Impact of Preoperative Thrombocytopenia on the Outcome after Coronary Artery Bypass Grafting

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Abstract

The impact of thrombocytopenia on postoperative bleeding and other major adverse events after cardiac surgery is unclear. This issue was investigated in a series of patients who underwent isolated coronary artery bypass grafting (CABG) from the prospective, multicentre E-CABG registry. Preoperative thrombocytopenia was defined as preoperative platelet count <150 x 10^9/L and it was considered moderate-severe when preoperative platelet count was <100 x 10^9/L. Multilevel mixed-effects regression analysis was performed to adjust the effect of thrombocytopenia on outcomes for baseline and operative covariates as well as inter-institutional differences in patient-blood management. Among 7189 patients included in this analysis, 599 (8.3%) had preoperative thrombocytopenia. Patient with preoperative thrombocytopenia had an increased chest drainage output at 12 hours (mean, 519 vs. 456 mL, adjusted coeff. 39, 95%CI 18-60) and rates of severe-massive bleeding (UDPB bleeding severity grades 3-4: 12.7% vs. 8.1%, adjusted OR 1.47, 95%CI 1.11-1.93; E-CABG bleeding severity grades 2-3: 10.4% vs. 6.1%, adjusted OR 1.78, 95%CI 1.30-2.43). Thrombocytopenia was associated with an increased risk of hospital/30-day death (3.2% vs. 1.9%, adjusted OR 2.02, 95%CI 1.20-3.42), 1-year death (5.7% vs. 3.4%, adjusted HR 1.68, 95%CI 1.16-2.44), deep sternal wound infection (3.5% vs. 2.4%, adjusted OR 1.65, 95%CI 1.02-2.66), acute kidney injury (28.1% vs. 22.2%, OR 1.45, 1.18-1.78) and prolonged stay in the intensive care unit (mean, 3.6 vs 2.8 days, adjusted coeff. 0.74, 95%CI 0.40-1.09). Similar results were observed in a subset of patients with moderate-severe thrombocytopenia (51 patients, 0.7%). In particular, these patients had a markedly higher rate of acute kidney injury (40%, adjusted OR, 1.94, 95%CI 1.05-3.57), resternotomy for bleeding (7.8%, adjusted OR 3.49, 95%CI 1.20-10.21), and severe-massive bleeding (UDPB bleeding severity grades 3-4: 23.5%, adjusted OR 3.08, 95%CI 1.52-6.22; E-CABG bleeding severity grades 2-3: 23.5%, adjusted OR 4.43, 95%CI 2.15-9.15) compared to patients with normal preoperative platelets count. Mild preoperative thrombocytopenia is associated with increased risk of severe-massive bleeding, mortality and other major adverse events after CABG. Such risks are markedly increased in patients with moderate-severe preoperative thrombocytopenia.

Introduction

Major bleeding is a common complication after cardiac surgery. It is associated with an increased use of blood products, re-exploration for bleeding, stroke, acute kidney injury, perioperative myocardial infarction, with consequent increase in mortality and excessive use of resources [1,2]. Impaired platelet function, mostly due to preoperative use of potent antiplatelet medications, is a well-recognized cause of major bleeding following cardiac surgery [3,4]. Randomized trial data suggested that point-of-care platelet function testing in an integrated transfusion algorithm reduces postoperative major bleeding and blood product transfusion [5]. Yet, a meta-analysis of randomized trials demonstrated that point-of-care platelet function testing to guide blood product transfusion did not improve the main clinical endpoints, although it reduced red blood cell and platelet transfusions [6]. Little is known about the impact of preoperative platelet count on postoperative major bleeding after cardiac surgery. We sought to explore the effect of preoperative thrombocytopenia on the incidence of postoperative major bleeding events in patients who underwent isolated coronary artery bypass grafting (CABG) from the multicentre E-CABG registry.

Methods

Study Cohort

E-CABG registry is a prospective, multicenter study that enrolled patients undergoing isolated CABG at 16 European centers of cardiac surgery from Finland, France, Italy, Germany, Sweden and United Kingdom. The detailed protocol and definition criteria were published before [7]. Data were collected prospectively and underwent robust validation and checking of its quality. Data submissions were constantly verified with regular data quality reports, with review of administrative and medical chart audits in order to correct clinical and temporal conflicts and/or discrepancies. The study was approved by the Institutional Review Board of the participating centers, and it was not supported financially. Informed consent was obtained in institutions where it was specifically required by the internal

Institutional Review Board, otherwise it was waived. The study is registered in clinicaltrials.gov (Identifier: NCT02319083).

