Original Research

Patient - prosthesis mismatch and its influence on immediate postoperative Von Willebrand factor levels in aortic valve replacement surgery

Andrei Emanuel Grigorescu[1,2,3,4], Andrei Anghel[5], Anamaria Matichescu[6,7], Horea Feier[1,2,3]

1) Department of Cardiology, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

2) Research Center of the Institute of Cardiovascular and Heart Disease of Timisoara, Timisoara, Romania

3) Division of Cardiovascular Surgery, Institute for Cardiovascular Diseases, Timisoara, Romania

4) Doctoral School Medicine - Pharmacy, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

5) Department of Biochemistry, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

6) Department of Preventive, Community and Oral Health Dentistry, Faculty of Dentistry, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

7) Translational and Experimental Clinical Research Centre in Oral Health (TEXCE-OH), Timisoara, Romania

Abstract

Background and aims. Aortic stenosis (AS) often requires surgical aortic valve replacement (SAVR). Patient-prosthesis mismatch (PPM) can lead to suboptimal outcomes. Von Willebrand factor (VWF), crucial for hemostasis, is altered in AS patients. As part of an ongoing study, this research focuses on the impact of PPM on immediate postprocedural VWF levels in SAVR patients, building upon our previous publication on short-term VWF dynamics in SAVR and TAVR.

Methods. This prospective study included 31 consecutive patients with severe AS undergoing SAVR. Preoperative and postoperative VWF levels were measured. PPM was assessed based on the indexed effective orifice area of the implanted valve.

Results. PPM was observed in 61.29% of patients. Postoperative VWF antigen levels increased significantly (131.37 ± 64.82 IU/dL to 311.01 IU/dL, $p<0.01$). However, PPM did not significantly influence postoperative VWF antigen levels (285.43 IU/dL vs. 293.30 IU/dL, $p=0.88$), VWF activity (178.33% vs. 204.76%, $p=0.56$), or Factor VIII levels (100.38 IU/dL vs. 97.10 IU/dL, $p=0.79$).

Conclusions. While SAVR led to increased VWF levels, PPM did not impact short-term VWF dynamics. This study provides insights into PPM and VWF relationships in SAVR patients, informing valve selection and perioperative management strategies. A future paper will reveal long-term follow-up results, completing this comprehensive investigation of VWF dynamics in aortic valve interventions.

Keywords: patient-prosthesis mismatch, aortic valve replacement, Von Willebrand factor, prosthetic valve size

Introduction

Aortic stenosis (AS) is a common valvular heart disease that disproportionately affects older individuals, with severe cases often necessitating surgical intervention to mitigate symptoms and prolong life [1]. For patients with symptomatic severe AS, surgical aortic valve replacement (SAVR) has long been considered the gold standard treatment, offering substantial improvements in quality of life and long-term survival [2–6]. However, the overall success of SAVR can be hindered by patient-prosthesis mismatch (PPM), a phenomenon that occurs when the implanted prosthetic valve is too small in relation to the patient's body size and hemodynamic requirements [7–9].

PPM can lead to a range of adverse consequences, including elevated transvalvular gradients, reduced left ventricular mass regression, and increased cardiac workload [10,11]. These hemodynamic abnormalities have been linked to poorer clinical outcomes, such as higher rates of mortality, rehospitalization, and heart failure symptoms [12,13]. While the impact of PPM on hemodynamics and clinical endpoints has been extensively

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Address for correspondence:
Anamaria Matichescu
matichescu.anamaria@umft.ro

studied, its potential influence on hemostatic parameters, particularly the von Willebrand factor, remains largely unexplored.

VWF is a multimeric glycoprotein that plays a pivotal role in primary hemostasis by mediating platelet adhesion and aggregation at sites of vascular injury [14–18]. Abnormalities in von Willebrand factor levels and function are influenced by aortic stenosis, where they may have a contribution to the development of bleeding or thrombotic complications [15–17,19–21]. Given the complex interplay between hemodynamic factors and hemostatic pathways, it is plausible that PPM could modulate VWF dynamics in patients undergoing SAVR, potentially impacting their perioperative and long-term outcomes.

Despite the potential significance of this relationship, there is a paucity of data on the effects of PPM on postoperative VWF levels in SAVR patients. A better understanding of how PPM influences VWF dynamics could provide valuable insights into the hemostatic consequences of PPM and guide the development of tailored strategies for optimizing valve selection, perioperative management, and long-term follow-up in this high-risk population.

