Comparative Evaluation of 'Will Bleed, Papworth, Track and Trust' Bleeding Risk Scores in Diabetic Isolated Coronary Bypass Graft Surgery Patients and Laying the Foundations for Optimum Risk Score for Bleeding After Coronary Bypass Graft Surgery

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February 23, 2021

Abstract

Background: One of the most undesired complications after open heart operations is bleeding. In our study, we set ourselves two different goals: examining 'Papworth, Will-Bleed, Track and Trust' bleeding scoring systems to determine the most predictive one among diabetic patients undergoing isolated coronary bypass surgery, and determining the variables that should be included in the new scoring systems to be established for this patient group. Methods: The files of 297 diabetic patients who underwent isolated coronary artery bypass operation between 2017-2019 were retrospectively reviewed. Patients who underwent emergency surgery with a beating heart, those with reoperated open hart surgery, those with ticagrelor use, and those who died within the first 24 postoperative hours were excluded from the study. Drainage from the thorax and mediastinal tubes and blood product transfusions to the patients within the first 24 hours were noted and analyzed according to scoring systems. Results: Scoring systems are evaluated based on 'European Multicenter Study on Coronary Artery Bypass Grafting Bleeding Severity (E-CABG)'. In this study including diabetic patients only, Papworth was better predictive of E-CABG bleeding Grade 2-3. We found that Will-Bleed, Track, Trust, the other scoring systems we examined had discriminatory value in terms of E-CABG bleeding Grade 2-3 in our study group. Among the parameters in the scoring systems, we concluded that gender, preoperative hemoglobin (or hematocrit) value, preoperative platelet count, use of antiplatelets until less than five days prior to the operation, and preoperative creatinine (or eGFR) values should be included in the scoring system we aim to establish in the future, called the "Optimum Risk Score for Bleeding (ORS)." Conclusion: Considering the possible risks of bleeding and blood product transfusion, scoring systems that will provide accurate results for patient blood management will be lifesaving and increase the cost-effectiveness of the treatment.

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Conclusion: Considering the possible risks of bleeding and blood product transfusion, scoring systems that will provide accurate results for patient blood management will be lifesaving and increase the cost-effectiveness of the treatment.

Key Words: coronary artery bypass graft, will bleed. track, trust, E-CABG, papworth, bleeding

What's known

1-Despite the developing technique and technology, bleeding is still a serious problem after open heart surgery.

2- Bleeding; may cause mortality from cardiac tamponade and hypovolemic shock

3- Success in surgical treatment is not only operational success. Management of postoperative bleeding is at least as important as the surgical procedure.

What's new

1- New bleeding prediction scores are needed for isolated coronary bypass operations.

2- Although it causes vascular pathologies; we couldn't find relations between postoperative bleeding and DM

3-The bleeding scores examined in this study were insufficient to calculate the risk of postoperative bleeding in patients with DM.

Examination of variables that can be intervened by the clinician such as htc, creatinine, platelet in the preoperative period may decrease the postoperative bleeding level.

1 Introduction

In the light of the studies in the literature, we now know that postoperative bleeding is a serious cause of mortality and morbidity that disrupts the function and structural integrity of organs^{1,2} Bleeding can occur due to many different surgical procedures. However, the fact that atherosclerotic patients receive antiplatelet treatment is significant for cardiac surgeons, whose working area consists of blood and the circulatory system³. Conditions such as hemodilution, number and structural changes in platelets, and hypothermia which occur during cardiac operations performed with a heart-lung machine may also cause impairment of the coagulation system⁴. The need for blood transfusion in cardiac operations varies between 20% and 80% ⁵. This wide transfusion margin is because post-operative hemorrhagic drainage is considered normal for a certain period and amount unless the patient is hemodynamically unstable^{1,3}. While drains that do not disrupt hemodynamics do not require re-exploration, bleeding that causes hypovolemia can lead to permanent damage to vital organs and life-threatening consequences ⁶. As it requires more fluid replacement, postoperative volume loss increases the need for transfusion and related complication rates. In addition, postoperative bleeding has also been shown to increase ICU stay, infection rate, intubation time and hospital costs ^{7,8}. Postoperative bleeding may occur due to coagulopathy, or surgical technique and related problems. Whatever the reason, guidelines on blood management have been established ⁹ based on numerous studies performed on coronary bypass operations over the years. For successful postoperative bleeding control, the process needs to begin from the preoperative period ⁵. A thorough analysis of preoperative demographic data and drug use will help the postoperative process to proceed more smoothly. Detection of anemia, initiation of erythropoietin therapy and practices to increase preoperative blood reserve, such as blood donation, may help reduce the need for postoperative transfusion⁵. The need for transfusion can be significantly reduced with perioperative cell salvage methods¹⁰.