Definitions and endpoints

Preoperative thrombocytopenia was defined as preoperative platelet count <150 x 10^9/L. Thrombocytopenia was considered moderate-severe when preoperative platelet count was <100 x 10^9/L. All the end-points of this registry were pre-specified [7]. The primary outcomes were chest drainage output at 12 hours after surgery, reoperation for bleeding, use of blood products, nadir levels of hemoglobin and hematocrit, as well as the severity of bleeding as graded by the E-CABG [7] and Universal Definition of Perioperative Bleeding (UDPB) bleeding severity stratification methods [1]. Secondary endpoints included hospital/30-day mortality, 1-year mortality, stroke, prolonged inotropic support, need of intra-aortic balloon pump and/or extra-corporeal membrane oxygenation, deep sternal wound infection, atrial fibrillation, acute kidney injury, de novo dialysis and length of stay in the intensive care unit. In this study, the length of hospital stay was not considered as an endpoint since the timing of patient discharge could have been influenced by the resources of postoperative rehabilitation.

Statistical Analysis

Statistical analysis was performed using a SPSS v. 24.0 (IBM Corporation, New York, USA) and Stata v. 14.2 (StataCorp LLC, Texas, USA). Covariates and outcomes were reported as counts and percentages, and as mean and standard deviation. The Mann-Whitney, Kruskal-Wallis, Chi-square and Fisher Exact tests were used to compare baseline and operative covariates between the study cohorts. In view of the significant baseline differences between patients with and those without preoperative thrombocytopenia as well as interinstitutional differences in perioperative bleeding and patient-blood management strategies, the outcomes were adjusted in multilevel mixed-effects logistic, linear and Cox proportional hazard regression models for the following covariates: age, gender, baseline

hemoglobin, estimated glomerular filtration rate, $P2Y_{12}$ inhibitors administered within 5 days from surgery, aspirin administered within 7 days from surgery, oral anticoagulants administered within 3 days from surgery, diabetes, stroke or transient ischemic attack, atrial fibrillation, pulmonary disease, extracardiac arteriopathy, number of diseased coronary arteries, urgent procedure, left ventricular ejection fraction ≤50%, critical preoperative state, prior cardiac surgery, prior percutaneous coronary intervention, off-pump surgery, bilateral internal mammary artery grafting and number of distal anastomoses. We did not include the duration of cross-clamping and cardiopulmonary bypass, because a significant number of patients in this series underwent off-pump CABG. The Kaplan-Meier method with the log-rank test was used to evaluate the differences in mid-term survival in the study cohorts. Since moderate-severe thrombocytopenia (platelets count <100 x 10^9/L) was present in a limited number of patients, but still might have had an impact on the study outcomes, further analyses were performed in three study cohorts with the following preoperative platelet counts: <100 x 10^9/L, 100-149 x 10^9/L and ≥150 x 10^9/L. All tests were 2-sided and $p<0.05$ was set for statistical significance.

Results

Baseline data

Of the 7352 patients enrolled in the registry, 7189 (97.8%) with data on preoperative platelet count were included in the final analysis. Mean age of the cohort was 67.3 ± 9.4 years; 16.1% were females; 31.0% diabetics; 45.8% underwent urgent procedure; 20.4% underwent off-pump surgery. Mean preoperative EuroSCORE II was 2.8±4.1%. Of the enrolled cohort, 599 patients (8.3%) had a platelet count <150 x 10^9 /L, 51 patients (0.7%) had a platelet count <100 x 10^9 /L and 18 patients (0.3%) had a platelet count <75 x 10^9 /L. In patients with preoperative thrombocytopenia, mean platelet count was 127.5 ± 19.7 x 10^9 /L (median, 133 x 10^9 /L; range, 30 x 10^9 /L – 149 x 10^9 /L). Baseline characteristics and operative data of these cohorts are summarized in Table 1.

Multilevel mixed-effects logistic regression showed that advanced age (per year, OR 1.02, 95%CI 1.01-1.03) and low hemoglobin level (per unit, OR 0.99, 0.98-0.99) were predictive of preoperative platelets

level <150 x 10^9 /L), whereas female gender (OR 0.43, 95%CI 0.31-0.56) and chronic obstructive pulmonary disease (OR 0.72, 95%CI 0.52-0.98) were associated with a significantly lower risk of thrombocytopenia.