Von Willebrand factor deficiency may have an impact on the risk of thrombotic or hemorrhagic complications during surgical aortic valve replacement. In patients with severe aortic stenosis, the high shear stress leads to a loss of high molecular weight VWF multimers, which are crucial for platelet adhesion and aggregation. This acquired von Willebrand syndrome can result in an increased bleeding tendency, particularly from mucosal surfaces. Conversely, after valve replacement, the sudden normalization of shear stress can lead to a rapid increase in VWF levels, potentially increasing the risk of thrombotic events. The balance between these opposing risks is delicate and can be further complicated by factors such as cardiopulmonary bypass, which can independently affect VWF levels and platelet function.

To address this knowledge gap, the present prospective study aims to investigate the association between PPM and postoperative VWF levels in patients who undergo SAVR for severe aortic stenosis. Through investigating the relationship between PPM and von Willbrand factor leves, this study seeks to contribute to the growing body of evidence on the multifaceted impact of PPM and inform the development of personalized approaches for improving outcomes and minimizing complications in patients undergoing SAVR.

Methods

Patient selection and study protocol

This prospective investigation recruited 31 patients consecutively diagnosed with severe aortic stenosis who subsequently underwent surgical aortic valve replacement. The study's inclusion criteria mandated the presence of severe AS, confirmed by echocardiographic evaluation, and the patient's suitability for SAVR.

The indication for surgical correction of aortic stenosis was based on established guidelines. Specifically, patients were considered for SAVR if they met the following criteria:

1. Symptomatic severe AS (aortic valve area < 1.0 cm^2, mean gradient > 40 mmHg, or peak aortic jet velocity > 4.0 m/s)
2. Asymptomatic severe AS with left ventricular ejection fraction < 50%
3. Severe AS undergoing cardiac surgery for other indications
4. Low-flow/low-gradient severe AS, in symptomatic patient
5. Moderate AS undergoing cardiac surgery for other indications

Data acquisition and evaluation

A set of preoperative data was gathered for each patient, encompassing demographic information (age and gender), comorbid conditions (hypertension, diabetes, coronary artery disease, valvular pathologies, and aortic disorders), echocardiographic measurements (aortic valve area and mean transvalvular pressure gradient), and relevant laboratory parameters (hemoglobin levels, platelet counts, and coagulation profiles). Records were maintained regarding intraoperative details, with a particular attention to the classification (bioprosthetic or mechanical) and physical specifications of the surgically implanted valve.

Echocardiographic evaluation and aortic stenosis grading

Transthoracic ultrasound imaging was employed to evaluate the extent of aortic valve narrowing. Upon patient entry, we measured the maximum blood flow speed, calculated the mean pressure gradient through the aortic valve, and determined the functional opening area of the valve. Established guidelines were employed to categorize the severity of aortic stenosis as mild, moderate, or severe [10,11].

Prosthetic valve characteristics and patient-prosthesis mismatch assessment

We obtained the effective orifice area (EOA) values for the implanted prosthetic aortic valves by consulting the manufacturer, which provided charts and existing literature (Table I) [12,13,15]. We determined body surface area (BSA) for all patients using the Dubois formula. The calculated BSA was used to calculate the indexed EOA (EOAi) of the prosthesis and the indexed aortic valve area prior to the surgical intervention (SOAi).

The presence and extent of patient-prosthesis mismatch were evaluated based on the criteria put forth by Pibarot and Rahimtoola [2,15,22]. The EOAi of the prosthetic valve was used to classify the severity of PPM into mild (EOAi > 0.85 cm^2/m^2), moderate (EOAi between 0.65 and 0.85 cm^2/m^2), and severe (EOAi < 0.65 cm^2/m^2) categories.

Table I. Standard values of EOA for the prosthesis in aortic position. Adapted from [12,13,15,18].

