time vWF:Ac/Ag ratio increased significantly (0.79 [IQR: 0.70–0.88] at baseline to 0.85 [IQR: 0.77–0.96] 6 h after TAVR, $p < 0.001$, Table 2). Median ΔvWF 6 h after TAVR was +7.8% and showed a significant negative correlation with platelet change ($r = -0.254$, $p = 0.002$, Figure 3). DPC > 20% was associated with a significantly higher ΔvWF 6 h after TAVR ($p = 0.021$). Patients with AVWS at baseline also showed significantly higher ΔvWF ($p < 0.001$). Twenty-four patients (17%) with insufficient vWF restoration (AVWS 6 h after TAVR) had a significantly lower DPC (9.5% [IQR: 0.5–19.7] versus 18.9% [IQR: 9.8–26.5], $p = 0.009$, Figure 4).

4.4 | BMI

Median BMI was 27.1 kg/m^2 (IQR: 24.0–29.6), two patients (1.4%) were underweight and 31 patients (22%) obese. The negative correlation between BMI and age was not significant ($r = -0.165$, $p = 0.051$). BMI did not correlate significantly with DPC after 6 h ($r = 0.139$, p = n.s.). Obese patients (BMI ≥ 30 kg/m^2) showed a significantly less pronounced DPC 6 h after TAVR than others (11.8% vs. 19.9%, $p = 0.001$, Figure 5). There was no significant correlation between BMI and ΔvWF (p = n.s.).

4.5 | CM volume

The median CM use was 110 mL (IQR: 89–134) and did not show a significant correlation with DPC 6 h after TAVR (p = n.s.). In five patients (3.5%) CM volume was >200 mL, these patients showed a significantly higher ΔvWF 6 h after TAVR ($p = 0.016$).

4.6 | Balloon-expandable valve (BEV) versus self-expandable valves (SEV)

Seventy-three patients (51.8%) received a self-expandable valve (Symetis Acurate Neo 46.1%, Medtronic Evolut R 5.7%), a balloon-expandable valve (Edwards Sapien) was used in 68 patients (48.2%). There was no significant difference between BEV and SEV concerning DPC or ΔvWF 6 h after TAVR (p = n.s.).

4.7 | Predictors for DPC after TAVR

Binary logistic regression analysis for DPC > 20% was conducted with the potential influencing factors ΔvWF, BMI, BEV, and CM volume. ΔvWF was the only significant predictor for DPC > 20% 6 h after

TABLE 1 Baseline characteristics.