Less postoperative drainage results in the use of less blood product transfusions. Thus, complications related to blood product transfusion are also reduced. It is for this reason that scoring systems have been defined for the bleeding modality. The ones we investigate in this study, i.e., PAPWORTH, was developed by Vuylsteke et al ¹¹, WILL-BLEED, by Biancari et al. ³, ACTA-PORT, by Klein et al ¹², TRACK, by Ranucci et al ¹³, and TRUST was developed by Alghamdi et al ¹⁴.

For this retrospective study, the need to obtain informed consent was exempted. Our aim in this study was to review the scoring systems that can be used to predict early massive bleeding after CABG in diabetic patients undergoing isolated coronary bypass surgery and determine the parameters of the ORS, which is currently an ongoing project. The reason we chose this patient population is because diabetes causes microvascular endothelial dysfunction ^{15,16} and impairments have been shown in the fibrinolytic system and coagulation factor functions in diabetic patients ¹⁷. Endothelial damage, increased oxidative stress, chronic inflammation and impaired fibrinolytic system seen in patients with DM are its main causes¹⁷. Surgical technique-induced bleeding such as anastomotic leak, and non-ligatured vascular structures were found in the operation notes and these patients were excluded from our study.

2 Methods

We organized our study as a retrospective archive scan. Following the permission we received from the local ethics committee to scan the patient files (decision no: 2020/85), patients who underwent isolated coronary bypass operation at Kütahya Health Sciences University Evliya Çelebi Training and Research Hospital between 2017-2019 were examined. Inclusion criteria comprised patients who were diagnosed with diabetes mellitus and underwent an isolated coronary bypass operation for the first time. Patients who underwent beating heart surgery, presented to the emergency department with acute MI and started 'ticagrelor' treatment, and those who died within the first 24 hours postoperatively were excluded. In addition, the amount of drainage before re-exploration was used for the scoring systems in patients who were explored due to bleeding. Demographic characteristics and hematological parameters were determined according to the blood samples obtained preoperatively, at the closest date to the operation day. Since our study is focused on early postoperative bleeding, it includes the first 24 hours of postoperative follow-up, because bleeding and related complications are likely to occur in the early period. The amount of drainage and blood products used in the first 24 hours postoperatively were recorded.

This study was based on a prospective multicenter study in Europe, e-CABG (clinicaltrials.govIdentifier:NCT02319083). The bleeding scores (Papworth, Will-Bleed, Track, Trust) were compared with the E-CABG bleeding grades and analyzed to find which was more convenient for our patient population. In addition, significant parameters were determined, and it was aimed to lay the foundations of the ORS by using these parameters in larger studies.

E-CABG is a multi-center study conducted across 6 European countries (Germany, Italy, England, France, Sweden, Finland) and 16 centers ¹⁸. In this study, risk was calculated by scoring after grouping according to the blood products and amounts transfused.

2.1 Clinical Management

In our center, cardiac operations were performed under general anesthesia (fentanyl $35\mu g / kg$, pancuronium 0.1mg / kg) with positive pressure ventilation. Median sternotomy was performed in all patients and aorto-

right atrial cannulation method was preferred. Before switching to cardiopulmonary bypass (CPB), 3 mg / kg heparin was administered to the patients and additional heparin dose was given if necessary, to keep activated clotting time (ACT)> 480. When switching to CPB, antegrade or antegrade + retrograde crystalloid solutions were used as prime solutions according to the patient's body mass index. Systemic hypothermia was achieved by cooling the patient to 32°C. During the surgical procedure, blood accumulated in the thoracic cavity and pericardial area was collected in the reservoir and re-infused to the patient. However, unfortunately, methods such as cell saver could not be used. The cardiac operation was completed, and bleeding was controlled with protamine sulphate (3.1 mg / kg) administration to keep ACT <120 s during weaning from CPB.