Valve Diameter (mm)	19	21	23	25
Biological prosthesis				
Medtronic HancockII	N/A	1.2 ± 0.2	1.3 ± 0.2	1.5 ± 0.2
Carpentier-Edwards Perimount	1.1 ± 0.3	1.3 ± 0.3	1.5 ± 0.4	1.8 ± 0.4
Biocor (Epic)	1.0 ± 0.3	1.3 ± 0.5	1.4 ± 0.5	1.9 ± 0.7
Mechanical prosthesis				
Carbomedics Standard and Top Hat	1.0 ± 0.4	1.5 ± 0.3	1.7 ± 0.3	2.0 ± 0.4

Blood sample collection and von Willebrand factor analysis

Blood samples were obtained within a 24-hour window prior to surgery and on the seventh postoperative day. We analyzed blood components using specialized assays: clotting factor VIII plasma levels were measured using reagents form Antibodies-online (Limerick, Pennsylvania), von Willebrand factor antigen levels were quantified with kits also sourced from Antibodies-online, and functional activity of von Willebrand factor in response to ristocetin was assessed usign HemosIL reagents (Bedford, Massachusetts).

Statistical methodology

The normality of the data was evaluated using the Shapiro-Wilk test. Continuous variables were reported as mean ± standard deviation and interquartile range, while categorical variables were expressed as frequencies and percentages. Spearman's rank test (Spearman's Rho) was used to assess correlations between variables. For sin-gle-variable comparisons, we employed different statistical methods based on data characteristics. Continuous variables were analyzed using either the Student's t-test or the Mann-Whitney U-test, depending on distribution normality. For discrete or categorical variables, we applied the chi-squared test to asses group differences. Multivariable analyses, including linear regression and analysis of variance (ANOVA), were performed to identify independent variables influencing continuous outcomes. Statistical significance was set at a p-value < 0.05. All statistical computations were carried out using a specialized software for data analysis and statistical modeling StataBE version 17.0 developed by StataCorp, headquartered in College Station, Texas).

Ethical considerations

Our research methodology adhered to the ethical guidelines established in the Helsinki Declaration. The Institutional Review Board of the Cardiovascular Institute and University of Medicine "Victor Babes" in Timisoara evaluated and approved our study design (reference: 33/09 December 2019). Before enrollment, each prospective participant was fully informed about the study's purpose and procedures. We secured signed documentation from all subjects, confirming their voluntary participation and consenting to the utilization of their anonymized data in subsequent academic publications.

Results

Patient characteristics and baseline data

Our study cohort comprised 31 individuals who received surgical aortic valve replacement (SAVR). The demographic profile revealed a female predominance (54.84%) and mean age 66.8 years (SD ± 9.15), ranging from 46 to 79 years old.

All participants exhibited severe AS, as evidenced by a mean aortic valve area of 0.81 ± 0.15 cm² and a mean pressure gradient of 52.24 ± 13.79 mmHg. Mean diameter for aortic annuli was 2.25 ± 0.20 cm, while mean EF was 48.44 ± 8%.

Analysis of cardiovascular risk factors and comorbidities revealed that hypertension was the most prevalent condition (67.74%), followed by diabetes mellitus (35.48%). Significant cardiac comorbidity included coronary artery disease in 12.90% of patients, all of whom underwent concurrent CABG procedure. Other comorbidities included chronic pulmonary disease (12.9%), chronic renal impairment (3.23%), and 9.68% of patients were active smokers at the time of surgery.

Regarding cardiovascular medications, most patients were receiving multiple agents preoperatively. Beta-blockers were the most commonly prescribed (77.4%), followed by ACE inhibitors/ARBs (70.9%) and statins (61.3%). Antiplatelet therapy was present in 45.2% of patients.

No significant correlations were found between demographic factors (age, gender, ethnicity) or comorbidities in perioperative changes in von Willebrand factor levels.

Table II. Cardiac ultrasound assessment.

Variable	Mean	Min	Max
Ao. Anulus (cm)	2.25	1.9	2.7
Pmax (mmHg)	80.35	16	134
Pmed (mmHg)	52.24	36	90
Valve area (cm²)	0.81	0.55	1.2
Indexed valve area (cm²)	0.43	0.28	0.58
EF (%)	48	25	55
VTD (ml)	109.87	70	215

Surgical procedure and prosthetic valve characteristics

The mean prosthesis size was 22.35 mm. The average cardiopulmonary bypass (CPB) time and aortic cross-clamp time were 103.13 minutes [IQR: 78-110.5] and 62.35 minutes [IQR: 45-78.5], respectively. The mean intensive care unit stay was 4 days.