	All ($n = 141$)	Platelet drop > 20% ($n = 56$)	Platelet drop ≤ 20% ($n = 85$)	p-Value
Age (years)	82 (interquartile range [IQR]: 78–85)	82 (IQR: 78–85)	82 (IQR: 77–85)	0.756
Sex, *n* (% male)	78 (55.3%)	31 (55.4%)	47 (55.3%)	0.994
Body mass index (BMI) (kg/m^2)	27.1 (IQR: 24.0–29.6)	27.1 (IQR: 23.9–28.3)	27.2 (IQR: 24.1–31.3)	0.319
STS-score (%)	2.8 (IQR: 1.9–4.7)	2.4 (IQR: 1.8-4.6)	3.0 (IQR: 1.9–4.8)	0.675
Hypertension, *n* (%)	128 (90.8%)	52 (92.9%)	76 (89.4%)	0.489
Diabetes, *n* (%)	46 (32.6%)	21 (37.5%)	25 (29.4%)	0.316
Obesity (BMI ≥ 30 kg/m^2), *n* (%)	31 (22.0%)	5 (8.9%)	26 (30.6%)	**0.002**
History of PCI, *n* (%)	30 (21.3%)	10 (17.9%)	20 (23.5%)	0.421
History of CABG, *n* (%)	11 (7.8%)	3 (5.4%)	8 (9.4%)	0.380
Peripheral artery disease, *n* (%)	24 (17.0%)	9 (16.1%)	15 (17.6%)	0.808
COPD, *n* (%)	19 (13.5%)	7 (12.5%)	12 (14.1%)	0.783
History of stroke/TIA, *n* (%)	21 (14.9%)	12 (21.4%)	9 (10.6%)	0.077
Permanent dialysis, *n* (%)	3 (2.1%)	1 (1.8%)	2 (2.4%)	0.819
Medication, n (%)				
Acetylsalicyclic acid	73 (51.8%)	29 (51.8%)	44 (51.8%)	0.998
Clopidogrel	20 (14.2%)	9 (16.1%)	11 (12.9%)	0.602
Ticagrelor	3 (2.1%)	2 (3.6%)	1 (1.2%)	0.335
Prasugrel	-	-	-	-
Phenprocoumon	20 (14.2%)	6 (10.7%)	14 (16.5%)	0.338
NOAC	21 (14.9%)	7 (12.5%)	14 (16.5%)	0.517
LMWH	7 (5.0%)	3 (5.4%)	4 (4.7%)	0.862
Beta-blocker	91 (64.5%)	34 (60.7%)	57 (67.1%)	0.441
Digitalis	6 (4.3%)	-	6 (7.1%)	**0.042**
Ca-channel blocker	46 (32.6%)	18 (32.1%)	28 (32.9%)	0.921
ACE-I/ARB	103 (73.0%)	44 (78.6%)	59 (69.4%)	0.230
Diuretics	100 (70.9%)	38 (67.9%)	62 (72.9%)	0.515
Aldosterone antagonist	26 (18.4%)	11 (19.6%)	15 (17.6%)	0.765
Aortic Valve				
Pmean (mmHg)	42 (IQR: 33–53)	44 (IQR: 35–56)	40 (IQR: 31–53)	**0.039**
Stroke volume index (SVI) (mL/m^2)	36 (IQR: 30–43)	36 (IQR: 31–43)	36 (IQR: 29–43)	0.428
Ejection fraction (EF) (%)	56 (IQR: 51–62)	57 (IQR: 54–64)	55 (IQR: 50–60)	0.213
Effective orifice area (EOA) (cm^2)	0.7 (IQR 0.6–0.8)	0.7 (IQR 0.6–0.8)	0.7 (IQR 0.6–0.8)	0.328
Procedural parameters				
Balloon-expandable valve, *n* (%)	68 (48.2%)	29 (51.8%)	39 (45.9%)	0.492
Access site, *n* (%)				
– Transfemoral	130 (92.2%)	52 (92.9%)	78 (91.8%)	0.813
– Transapical	9 (6.4%)	4 (7.1%)	5 (5.9%)	0.764
– Subclavian	2 (1.4%)	-	2 (2.4%)	0.248

TABLE 1 (Continued)

	All (n = 141)	Platelet drop > 20% (n = 56)	Platelet drop ≤ 20% (n = 85)	p-Value
Contrast medium volume (mL)	110 (IQR: 89–134)	112 (IQR: 87–134)	109 (IQR: 92–137)	0.712
Major vascular complication, n (%)	5 (3.5%)	3 (5.4%)	2 (2.4%)	0.345
Major bleeding complication, n (%)	6 (4.3%)	3 (5.4%)	3 (3.5%)	0.599
Pmean after transcatheter aortic valve replacement (TAVR) (mmHg)[a]	10 (IQR: 7–12)	10 (IQR: 8–13)	9 (IQR 7–12)	0.156
Paravalvular leak (≥II°)	11 (7.8%)	4 (7.1%)	7 (8.2%)	0.813
Permanent pacemaker after TAVR	15 (10.6%)	9 (16.1%)	6 (7.1%)	0.089

Note: Bold values are below significance threshold of 0.05.

[a]Mean transvalvular gradient (Pmean) after TAVR was not assessed in three patients (decrease in platelet count [DPC] > 20% n = 55, DPC ≤ 20% n = 83).

TABLE 2 Hemostatic parameters.

	Hemostatic parameters	All (n = 141)	Platelet drop > 20% (n = 56)	Platelet drop ≤ 20% (n = 85)	p-Value
Baseline	Platelet count (/nL)	214 (IQR: 176–261)	238 (IQR: 184–298)	210 (IQR: 174–253)	0.057
	Thrombocytopenia, n (%)	18 (12.8%)	7 (12.5%)	11 (12.9%)	0.939
	vWF:Ac/Ag ratio	0.79 (IQR: 0.70–0.88)	0.79 (IQR: 0.70–0.89)	0.80 (IQR: 0.70–0.88)	0.830
	acquired von Willebrand syndrome (AVWS), n (%)	36 (25.5%)	14 (25.0%)	22 (25.9%)	0.906
6 h	Platelet count (/nL)	184 (IQR: 145–222)	164 (IQR: 132–205)	196 (IQR: 159–235)	**0.004**
	Thrombocytopenia, n (%)	41 (29.1%)	24 (42.9%)	17 (20.0%)	**0.003**
	vWF:Ac/Ag ratio	0.85 (IQR: 0.77–0.96)	0.89 (IQR: 0.80–0.99)	0.85 (IQR: 0.72–0.95)	0.067
	AVWS, n (%)	24 (17%)	5 (8.9%)	19 (22.4%)	**0.038**
Δ	Decrease in platelet count (DPC) (%)	17.8 (IQR: 8.5–25.7)	27.5 (23.8–35.3)	10.1 (1.0–15.8)	-
	ΔvWF (%)	7.8 (−0.1-19.0)	10.9 (2.5–24.8)	6.5 (−2.0 to 17.4)	**0.021**