The left hemithorax was opened with left pleural incision in all patients. The right hemithorax may have been opened in some patients, however, bleeding was monitored in the intensive care unit with 32 French drains placed in all hemithoracic cavities and 36 French drains placed in the mediastinum. After the sternum was closed with sternal wires, the subcutaneous and skin tissues were closed, and the intubated patient was transported to the intensive care unit. In our center, the surgical team is responsible for the intensive care of the patients were extubated in the intensive care unit based on the extubation criteria. According to the institution's protocol, patients with high volumes of drainage and/or hemodynamic instability were not extubated. In cases where the drainage was voluminous enough to impair hemodynamics, the patients were re-explored for bleeding revision. Fresh frozen plasma (FFP) was transfused to the patients if the central venous pressure was <8, or when the patient had more drainage than expected. Colloid solutions can be used instead of FFP, but FFP is primarily used due to clinical preference. Erythrocyte transfusion was performed when Hg <8 gm%. Platelet suspensions were administered according to the platelet count in the hemogram obtained postoperatively as the patient entered the intensive care unit.

Descriptive parameters of the scoring systems used in the study are shown in Table (Table 1).

2.2 Statistical analysis

Statistical analyses were performed using Jamovi Statistics (version 1.2.27solid) software. Shapiro-Wilk test, histograms, and Q/Q plots were used to identify the distribution patterns. Nominal variables were presented as number and percentage, normally distributed continuous variables as mean and standard deviation, and non-normally distributed continuous variables, as median and interquartile range. In addition to descriptive statistics, Chi-Square test was used for nominal values in the comparison of groups, Independent Samples t-test, for comparison of parametric data, and Mann-Whitney U test, for comparison of nonparametric data. Significant factors in univariate analysis were carried onto multivariate logistic regression analysis. P value <0.05 was considered statistically significant.

3 Results:

This study included the data of 297 diabetic patients who underwent isolated coronary bypass surgery. Since our study focuses entirely on postoperative bleeding, patients who died due to any other reason within the first 24 postoperative hours were excluded from the study, along with patients who were re-explored for any reason other than bleeding. We based our study on the E-CABG study and evaluated the bleeding prediction scores accordingly. In addition, we examined the average drainage amount of the patients and analyzed the data.

The patients were divided into two groups according to their E-CABG grades (Table 2). E-CABG Grades 0 and 1 (n = 260) were evaluated in the same group, just as Grades 2 and 3 (n = 37). Grade 2-3 patients had lower BMI (p <0.001), and higher drainage amounts in first 24 hours postoperatively (p<0.001), higher postoperative creatinine values (p = 0.02), higher amounts of postoperative blood product transfusion (RBC transfusion (p <0.001), FFP transfusion (p <0.001) and platelet transfusion (p <0.001)), and a higher ratio of female patients (p = 0.026).

Patients were grouped according to the amount of drainage from thoracic tubes and re-evaluated (Table 3). The median drainage was 600 ml (450ml and 850ml for 25% and 75% percentiles, respectively). A cut-off value of 850 ml (75% percentile) indicated massive drainage in our study group, and when grouped

accordingly, preoperative platelet count (p <0.001), creatinine clearance (p = 0.025), eGFR (p = 0.004) and BMI (p <0.001) values were significantly higher among patients with drainages of less than 850 ml/day. Postoperative creatinine values (p = 0.008) and female gender (p = 0.001) were higher in patients with a drainage of more than 850 ml/day.

Significant variables in univariate analysis or those confirmed as significant in clinical practice were carried onto multivariate analysis (Table 4). Risk factors for E-CABG II-III scores were analyzed in Models 1A and 2A, and risk factors for massive postoperative drainage were analyzed in Models 1B and 2B (Model 2A: Nagelkerke R² : 14.5%, Accuracy: 87.2%; Model 2B Nagelkerke R² : 15.1%, Accuracy: 74.4%). Accordingly, female gender (p = 0.01) and BMI (p < 0.001) were significant in E-CABG Group 2-3. In the multivariate analysis performed according to the amount of drainage, female gender (p = 0.015), preoperative platelet values (p = 0.037) and BMI (p < 0.001) were significant.