Impact of preoperative thrombocytopenia on postoperative outcome

Patient with preoperative thrombocytopenia had increased chest drainage output at 12 hours postoperatively (mean, 519 vs. 456 mL, adjusted coeff. 39, 95%CI 18-60) and an increased risk of major-massive bleeding (UDPB bleeding severity grades 3-4: 12.7% vs. 8.1%, adjusted OR 1.47, 95%CI 1.11-1.93; E-CABG bleeding severity grades 2-3: 10.4% vs. 6.1%, adjusted OR 1.78, 95%CI 1.30-2.43) (Tab. 2). Patients with thrombocytopenia had a significantly increased risk of hospital/30-day death (3.2% vs. 1.9%, adjusted OR 2.02, 95%CI 1.20-3.42), 1-year death (5.7% vs. 3.4%, adjusted HR 1.68, 95%CI 1.16-2.44), deep sternal wound infection (3.5% vs. 2.4%, adjusted OR 1.65, 95%CI 1.02-2.66), acute kidney injury (28.1% vs. 22.2%, OR 1.45, 1.18-1.78) and prolonged length of stay in the intensive care unit (mean, 3.6 vs 2.8 days, adjusted coeff. 0.74, 95%CI 0.40-1.09).

Similar results were observed in a subset of patients with preoperative platelet count <100 x 10^9/L (51 patients, 0.7%) (Tab. 3). In particular, patients with moderate-severe thrombocytopenia had a significantly higher rate of acute kidney injury (40%, adjusted OR, 1.94, 95%CI 1.05-3.57), resternotomy for bleeding (7.8%, adjusted OR 3.49, 95%CI 1.20-10.21), and had higher rate of severe-massive bleeding (UDPB bleeding severity grades 3-4: 23.5%, adjusted OR 3.08, 95%CI 1.52-6.22; E-CABG bleeding severity grades 2-3: 23.5%, adjusted OR 4.43, 95%CI 2.15-9.15) compared to patients with normal preoperative platelets count.

Discussion

In the current analysis of the multicentre E-CABG registry data, preoperative thrombocytopenia was not uncommon in patients undergoing contemporary isolated CABG and it was associated with increased early postoperative blood loss, severe-massive bleeding and other major adverse events.

Such risks seem increased particularly in patients with preoperative platelets count <100 x 10^9/L. Indeed, one fourth of them experienced severe-massive bleeding as defined by the E-CABG and UDPB bleeding severity stratification criteria. It is worth noting that the impact of thrombocytopenia on these outcomes was adjusted for baseline and operative covariates as well as preoperative use of antithrombotics and any possible interinstitutional differences in patient-blood management using multilevel mixed-effects regression methods.

Investigation of factors associated with bleeding after CABG is crucial for reduction of the bleeding events and improvement of the outcome after cardiac surgery. Many preoperative factors such as prior bleeding history, preoperative hemoglobin, platelet dysfunction, time of discontinuation of antiplatelet medications before surgery are independently associated with perioperative bleeding and allogenic blood product transfusion [8]. Thrombocytopenia may intuitively be associated with increased perioperative bleeding. In a single-centre observational study, lower preoperative platelet count was independently associated with excessive bleeding after cardiac surgery [9]. However, the mean value of platelet count in patients who experienced excessive bleeding was within the normal range; the cutoff value of platelet count associated with postoperative bleeding risk was 214 x 10^9/L [9]. Other abnormalities of the coagulation system might have probably contributed to episodes of excessive bleeding in that study. In another study by the same investigators, lower preoperative platelet count was associated with re-exploration for bleeding in univariate, but not in multivariate analysis [10]. In a previous observational study of children undergoing cardiac surgery, lower platelet count during cardiopulmonary bypass was the variable most significantly associated with intraoperative and 12-hour blood loss in linear regression analysis (cutoff value was platelet count of 108 x 10^9/L) [11]. Other observational studies showed that lower post-bypass platelet count independently predicted early postoperative blood loss [12-14]. These findings are of clinical importance in view of the expected reduction of platelets count after cardiopulmonary bypass [15].