Note: Platelet count and vWF parameters at baseline, 6 h after TAVR and its percentual change: DPC and change in vWF:Ac/Ag ratio (ΔvWF). Bold values are below significance threshold of 0.05.

TAVR (p = 0.017). BMI, BEV, and CM volume were no significant predictors (p = n.s., Table 3).

5 | DISCUSSION

Previous studies have shown that TAVR often leads to a temporary thrombocytopenia.[2] The reasons leading to DPC however remain unclear.[3–5]

In the present cohort platelet count decreased significantly after TAVR and the number of patients with thrombocytopenia more than doubled within 6 h compared to baseline. The present study showed for the first time a correlation between the restoration of vWF function and the DPC.

5.1 | Restoration of vWF

TAVR induces a fast increase in high molecular weight vWF multimers (HMWM), even within minutes.[22] Van Belle et al. proposed the explanation that besides the decrease in vWF cleavage, TAVR could lead to a vWF release from the endothelium due to an alteration in luminal pressure during the procedure.[22] vWF is released from platelets and endothelial cells as an ultra-large multimer (ULVWF) anchored to the endothelial surface which is then cleaved by ADAMTS13 into smaller fragments.[23] Arya et al. showed that ULVWF even spontaneously bind circulating platelets, whereas plasma vWF required exogenous modulators to bind cells in absence of shear stress.[24] Therefore, vWF release could induce platelet activation even in flow and consequently lead to platelet consumption and DPC.

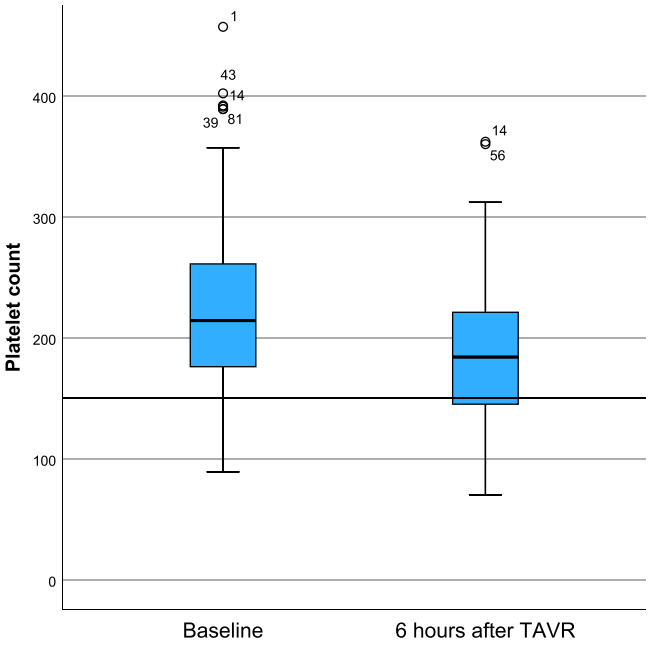


FIGURE 2 Decrease in platelet count after transcatheter aortic valve replacement (TAVR). Boxplots: Platelet count at baseline and 6 h after TAVR. Significant change in platelet count from 214/L: (interquartile range [IQR]; 176–261) at baseline to 184/n: (IQR: 145–222) 6 h after TAVR ($p < 0.001$). [Color figure can be viewed at wileyonlinelibrary.com]