Examinations of risk scores (Table 5) determined that 'PAPWORTH' was significant for E-CABG Group 2-3 (p = 0.03). In our study, other scoring systems were not significant in predicting postoperative bleeding. However, all bleeding risk scores were insignificant in terms of drainage amount. Among the scoring parameters, preoperative hemogram (or hematocrit) value, platelet count, creatine (or eGFR), female gender, and antiplatelet use could be included into ORS.

4 Discussion

After coronary bypass (CABG) operations became routine procedures in many centers, various scientific studies were conducted on each phase of CABG operations. We now know that postoperative bleeding is a serious cause of mortality and morbidity^{19,20,21}. Bleeding may cause end organ damage due to low perfusion, which may lead to increased intensive care stay and hospital costs, cerebrovascular events, renal failure, mesentery ischemia, liver damage and ultimately, mortality^{19,20,21}. Therefore, postoperative bleeding is one of the nightmares of surgeons. Blood product transfusion, performed to avoid these complications caused by hypovolemia and low oxygen supply, is a risky procedure itself. Studies have shown that febrile reactions, renal dysfunction, respiratory distress, immunosuppression, infections, and even low cardiac output can occur after blood product transfusion^{22,23}. Our aim in this study was not to re-prove all this information, but by including only diabetic patients treated with CABG, to predict more clearly the risk of bleeding in the early period in a limited patient population. The progression of massive bleeding is clear. The reason we included only diabetic patients in our study is that diabetes is one of the biggest vascular damage predictors ²⁴, its association with atherosclerotic heart disease is high^{25,} and cardiovascular disease is the cause of mortality in approximately 75% of diabetic patients ²⁶.

The mean BMI values of patients in the E-CABG Group 2-3 is lower than those in Group 1-2. In PAPWORTH risk scoring, low BMI is a risk factor for postoperative bleeding ¹¹. Frankly, we could not find the mechanism explaining the relationship between BMI and bleeding in our literature review. However, BMI is calculated as kg/m^2 ORS' as a risk parameter.

^{1,3}. It can be suggested that patients with normal preoperative hemogram (or hematocrit) values will need less transfusion in the postoperative period. The number of platelets, which are the basic elements of the coagulation system, and their functional capacity, are also effective on postoperative bleeding 27,28,29

Our study included on-pump CABG patients. It is a known fact that the heart-lung machine causes end organ damage ³⁰ due to changes in microcirculation and blood pressure, as well as microthrombi^{31,3233} RS list. Among the bleeding scores, only Will-Bleed and Trust scores examine kidney functions. We believe this to be deficiency of Papworth and Track.

There may be differences between genders in terms of clinical course and diseases. In the evaluation of postoperative bleeding, the female gender was at higher risk 34,35

In our study, age, hypertension, pulmonary hypertension, COPD, and peripheral vascular diseases were not associated with postoperative bleeding. Interestingly, no significant results were obtained in terms of the tendency to bleed postoperatively in patients who were taken to emergency surgery. Antiplatelet agents are one of the main therapeutic agents in coronary artery diseases 36 . While discontinuation of acetylsalicylic acid (ASA) before the operation is not recommended, clopidogrel and the less frequently used ticagrelor should be discontinued at least 5 days before the operation 36 . Patients receiving ticagrelor were not included in the study. However, those using clopidogrel and ASA were not evaluated in separate groups. This can be considered the biggest limitation of our study. We can attribute the lack of statistically significant bleeding in patients undergoing emergency surgery to two reasons: The fact that the number of patients undergoing emergency operation is lower than those using ASA, and patients undergoing emergency surgery have recently been diagnosed with CAD and therefore have not received antiplatelet therapy before the operation. Ultimately, as clearly shown in the guidelines, the amount of postoperative bleeding may vary depending on the type of antiplatelet agent, and this is a proven fact that cannot be ignored for the timing of the operation 36 . Therefore, preoperative use of antiplatelets will be included in our ORS, which we plan to present with larger case numbers in the future.

5 Conclusion

Current risk scores have been created for all open-heart surgery operations. Therefore, scoring may not yield accurate results for every type of surgery. We think that specific risk scores are needed for isolated CABG for a smoother surgical recovery process.

Disclosure

The authors declare that they have no conflict of interest.