Similarly, in registry data of patients with atrial fibrillation who underwent percutaneous coronary intervention, preprocedural thrombocytopenia (<150 x 10^9/L) was not associated with postprocedural

bleeding, thromboembolic event rates and mortality [16]. Remarkably, in that registry study, prescribed antithrombotic medications were comparable between the two groups. Yet, in another registry data analysis, preprocedural thrombocytopenia before percutaneous coronary intervention was associated with more in-hospital major bleeding events, and independently predicted in-hospital mortality after urgent procedures [17].

Preoperative thrombocytopenia is recognized as a risk factor for bleeding and other adverse outcomes after non-cardiac surgery [18]. The evidence of an increased risk of perioperative bleeding after cardiac surgery associated preoperative thrombocytopenia is derived from a few studies [19-22]. A recent study by Ranucci and collegues [19] demonstrated that preoperative platelet count and $P2Y_{12}$-dependent platelet function were linearly associated along the whole spectrum of platelet count, and both were independent predictors of postoperative bleeding in multivariable analysis. In the current study, a preoperative platelet count <150 x 10^9/L as adjusted for baseline and operative covariates by propensity score matching was associated with greater chest drainage output at 12-hour and a trend toward increased rate of reoperation for bleeding, but it had no significant effect on postoperative severe-massive bleeding as defined by the E-CABG [7] and UDPB [1] bleeding severity criteria. Furthermore, patients with thrombocytopenia received similar amounts of red blood cell units either intra- or perioperatively even after propensity score matching. However, when only patients with a preoperative platelet count <100 x 10^9/L were compared, despite its low prevalence, it was invariably associated with an increased risk of blood loss, use of blood products and reoperation for bleeding. Importantly, one fourth of these patients experience severe-massive bleeding defined according to the E-CABG and UDPB bleeding severity classifications.

Recent studies from the Duke University Medical Center showed that postoperative thrombocytopenia were associated with increased risk of stroke, acute kidney injury and mortality after CABG [21,22]. The present study confirms these prior findings as thrombocytopenia was associated with an increased risk of early and 1-year mortality, deep wound infection, acute kidney injury and atrial fibrillation along with longer stay in the intensive care unit. The direct role of decreased platelet count on these major

adverse events is unclear. However, since perioperative thrombocytopenia was associated with significantly greater exposure to blood products and likely to increased blood loss and anemia [21,22], we speculate that thrombocytopenia may exert its negative effects through an increased risk of perioperative bleeding and use of prothrombotic agents. Other studies are needed to confirms these findings and investigate any direct effect of thrombocytopenia on postoperative end-organ injury.

Limitations

The current study has some limitations including unmeasured confounders and selection bias, which might have influenced the results. First, platelet dysfunction, fibrinogen level, thrombin generation, excessive fibrinolysis, and the viscoelastic properties of whole blood might have influenced major bleeding events in our cohort. Second, this registry did not collect data on preoperative use of blood products, therefore it is unclear whether some of these patients had their thrombocytopenia corrected before surgery. Third, the lack of intra- and postoperative levels of platelets prevented an analysis of the impact of perioperative thrombocytopenia on bleeding and other adverse events.

Conclusions

The results of this large multicentre study showed that preoperative thrombocytopenia is associated with increased risk of severe-massive perioperative bleeding, mortality and other major adverse events after CABG. Such risks are markedly increased in patients with moderate-severe preoperative thrombocytopenia.

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Table 1. Baseline characteristics and operative data.