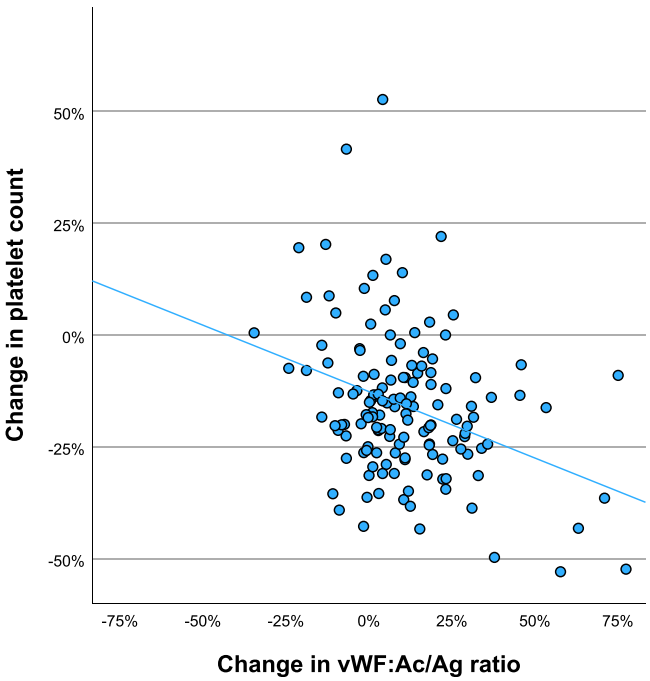


FIGURE 3 Decrease in platelet count and change in vWF:Ac/Ag ratio (ΔvWF). Scatter plot: Significant negative correlation of vWF:Ac/Ag ratio change (%) with change in platelet count (%) ($r = -0.254$, $p = 0.002$). [Color figure can be viewed at wileyonlinelibrary.com]

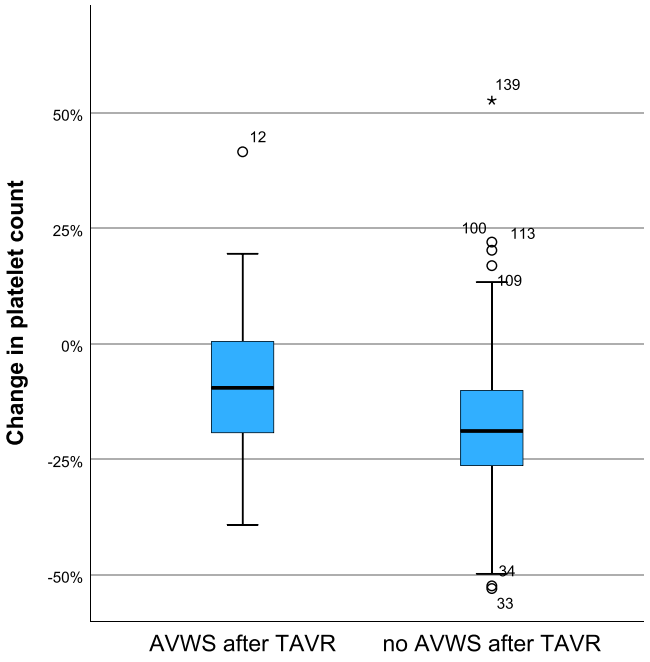


FIGURE 4 Decrease in platelet count (DPC) in patients with acquired von Willebrand syndrome (AVWS) after transcatheter aortic valve replacement (TAVR). Boxplots: Change in platelet count in patients with and without AVWS 6 h after TAVR (median DPC 9.5% vs. 18.9%, $p = 0.009$). [Color figure can be viewed at wileyonlinelibrary.com]

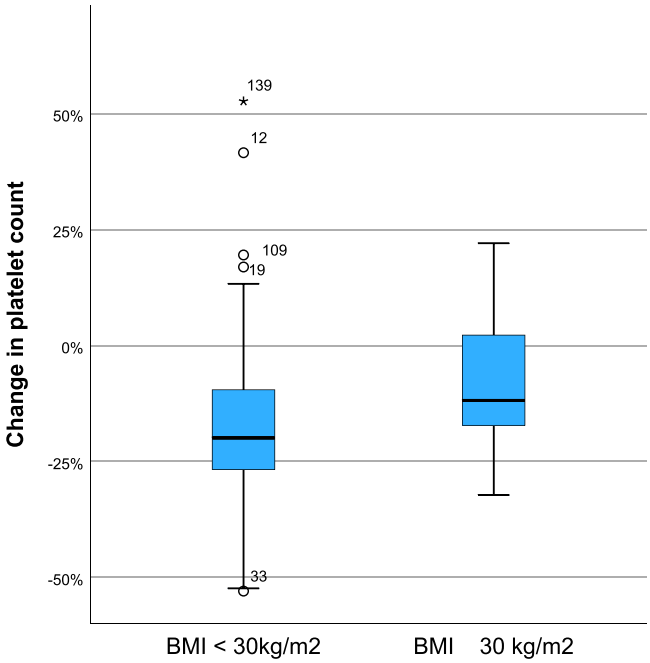


FIGURE 5 Decrease in platelet count (DPC) and obesity. Boxplots: Change in platelet count in obese patients versus others 6 h after transcatheter aortic valve replacement (TAVR) (median DPC 11.8% vs. 19.9%, $p = 0.001$). [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Predictors for decrease in platelet count (DPC).