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Table 1: Descriptive parameters	of t	he scoring	systems	used	in '	the s	study	Ţ
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Trust Score	Score	Track Score	Score
Hb < 13.5 g/dl	1	Age > 67 years	6
Weight < 77 kg	1	Weight: $<60 \text{ kg}$ (female) < 85 kg (male)	2
Female Sex	1	Female Sex	4
Age > 65 years	1	Complex Surgery	7
Nonelective Surgery	1	Hematocrit (Continuous)	1 point per each value $(\%)$ below 40%
Creatinine > 1.36 mg/dl	1		
Previous Cardiac Surgery	1		
Nonisolated Operation	1		
Will-Bleed Score	Score	Papworth Score	Score
LMWH, UFH,Fpx Usage	1	Surgery Priority: urgency/ emergency	1
Potent antiplatelet drug pause	2	Surgery Type: Other than CABG or single valve	1
Female Sex	2	Aortic valve disease: stenosis, regurgitation or both	1
Acute Coronary Syndrome	2	BMI: < 25	1
	3	Age	1
eGFR < 45 mL/min/173m ²	3		
Critical preoperative state	5		

E-CABG Bleeding Classification	Intervention for the treatment of bleeding	Intervention for the treatment of bleeding	Additive Score
Grade 0	No transfusion of blood products except 1 unit of RBCs	No transfusion of blood products except 1 unit of RBCs	0
Grade 1	Transfusion of platelets Transfusion of fresh frozen plasma or	Transfusion of platelets Transfusion of fresh frozen plasma or	233
	Octaplas Transfusion of 2-4 units of RBCs	Octaplas Transfusion of 2-4 units of RBCs	
Grade 2	Transfusion of 5-10 units of RBCs Reoperation for	Transfusion of 5-10 units of RBCs Reoperation for	5 5
Grade 3	bleeding Transfusion of >10 units of RBCs	bleeding Transfusion of >10 units of RBCs	7

LMWH: Low molecular weight heparin, UFH: un fractionated heparin, FPX: fondaparinux

 ${\bf Table} \ {\bf 2}: \ {\rm Determination} \ {\rm of} \ {\rm demographic} \ {\rm characteristics} \ {\rm and} \ {\rm hematological} \ {\rm parameters} \ {\rm according} \ {\rm to} \ {\rm E-CABG}$

Variables	E-CABG Grade	E-CABG Grade	E-CABG Grade	E-CABG Gr
	Grade 0-1 $(n=260)$	Grade 0-1 $(n=260)$	Grade 2-3 (n=37)	Grade 2-3 (r
	$Mean \pm SD$	Median (IQR)	$Mean \pm SD$	Median (IQI
Age	63.4 ± 9.3	64.5(58-69)	64.2 ± 9.3	65.0(57.0-69)
Postoperative Drainage (0-24h)	600 ± 218	550 (450 - 750)	1332 ± 453	1450(1100 - 1)
Preoperative Hemoglobin (g/dl)	13.4 ± 1.9	13.6 (12.0 - 15.0)	13.9 ± 1.7	14.2(13.0 - 14)
Preoperative Hemotocrit (%)	39.1 ± 5.7	$39.4 \ (35.0 - 43.8)$	40.3 ± 5.0	41.0(38.2 - 43)
Preoperative Platelet $(10^3/ul)$	248 ± 77.4	$237\ (198-290)$	229 ± 102	222 (190 - 252)
Preoperative MPV (fl)	$9.63{\pm}1.05$	$9.60\;(8.9-10.3)$	$9.81{\pm}~1.18$	9.90 (8.9 - 10.
Preoperative Creatinine (mg/dl)	1.09 ± 0.51	$1.00\ (0.86-1.16)$	1.1 ± 0.33	1.04 (0.90 - 1.
Preoperative Creatinine Clearance	80.9 ± 27.0	79.3(64.8 - 98.3)	73.8 ± 22.8	71.7 (57.1 - 88)
Postoperative Creatinine (mg/dl)	$1.15 \pm\ 0.51$	$1.06\ (0.93-1.22)$	$1.35 \pm \ 0.34$	1.31 (1.20 - 1.)
$eGFR (ml/dk/1.73m^2)$	64.5 ± 20.8	$63.3\ (50.2-76.4)$	58.6 ± 19.7	55.3(44.4 - 71)
BMI	$28.1 {\pm} 4.0$	28.0(25.6-30.5)	$25.3 \pm \ 3.3$	25.5(23.5-26.
BSA	$1.85 \pm \ 0.16$	1.85 $(1.74 - 1.96)$	$1.83 \pm \ 0.13$	1.86(1.72 - 1.5)
Euroscore II	3.92 ± 5.78	$2.08\ (1.34 - 3.84)$	$4.06 \pm \ 5.03$	2.35(1.48 - 4.
Ejection Fraction	48.8 ± 10.0	50(40-60)	$48.4 \pm \ 10.2$	50(40-55)
RBC transfusion	1.4 ± 1.0	1(1-2)	$4.6{\pm}~1{,}8$	5 (1-2)
FFP transfusion	2.7 ± 1.2	3(2-3)	$4.8{\pm}~1.6$	5(2-3)
Platelet transfusion	0.2 ± 0.4	0(0-0)	$0.9\pm$ 1.0	1 (0 - 1)
Variables	E-CABG Grade	E-CABG Grade	E-CABG Grade	E-CABG Gr
	Grade 0-1 (n=260)	Grade 0-1 (n=260)	Grade 2-3 (n=37)	Grade 2-3 (n
	n	%	n	%
Gender (Female)	193	74.2	35	94.6
Reexploration for bleeding	0	0	29	78.4
DM (OAD)	127	48.8	17	45.9
DM (insulin dependent)	133	51.2	20	54.1
Hypertension	112	43.1	17	45.9
Peripheral vascular disease	60	23.1	8	21.6
Pulmonary HT (>60mmHg)	19	7.3	2	5.4
Preoperative IABP	18	6.9	4	10.8