The group presented with distinctive anthropometric features that contributed to the challenge of achieving optimal prosthesis sizing. Average height was 1.67 ± 0.08 m, weight 82.25 ± 20.9 kg, with a calculated BSA of 1.90 ± 0.24 m². Crucially, their aortic annulus had a mean diameter size of 2.25 ± 0.20 cm, being insufficiently related to their calculated BSA (Table III). This disparity between a small aortic root and high BSA complicated the prosthesis selection process.

Table III. Anthropometric features.

	Value
Height (mean m)	1.67 (±0.08)
Weight (mean cm)	82.25 (±20.9)
BSA (m^2)	1.90 (±0.24)
Aortic anulus (cm)	2.25 (±0.20)

Bioprosthetic valves were implanted in 51.61% (n=16), while mechanical valves were used in 48.39% (n=15). The Carbomedics Top Hat was the most frequently utilized valve model (51.61%, n=16), followed by the Edwards Lifesciences CE Perimount (32.26%, n=10). The mean effective orifice area of the aortic prostheses was 1.52 cm² [IQR: 1.3-1.7], with a mean indexed EOA of 0.79 cm²/m² [IQR: 0.71-0.92].

Table IV. Intraprocedural and postprocedural outcomes.

	Mean	Median	Q1	Q3
Prosthesis size	22.35	23	21	23
CBP time (min)	103.13	94.5	78	110.5
Cross-clamp time (min)	62.35	57	45	78.5
Drainage (ml)	377.69	310	230	450
Days ICU	4	2	1	3
Days postprocedural	5.96	6	5	7

In 12.90% of cases (n=4), concurrent coronary artery bypass grafting (CABG) was performed along with SAVR due to significant coronary artery disease.

In our cohort postoperative bleeding was quantified within the first 24 hours following the procedure. The mean drainage was 377.69 ml [IQR: 230-450]. Notably, our analysis revealed a significant inverse relationship between preoperative von Willebrand factor antigen levels and postoperative drainage. Specifically, baseline vWF:Ag emerged as an independent negative predictor of bleeding volume.

Table V. Multivariate analysis of factors influencing bleeding.

	Coefficient	95% CI	p
Initial Von Willberand factor antigen levels	-1.12	-2.09 - -0.14	0.02
Initial factor VIII levels	0.80	-0.38 - 1.98	0.17

Patient-prosthesis mismatch

PPM, defined as an indexed EOA < 0.85 cm²/m² BSA, was observed in 61.29% (n=19) of patients. We graded PPM into three categories: no/insignificant PPM(EOAi>0.85 cm2/m2), moderate PPM (EOAi 0.65-0.85 cm^2/m^2), and severe PPM (EOAi<0.65 cm^2/m^2 (Table VI).

Table VI. The distribution of PPM severity.

PPM Classification	EOAi (cm^2/m^2)	Number of patients (%)
No/ Insignificant	>0.85	12 (38.71%)
Moderate	0.65-0.85	14 (45.16%)
Severe	<0.65	5 (16.13%)

Statistical analysis revealed no significant association between patient-prosthesis mismatch and postoperative levels of VWF antigen. Von Willebrand factor antigen concentrations demonstrated comparable distributions in both cohorts (285.43IU/dL[IQR:135.65-382.9] versus 293.30IU/dL[IQR:222.9-345.4], p=0.88). Similarly, von Willebrand factor activity exhibited no statistically meaningful difference (178.33%[IQR:119.2-130.9] versus 204.76% [IQR:115.8-399.2], p=0.56). Levels of Factor VIII remained consistent irrespective of prosthetic fit (100.38 IU/dL[IQR:75.3-111.5] versus 97.10 IU/dL[IQR:80.4-111.2], p=0.79).

Further analysis of PPM severity subgroups also showed no statistically significant differences in these parameters (Table VII).

Table VII. Impact of PPM severity.