	Odds ratio	95% confidence interval		*p*-Value
Change in vWF:Ac/Ag ratio	0.087	0.012	0.642	**0.017**
Body mass index	1.069	0.991	1.153	0.083
Balloon-expandable valve	1.341	0.665	2.707	0.412
Contrast medium volume	1.000	0.991	1.009	0.997

Note: Binary logistic regression analysis: Of all analyzed potential influencing factors ΔvWF was the only significant predictor for DPC > 20% 6 h after transcatheter aortic valve replacement (TAVR). Bold values are below significance threshold of 0.05.

The finding, that patients with DPC > 20% had higher transvalvular gradients before TAVR (Table 1) could be explained by the association of high gradient stenosis with AVWS,[16] as patients with AVWS at baseline then show a significantly higher increase in vWF function after TAVR.

Sedaghat et al. analyzed further hemostasis-related biomarkers in the context of post-TAVR thrombocytopenia.[25] Studies evaluating a potential influence of vWF on thrombocytopenia after TAVR however have not yet been reported in current literature.

5.2 | Thrombocytopenia after surgical aortic valve replacement (SAVR)

DPC after aortic valve replacement is not unique to TAVR, postprocedural thrombocytopenia is even more frequent in patients undergoing SAVR.[4,9,26] Furthermore, several studies found that patients receiving a mechanical prosthesis had a lower risk to develop postprocedural thrombocytopenia than patients with bioprosthetic valves.[6,7,27] Kizilay et al. hypothesized that glutaraldehyde, which is used to increase the durability of bioprostetic valves, could have a toxic effect on platelets.[6] The present study suggests a further hypothesis in context with the change in vWF parameters: Differences in hemodynamics, with mechanical prostheses being associated with higher peak systolic wall shear stress (WSS_{peak}),[28] could have an impact on platelet activation. Several studies also reported greater DPC in patients treated with stentless compared to stented SAVR-prostheses.[7,29] Further interpretation requires the comparison of vWF restoration in patients receiving different types of prostheses.

5.3 | Impact of pharmacological agents on platelet count after TAVR

Following the presented hypothesis, an increased vWF release caused by other factors, as after desmopressin administration, would also lead to thrombocytopenia. On the other hand, periprocedural platelet inhibition would reduce platelet activation and thrombocytopenia in consequence.

The influence of vasopressin analogs on platelet count was investigated in context of shock therapy. Patients treated with arginine vasopressin showed a significant DPC opposed to patients receiving norepinephrine.[30,31] DPC was also shown in patients with von Willebrand disease type 2b, where a gain-of-function mutation in the A1 domain causes increased vWF binding to GP1bα on the platelet surface, which leads to increased platelet activation.[32] For this reason, desmopressin administration is even generally contraindicated in these patients.[32,33]

Ibrahim et al. found that patients receiving a clopidogrel loading dose before TAVR showed a significantly lower DPC.[20] This finding supports the hypothesis of an increased platelet consumption through activation, since clopidogrel inhibits platelet aggregation.