CPD	42	16.2	2	5.4
Emergent Surgery	23	8.8	4	10.8

BMI: Body mass index, BSA: Body surface area, RBC: Red blood cell, FFP: Fresh frozen plasma, DM: Diabetes mellitus, CPD: Chronic pulmonary disease

 $\label{eq:table 3} \textbf{Table 3}: Determination of demographic characteristics and hematological parameters according to drainage amount$

Variables	Groups	Groups	Groups
	Drainage < 850 ml/day (n=218)	Drainage<850ml/day (n=218)	Drainage [?]850ml/d
	Mean \pm SD	Median (IQR)	Mean \pm SD
Age	63.2 ± 9.3	65(57-69)	64.4 ± 9.1
Postoperative Drainage (0-24h)	525 ± 161	550(400-650)	$1149 \pm \ 338$
Preoperative Hemoglobin (g/dl)	13.5 ± 1.88	13.7(12.0-15.0)	13.5 ± 1.97
Preoperative Hemotocrit (%)	39.3 ± 5.6	39.5(35.0-44.0)	39.1 ± 5.7
Preoperative Platelet (10 ³ /ul)	253 ± 76	$242 \ (206 - 296)$	$227 \pm \ 91$
Preoperative MPV (fl)	9.68 ± 1.02	$9.65 \ (8.93 - 10.4)$	9.58 ± 1.18
Preoperative Creatinine (mg/dl)	1.06 ± 0.50	1.00 (0.84 - 1.16)	1.15 ± 0.48
Preoperative Creatinine Clearance	82.1 ± 26.9	$81.9\ (64.8-99.4)$	74.3 ± 23.8
Postoperative Creatinine (mg/dl)	1.13 ± 0.50	1.05(0.91-1.22)	1.30 ± 0.49
$eGFR (ml/dk/1.73m^2)$	65.9 ± 21.1	63.6(50.9-78.5)	$58.0 \pm \ 18.8$
BMI	28.4 ± 4.1	$28.1 \ (25.7 - 30.9)$	26.1 ± 3.1
BSA	1.85 ± 0.16	1.85(1.73-1.96)	$1.85 \pm \ 0.13$
Euroscore II	3.88 ± 5.15	2.09(1.34-3.98)	$4.09 \pm \ 6.98$
Ejection Fraction	48.6 ± 10.0	50 (40-60)	48.9 ± 10.1
RBC transfusion	1.3 ± 1.0	1 (1-2)	3.1 ± 1.9
FFP transfusion	2.7 ± 1.2	2(2-3)	3.9 ± 1.6
Platelet transfusion	0.2 ± 0.4	0(0-0)	$0.5\pm$ 0.8
Variables	Groups according to drainage	Groups according to drainage	Groups according to
	Drainage < 850 ml/day (n=218)	Drainage < 850 ml/day (n=218)	Drainage [?]850ml/d
	n	%	n
Gender (Female)	157	72.0	71
Reexploration for bleeding	1	0.5	28
DM (OAD)	103	47.2	41
DM (insulin dependent)	115	52.8	38
Hypertension	96	44.0	33
Peripheral vascular disease	52	23.9	16
Pulmonary HT (>60mmHg)	17	7.8	4
Preoperative IABP	16	7.3	6
CPD	35	16.1	9
Emergent Surgery	21	9.6	6