	Platelets count 150-450 x 10^9/L (N=6590)	Platelets count <150 x 10^9/L (N=599)	p-value
Age (years)	67.2±9.4	68.9±9.2	<0.001
Female	1081 (16.6)	56 (9.4)	<0.001
Body mass index	27.6±4.1	27.6±4.0	0.95
Hemoglobin (g/L)	137±16	134±19	0.001
eGFR (mL/min/1.73 m^2)	81.5±25.0	81.8±29.6	0.82
Dialysis	68 (1.0)	12 (2.0)	0.03
Hypertension	5181 (79.5)	481 (81.1)	0.36
Diabetes	2035 (31.2)	177 (29.8)	0.48
Recent myocardial infarction	2093 (32.1)	179 (30.2)	0.32
Prior stroke/transient ischemic attack	380 (5.8)	31 (5.2)	0.54
Atrial fibrillation	520 (8)	58 (9.8)	0.12
Pulmonary disease	681 (10.5)	48 (8.1)	0.06
Extracardiac arteriopathy	1473 (22.6)	139 (23.4)	0.64
Ejection fraction ≤50%	1886 (29.0)	170 (28.7)	0.87
Prior percutaneous coronary intervention	1340 (20.6)	154 (26.0)	0.002
Prior cardiac surgery	30 (0.5)	8 (1.3)	0.004
Poor mobility	168 (2.6)	12 (2.0)	0.40
Critical preoperative state	404 (6.2)	54 (9.1)	0.005
Urgency of surgery			0.445
Elective	3552 (54.5)	307 (51.8)	
Urgent	2655 (40.8)	259 (43.7)	
Emergency	305 (4.7)	27 (4.6)	
Aspirin within 7 days	5747 (88.2)	512 (86.3)	0.17
P2Y12 within 5 days	979 (15.1)	72 (12.2)	0.06
Oral anticoagulation within 3 days	51 (0.8)	6 (1.0)	0.54
WILL-BLEED score	3.9±3.6	4.2±3.7	0.14
EuroSCORE II	2.8±4.1	3.0±3.9	0.16
CathPCI score	43.5±21.0	44.0±19.7	0.55
Number of aortic anastomoses	0.9±0.9	1.0±0.8	0.003
Number of distal anastomoses	2.7±0.9	2.7±0.9	0.99
Cardiopulmonary bypass time (min)	84.7±34.7	86.6±38.8	0.29
Aortic clamping time (min)	57.1±25.6	56.6±26.0	0.67
Off-pump surgery	1344 (20.6)	104 (17.5)	0.07
Bilateral internal mammary artery graft	2399 (36.8)	191 (32.2)	0.02

Continuous variables are reported as mean and standard deviation. Nominal variables are reported as counts and percentages. Clinical variables are according to the EuroSCORE II definition criteria. eGFR indicates estimated glomerular filtration rate according to the MDRD equation.

Table 2. Outcomes in the study cohorts.

Outcomes	Platelets count 150-450 x 10^9/L (N=6590)	Platelets count <150 x 10^9/L (N=599)	Univariate analysis p-value	Multivariate analysis p-value	Mixed-effects multivariate analysis Estimates
Hospital/30-day mortality	123 (1.9)	19 (3.2)	0.028	**0.009**	**2.02, 1.20-3.42**
1-year mortality (%)	3.4	5.7	0.009	**0.006**	**1.68, 1.16-2.44**
Intensive care unit stay (days)	2.8±3.6	3.6±8.7	0.045	**<0.0001**	**0.74, 0.40-1.09**
Stroke	75 (1.1)	7 (1.2)	0.946	0.947	1.03, 0.46-2.28
Prolonged inotropic support	1784 (27.1)	214 (35.7)	<0.0001	0.115	1.20, 0.96-1.49
Intra-aortic balloon pump	291 (4.4)	27 (4.5)	0.917	0.471	0.84, 0.52-1.36
Postoperative ECMO	42 (0.6)	3 (0.5)	0.685	0.843	0.88, 0.26-3.03
Deep sternal wound infection	157 (2.4)	21 (3.5)	0.090	**0.041**	**1.65, 1.02-2.66**
KDIGO acute kidney injury	1442 (22.2)	164 (28.1)	0.001	**<0.0001**	**1.45, 1.18-1.78**
De novo dialysis	112 (1.7)	18 (3.1)	0.019	**0.025**	**1.90, 1.08-3.17**
Postoperative atrial fibrillation	1736 (26.3)	197 (32.9)	0.001	**0.033**	**1.24, 1.02-1.51**
Drainage output at 12 hours (ml)	456±300	519±376	<0.0001	**<0.0001**	**43.01, 19.43-66.60**
Nadir hemoglobin (g/L)	99±16	100±17	0.747	0.075	0.98, -0.10-2.06
Nadir hematocrit (%)	30.0±4.8	30.0±4.8	0.819	0.100	1.04, -0.13-0.53
Reoperation for bleeding	168 (2.5)	21 (3.5)	0.161	0.164	1.44, 0.88-2.25
Blood products					
Red blood cells (units)	1.1±2.4	1.4±2.5	0.055	0.174,	0.13, -0.06-0.31
Fresh frozen plasma	398 (6.0)	57 (9.5)	0.001	**0.010**	**1.52, 1.11-2.08**
Platelets	478 (85.1)	89 (14.9)	<0.0001	**<0.0001**	**3.03, 2.27-4.03**
Fibrinogen	228 (3.5)	29 (4.8)	0.081	**0.001**	**2.02, 1.33-3.08**
Prothrombin	108 (1.6)	11 (1.8)	0.717	0.165	1.60, 0.82-3.10
Cryoprecipitate	20 (0.3)	0	0.405	1.000	-
rfVIIa	10 (0.2)	1 (0.2)	1.000	0.932	1.10, 0.13-9.46
E-CABG bleeding grades 2-3	404 (6.1)	62 (10.4)	<0.0001	**<0.0001**	**1.78, 1.30-2.43**
UDPB bleeding grades 3-4	529 (8.1)	75 (12.7)	<0.0001	**0.007**	**1.47, 1.11-1.93**