Variable	No/Insignificant PPM	Moderate PPM	Severe PPM
VWF:Ag levels (IU/dL)	285.43 [135.65-382.9]	290.78 [222.9-318]	302.77 [196.65-408.9]
VWF Activity (%)	178.33 [119.2-130.9]	183.62 [107.2-135.4]	284.05 [118.75-449.35]
Factor VIII (IU/dL)	100.38 [75.3-111.5]	94.86 [80.4-111.2]	105.5 [83.4-127.6]

Anticoagulation and thrombotic events

Anticoagulation protocols were standardized for all patients. Preoperatively, patients on oral anticoagulants were bridged with low molecular weight heparin. Postoperatively, patients with mechanical valves were started on warfarin with a target INR of 2.5-3.5, while those with bioprosthetic valves received aspirin 75-100 mg daily unless otherwise indicated. No clinically significant thromboses were observed during the immediate postoperative period, despite the observed increase in von Willebrand factor levels. Long-term follow-up for thrombotic events was beyond the scope of this study.

Von Willebrand factor

The mean preoperative VWF antigen (VWF:Ag) level was 131.37 ± 64.82 IU/dL [IQR: 77.3-198]. Preoperative VWF:Ag levels showed a significant inverse correlation with the SOAi (rho= -0.36, p <0.04). Post-surgical assessment revealed a marked elevation in von Willebrand factor antigen concentrations, with levels rising to 311.01 IU/dL [IQR: 172.2-387] (p<0.01). Notably, this increase demonstrated no significant correlation with the size-adjusted effective orifice area of the implanted valve prosthesis (Spearman's rho=-0.01, p=0.95).

VWF activity also increased significantly from 79.25% [IQR: 45.9-122] at baseline to 190.41% [IQR: 120-135.4] (p<0.01). However, no significant differences were observed in Factor VIII levels (95.3 IU/dL [IQR: 61.9-105.4] vs. 100.18 IU/dL [IQR: 79-111.2], p=0.21) or VWF:Ag/VWF: activity ratio (0.66 [IQR: 0.43-0.78] vs. 0.75 [IQR: 0.38-0.79], p=0.33) following the procedure.

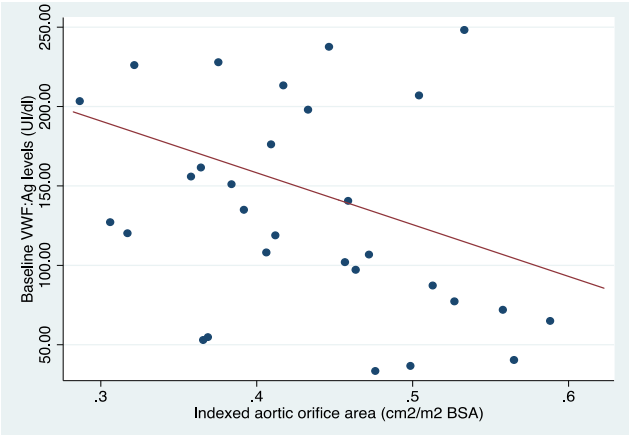

Figure 1. Correlation between initial levels of von Willebrand factor antigen and indexed aortic valve area.

At baseline, patients with blood group O had significantly lower VWF activity levels compared to those with a non-O blood group (1.20 ± 0.57 vs. 2.48 ± 1.98, p=0.03). However, no significant differences were found in preoperative VWF:Ag levels (99.51 IU/dL [IQR: 56.2-137.4] vs. 142.45 IU/dL[IQR:87.3-207], p=0.09) or levels of factor VIII (76.4 IU/dL[IQR:55.5-91.3] vs. 101.87 IU/dL [IQR: 66.6-120.6], p=0.42) between the two groups. These differences in VWF activity disappeared one week after SAVR (2.38 [IQR: 1.04-3.37] vs. 2.08 [IQR: 1.27-2.60], p=0.48), and no significant differences were observed in postoperative VWF:Ag levels (393.25 IU/dL [IQR: 212.3-506] vs. 282.40 IU/dL [IQR: 167.8-318.4], p=0.13) or Factor VIII levels (94 IU/dL [IQR: 69.5-92.3] vs. 102.33 IU/dL [IQR: 83.8-113.2], p=0.56) between blood group O and non-O patients.

To assess the potential impact of cardiopulmonary bypass on VWF levels, we analyzed the relationship between CPB times and the increase in VWF:Ag levels. We found no significant correlation between CPB duration and the magnitude of VWF:Ag increase (Spearman's rho = 0.20, p = 0.28). These data suggest that the observed increase in VWF levels is likely primarily due to the normalization of shear stress following valve re-placement, rather than being influenced by the cardiopulmonary bypass.