BMI: Body mass index, BSA: Body surface area, RBC: Red blood cell, FFP: Fresh frozen plasma, DM: Diabetes mellitus, CPD: Chronic pulmonary disease

Table 4: Determining the variables with multivariate analysis which were found statistically significant inunivariate analysis or confirmed to be significant in clinical practice

VariablesMultivariate analysis (E-CABG Group II-III)Multivariate analysis (E-CABG Group IIModel 1AModel 1A

Age Gender (Female) Preoperative Hb Preoperative Plt. eGFR BMI Emergent Surgery Variables Age Gender (Female) Preoperative Plt. eGFR	OR (95% CI)* $1.02 (0.97-1.06)^{NS}$ $4.04 (0.80-20.41)^{NS}$ $1.11 (0.90-1.37)^{NS}$ $1.00 (0.99-1.00)^{NS}$ $1.00 (0.98-1.02)^{NS}$ $0.81 (0.72-0.91)^{***}$ $1.59 (0.49-5.22)^{NS}$ Multivariate analysis (Drainage[?]850ml/day) Model 1B OR (95% CI)* $1.01 (0.98-1.04)^{NS}$ $2.17 (0.88-5.30)^{NS}$ $0.97 (0.99-1.00)^{*}$ $0.99 (0.98-1.01)^{NS}$	LR test statistics $X^{2}_{(1)}=0.62, p=0.43$ $X^{2}_{(1)}=3.58, p=0.06$ $X^{2}_{(1)}=0.98, p=0.32$ $X^{2}_{(1)}=0.56, p=0.45$ $X^{2}_{(1)}=0.001, p=0.97$ $X^{2}_{(1)}=1.44, p<.001$ $X^{2}_{(1)}=0.55, p=0.46$ Multivariate analysis (Drainage[?]850ml/o Model 1B LR test statistics $X^{2}_{(1)}=0.289, p=0.59$ $X^{2}_{(1)}=3.09, p=0.08$ $X^{2}_{(1)}=4.36, p=0.04$ $X^{2}_{(1)}=1.16, p=0.28$
eGFR	$0.99 (0.98-1.01)^{NS}$	$X^{2}_{(1)}=1.16, p=0.28$
BMI Emergent Surgery	$\begin{array}{c} 0.86 \ (0.80\text{-}0.94)^{***} \\ 0.77 \ (0.29\text{-}2.11)^{\text{NS}} \end{array}$	$X^{2}_{(1)}=14.3, \mathbf{p}<.001$ $X^{2}_{(1)}=0.25, \mathbf{p}=0.61$

Hb: Hemoglobin, Plt: Platelet, OR: Odds ratio, CI: Confidence interval, LR statistics: Omnibus Likelihood ratio test statistics and p value, *: p value (^{NS}: nonsense, *: p<0.05, **: p<0.01, ***: p<0.001) of Wald test statistics of logistic regression analysis

Table 5 : Univariate analysis of risk scores. Predictors of E-CABGII-III and Drainage[?]850ml/day

Assessments of risk scores for E-CABG Group II-III	Assessments of risk scores for E-CABG Group II-III Estimate
PAPWORTH TRUST TRACK WILL-BLEED ACTAPORT Assessments of risk scores for Drainage[?]850ml	0.592 0.055 -0.023 -0.050 -0.013 Assessments of risk scores for Drainage[?]850ml Estimate
PAPWORTH TRUST TRACK WILL-BLEED ACTAPORT	0.365 -0.074 -9.95e-4 -0.050 0.006

S.E.: standart error, O.R.: odds ratio, CI: confidence interval, L.E. lower end, U.E.: upper end