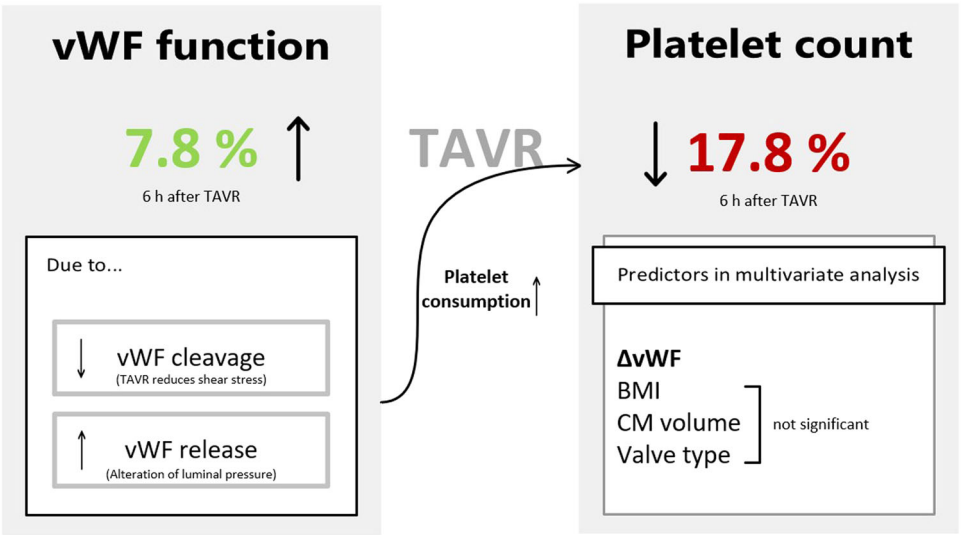
5.4 | BMI

A correlation between BMI and DPC with a more significant decrease in underweight patients was described in TAVR cohorts.[10] A causal relationship remains unclear, but earlier studies have also shown an association in other high-risk cardiac procedures. After primary angioplasty in acute myocardial infarction (AMI) obese patients develop less frequently thrombocytopenia.[34] This association was also observed in the present cohort, obese patients had a significantly lower DPC than others. There was no significant correlation between BMI and ΔvWF, they seem to be independent influencing factors. Nonetheless BMI was not a significant predictor for DPC > 20% in binary logistic regression analysis.

In the present TAVR cohort, there was only a nonsignificant negative correlation between age and BMI. The reason for this repeatedly described association of BMI with DPC remains unclear and requires further investigation.[34]

5.5 | CM volume

Mitrosz et al. reported a connection between CM use and thrombocytopenia after TAVR.[8] In the present cohort there was no significant correlation between CM volume and DPC. CM use was however associated with a higher ΔvWF 6 h after TAVR, but only in patients with a CM volume considerably above average. In five patients (3.5%) CM volume exceeded 200 ml and these patients showed a significantly higher ΔvWF. Likewise, in the study cohort of Mitrosz et al. CM use was considerably higher compared to the present cohort (229 mL ± 74 versus 110 mL (IQR: 89–134]).



CENTRAL ILLUSTRATION 1 vWF:Ac/Ag ratio increases by median 7.8% within 6 h after transcatheter aortic valve replacement (TAVR), median decrease in platelet count (DPC) is 17.8%. Especially freshly released von Willbrand factor is a very potent platelet activator and therefore could induce platelet consumption and thrombocytopenia after TAVR. [Color figure can be viewed at wileyonlinelibrary.com]

Based on the present findings the authors hypothesize that the correlation in earlier research may not represent a direct causal relationship. A higher CM volume is often necessary in complicated procedures and as vWF can be released by endothelial manipulation,[35] the increase in vWF function could represent the causal link between a high CM use and platelet consumption.

5.6 | TAVR prostheses

BEV was shown to be associated with a significantly higher DPC compared to SEV. Yamada et al. suggested that the use of the balloon in BEV implantation could cause greater shear stress leading to platelet activation.[10] This finding was not reproduced in the present cohort with an even distribution of BEV and SEV implantations.

5.7 | Clinical use

Fortunately, thrombocytopenia after TAVR rarely leads to severe bleeding complications[9] and mostly spontaneously recedes after reaching nadir on the second to fourth postoperative day.[2,10,13,25] Several studies did however report a worse midterm outcome in patients with severe postprocedural thrombocytopenia (platelet count < 50/nL).[2,12,15] In the present study no patient developed severe thrombocytopenia within 6 h after TAVR, but it is probable that some patients of the present cohort would also decrease to values below 50/nL in the following days. Further studies will be necessary for a better understanding of the underlying causes of thrombocytopenia and its prognostic implications. This could lead to an improvement of the periprocedural management for example concerning platelet inhibition before and after aortic valve replacement.

6 | CONCLUSION

The present study found that the restoration of vWF after TAVR is a significant predictor for the DPC after TAVR. In primary hemostasis vWF is crucial for platelet regulation. The authors therefore propose the hypothesis that an increased platelet consumption due to vWF restoration could cause thrombocytopenia after TAVR (Central Illustration 1).

7 | LIMITATIONS

The comparability between different publications is difficult, as many studies did not use the platelet count at a certain time point, but the lowest measured platelet count during hospitalization after TAVR. In the present study, platelet count was assessed only 6 h after TAVR, later development and patient's outcome was not analyzed. The study was conducted as a single-center study with a small cohort size and included only patients treated with TAVR. As thrombocytopenia after aortic valve replacement is common also after SAVR, further studies analyzing the potential impact of vWF change on platelet count comparing different valve types would be desirable.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in figshare at https://figshare.com/articles/dataset/Platelets_TAVI_data/23676414.

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