Discussion

Aortic stenosis is a well-known cause of acquired von Willebrand syndrome (AVWS), particularly type 2A, which is characterized by a deficiency in high-molecular-weight multimers (HMWM) of von Willebrand factor [15–18,23]. The elevated shear stress caused by the narrowed valve orifice in AS leads to structural changes in the VWF molecule, making it more susceptible to proteolysis [15–18,23]. As a result, patients with severe AS may experience a significant reduction in HMWM VWF levels, which can increase the risk of bleeding complications [15–18,24]. In fact, studies have shown that individuals with severe AS may have up to a 50% decrease in HMWM VWF levels compared to healthy individuals [15,19].

The severity of AVWS in AS patients has been found to correlate with the degree of valve stenosis and the transvalvular pressure gradient [18,19,25]. This highlights a crucial implication of high shear stress in HMWM of von Willebrand factor degradation .

Interestingly, systemic abnormalities in VWF have been linked to the pressure gradient across prosthetic valves following aortic valve replacement[15]. This suggests that patients who develop PPM after SAVR may continue to experience elevated shear stress, even if the prosthetic valve is functioning properly. Consequently, PPM could potentially contribute to the persistence or recurrence of AVWS even after valve re-placement surgery [15,18].

Impact of cardiovascular risk factors

Our analysis of patient characteristics revealed presence of cardiovascular risk factors and comorbidities, with more than two-thirds of patients having hypertension and over one-third having diabetes mellitus. Notably, 12.90% of our cohort had significant coronary artery disease requiring concurrent CABG procedure during their SAVR. While chronic conditions such as pulmonary

disease and renal impairment were present in our cohort, their prevalence was relatively low. Despite the presence of these conditions, we did not observe significant correlations between these factors and perioperative changes in VWF levels.

Preoperative cardiovascular medications, including antiplatelet and anticoagulant therapies, did not appear to significantly influence the VWF levels.

The VWF dynamics after SAVR

We observed a significant increase in VWF antigen levels following SAVR, indicating an improvement in hemostatic function. The mean preoperative VWF level was low at 131.37 ± 64.82 IU/dL [IQR: 77.3-198], reflecting the hemostatic impairment caused by AS. After surgery, VWF levels increased to 311.01 UI/dl ± 176.77 IU/dL [IQR: 172.2-387], suggesting a significant improvement. The resulted data confirms other studies findings that removing the stenosis in the aortic valve will decrease the degradation of von Willebrand factor [7,8,15,18,19].

Long CBP time, especially in associated procedures, could increase the risk of bleeding due to CPB-induced platelet dysfunction [26]. Although this factor does not directly influence VWF levels, it highlights the complex nature of hemostasis management in patients undergoing SAVR.

Impact of patient-prosthesis mismatch

Patient-prosthesis mismatch is a significant concern in aortic valve replacement procedures, as it can lead to suboptimal hemodynamics, increased shear stress on the prosthetic valve, and a higher risk of acquired von Willebrand factor deficiency [27–29]. PPM occurs when the effective orifice area of the implanted valve is smaller than that of the native stenotic valve, a concept first introduced by Rahimtoola in 1978 [27–29]. The prevalence of moderate PPM is estimated to range between 20% and 70%, while severe PPM occurs in 2% to 10% of cases [30].

When selecting the optimal prosthesis size, the effective orifice area is considered a more reliable measure than the geometric orifice area [2,18]. Bioprosthetic valves typically have smaller diameters and EOAs compared to mechanical prostheses or stentless prostheses [15,18,27,31].

Our study of 31 patients undergoing surgical aortic valve replacement revealed a significant incidence of patient-prosthesis mismatch, affecting more than half of the cohort. This high prevalence of PPM can be attributed to a complex interplay of patient characteristics and surgical considerations.

To address the varied needs of our SAVR patients, we employed a range of prosthetic valves. Bioprosthetic options included the Hancock II (Medtronic, Minneapolis, MN, USA) and the Edwards Perimount (Edwards Lifesciences, Irvine, CA, USA). The Hancock II, a porcine valve, was used in 23 mm and 25 mm sizes, offering effective orifice areas of 1.3 cm² and 1.5 cm², respectively. The Edwards Perimount, a bovine pericardial valve, was used in sizes 19-25 mm, with EOAs spanning from 1.1-1.8 cm². For patients receiving mechanical valves, we utilized the Carbomedics Standard and Top Hat models (LivaNova, London, UK) in sizes 21-25 mm, providing EOAs between 1.5-2.3 cm².