Continuous variables are reported as mean and standard deviation. Nominal variables are reported as counts and percentages. Estimates are odds ratios or coefficients with 95%confidence interval. CABG, coronary artery bypass grafting; ECMO, extracorporeal membrane oxygenation; KDIGO, Kidney Disease Improving Global Outcomes; UDPB, universal definition of perioperative bleeding; rVIIa, Recombinant factor VIIa. In bold are statistical significant values in multivariate analysis.

Table 3. Outcomes in cohorts with different preoperative platelet counts.

	Platelets count 150-450 x 10^9/L (N=6590)	Platelets count 100-149 x 10^9/L (N=548)	Platelets count <100 x 10^9/L (N=51)	Mixed-effects multivariate analysis p-value
Hospital/30-day mortality	123 (1.9)	17 (3.1)	2 (3.9)	**0.009**
1-year mortality (%)	3.4	5.7	4.3	**0.021**
Intensive care unit stay (days)	2.8±3.6	3.5±9.0	4.2±4.3	**<0.0001**
Stroke	75 (1.1)	6 (1.1)	1 (2.0)	0.803
Prolonged inotropic support	1784 (27.1)	196 (35.8)	18 (35.3)	0.112
Intra-aortic balloon pump	291 (4.4)	23 (4.2)	4 (7.8)	0.772
Postoperative ECMO	42 (0.6)	3 (0.5)	0	0.745
Deep sternal wound infection	157 (2.4)	19 (3.5)	2 (3.9)	**0.046**
KDIGO acute kidney injury*	1442 (22.2)	144 (27.0)	20 (40.0)	**<0.0001**
De novo dialysis	112 (1.7)	16 (3.0)	2 (4.0)	**0.021**
Postoperative atrial fibrillation	1736 (26.3)	178 (32.5)	19 (37.3)	**0.034**
Chest drainage output at 12 h (ml)	456±300	517±379	535±356	**<0.0001**
Nadir hemoglobin (g/mL)	99±16	100±17	93±13	0.152
Nadir hematocrit (%)	30±4.8	30±5	28±4	0.312
Resternotomy for bleeding	168 (2.5)	17 (3.1)	4 (7.8)	0.060
Blood products				
Red blood cells (units)	1.1±2.4	1.2±2.2	2.7±4.4	**0.027**
Fresh frozen plasma	398 (6.0)	45 (8.2)	12 (23.5)	**0.001**
Platelets	478 (7.3)	69 (12.6)	20 (39.2)	**<0.0001**
Fibrinogen	228 (3.5)	24 (4.4)	5 (9.8)	**<0.0001**
Prothrombin	108 (1.6)	8 (1.5)	3 (5.9)	**0.036**
Cryoprecipitate	20 (0.3)	0	0	1.000
rfVIIa	10 (0.2)	1 (0.2)	0	0.983
E-CABG bleeding grade 2-3	412 (6.3)	50 (9.1)	12 (23.5)	**<0.0001**
UDPB bleeding grade 3-4	537 (8.2)	63 (11.7)	12 (23.5)	**0.001**

Continuous variables are reported as median and interquartile range. Nominal variables are reported as counts and percentages. *, patients with CKD class 5 were excluded from the analysis. CABG, coronary artery bypass grafting; ECMO, extracorporeal membrane oxygenation; KDIGO, Kidney Disease Improving Global Outcomes; UDPB, universal definition of perioperative bleeding; rVIIa, Recombinant factor VIIa. In bold are statistical significant values.