The selection of appropriate valve size involved a delicate balance between minimizing PPM and avoiding more extensive surgical procedures like aortic root enlargement, which could potentially increase perioperative risks. Our strategy prioritized the safety of the patient and clinical improvement, sometimes engaging a grade of patient-prosthesis mismatch when the alternative poses a greater risks.

Interestingly, our analysis revealed that PPM did not significantly impact postoperative von Willebrand factor levels, VWF activity, or factor VIII levels in the short term. Further analysis of PPM severity subgroups (no/insignificant, moderate, severe) also showed no statistically significant differences in these parameters. This finding contradicts some previous studies [7,9,15] that suggested a relationship between PPM and VWF dynamics. The discrepancy might be attributed to the immediate hemostatic benefits of aortic valve replacement overshadowing any potential short-term effects of PPM on these parameters.

To further explore the implications of PPM in our cohort, we conducted additional analyses. We stratified patients based on the severity of PPM and examined correlations between the degree of mismatch and various clinical outcomes.

Our findings underscore the complexity of managing PPM. While the short-term VWF levels appeared unaffected, the long-term implications of PPM on hemostatic function, valve durability, and overall clinical outcomes remain uncertain. This highlights the need for extended follow-up studies to elucidate the full impact of PPM over time.

This observation suggests that the hemostatic recovery process following SAVR may be robust enough to overcome both blood group-related variations in VWF levels and any potential influences of PPM. It's important to note that this finding contradicts some earlier hypotheses that PPM might interfere with the normalization of hemostatic parameters post-surgery.

Our analysis revealed that baseline VWF levels, rather than the presence or severity of PPM, served as an independent negative predictor of postoperative bleeding. Specifically, patients with higher preoperative VWF levels tended to experience less postoperative bleeding, irrespective of whether they developed PPM.

While several studies have examined VWF dynamics in patients with aortic stenosis and after valve replacement, our study uniquely focuses on the specific relationship between PPM and immediate postoperative VWF levels. Previous research by Vincentelli et al. [8] and Frank et al. [19] demonstrated normalization of VWF

parameters after SAVR, but did not analyze the potential impact of PPM specifically. Similarly, Blackshear et al. [9] investigated VWF abnormalities in prosthetic valve dysfunction but did not address PPM specifically. Our study is therefore distinctive in examining PPM's influence on VWF dynamics, though our findings are limited to the immediate postoperative period. While we found no significant impact of PPM on VWF levels in this early phase, the long-term influence of PPM on VWF dynamics remains unknown and warrants further investigation through extended follow-up studies. Our ongoing research aims to address this knowledge gap by analyzing the long-term relationship between PPM and VWF parameters.

Conclusions

In conclusion, our study provides insights into the impact of patient-prosthesis mismatch on von Willebrand factor dynamics in patients undergoing surgical aortic valve replacement for severe aortic stenosis. While we did not observe a significant association between PPM and postoperative VWF levels in the short term, it is crucial to acknowledge that the persistent high shear stress caused by PPM could potentially lead to the re-emergence of acquired von Willebrand syndrome over time. Future result of our long follow-up study of this patients is warranted to elucidate the long-term implications of PPM on hemostatic function and clinical outcomes.

Limitations

Our investigation into patient-prosthesis mismatch among the 31 surgical aortic valve replacement patients faced several constraints that warrant consideration when interpreting the results.

A primary limitation was the short-term nature of our follow-up. This restricted timeframe allowed us to capture only the immediate post-operative effects of PPM, potentially missing longer-term hemostatic and clinical implications. The acute post-surgical period may not fully reflect the ongoing impact of PPM on valve function, hemodynamics, and patient outcomes. Extended observation periods in future studies could reveal whether PPM leads to progressive changes in von Willebrand factor levels or clinical endpoints that were not apparent in our short-term analysis.

The modest sample size of 31 patients, while providing valuable insights, limits the statistical power and generalizability of our findings. This constraint may have obscured subtle associations between PPM and VWF levels or clinical outcomes. Larger cohorts would enable more robust subgroup analyses, potentially uncovering PPM effects that vary based on factors such as prosthesis type, size, or patient characteristics.

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