POBS-Card, a new score of severe bleeding after cardiac surgery: Construction and external validation

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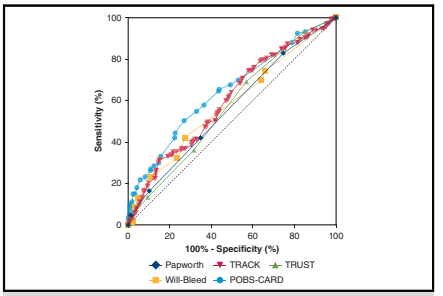
ABSTRACT

Objective: Bleeding after cardiac surgery leads to poor outcomes. The objective of the study was to build the PeriOperative Bleeding Score in Cardiac surgery (POBS-Card) to predict bleeding after cardiac surgery.

Methods: We conducted a retrospective cohort study in 2 academic hospitals (2016-2019). Inclusion criteria were adult patients after cardiac surgery under cardiopulmonary bypass. Exclusion criteria were heart transplantation, assistance, aortic dissection, and preoperative hemostasis diseases. Bleeding was defined by the universal definition for perioperative bleeding score $\geq$2. POBS-Card score was built using multivariate regression (derivation cohort, one center). The performance diagnosis was assessed using the area under the curve in a validation cohort (2 centers) and compared with other scores.

Results: In total, 1704 patients were included in the derivation cohort, 344 (20%) with bleeding. Preoperative factors were body mass index <25 kg/m^2 (odds ratio [OR], 1.48 [1.14-1.93]), type of surgery (redo: OR, 1.76 [1.07-2.82]; combined: OR, 1.81 [1.19-2.74]; ascendant aorta: OR, 1.56 [1.02-2.38]), ongoing antiplatelet therapy (single: OR, 1.50 [1.09-2.05]; double: OR, 2.00 [1.15-3.37]), activated thromboplastin time ratio >1.2 (OR, 1.44 [1.03-1.99]), prothrombin ratio <60% (OR, 1.91 [1.21-2.97]), platelet count <150 g/L (OR, 1.74 [1.17-2.57]), and fibrinogen <3 g/L (OR, 1.33 [1.02-1.73]). In the validation cohort of 597 patients, the area under the curve was 0.645 [0.605-0.683] and was superior to other scores (WILL-BLEED, Papworth, TRUST, TRACK). A threshold >14 predicted bleeding with a sensitivity of 50% and a specificity of 73%.

Conclusions: POBS-Card score was superior to other scores in predicting severe bleeding after cardiac surgery. Performances remained modest, questioning the place of these scores in the perioperative strategy of bleeding-sparing. (JTCVS Open 2024;19:183-99)



POBS-Card has highest predictive performance for severe bleeding after cardiac surgery.

CENTRAL MESSAGE

Bleeding after cardiac surgery is a major issue. In a cohort of 1700 patients, we developed a predictive score (POBS-Card). Its performance was better than other scores in a validation cohort.

PERSPECTIVE

This study highlights the difficulty of predicting the risk of bleeding during cardiac surgery, probably because of the high complexity of this setting. The use of scores must therefore be cautious and be part of an overall approach to risk prevention and patient blood management. Another aspect of the use of scores is their application as a matching tool for clinical trials.

Cardiac surgery creates a high risk of perioperative bleeding and can cause the need for blood product transfusion and reoperation. All of these factors may lead to poor outcomes, such as postoperative infection, kidney failure, shock, and even mortality, with subsequent increases in hospital length of stay and related health care costs.[1-4] Several factors are implicated in bleeding. Some are related to the specific characteristics of the patient, such as age, presence of malnutrition, anticoagulant or antiplatelet drugs, and preoperative coagulation disorders,

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Abbreviations and Acronyms

aPTT	= activated partial thromboplastin time
AUC	= area under the receiver operating characteristics curve
BMI	= body mass index
CPB	= cardiopulmonary bypass
eGFR	= estimated glomerular filtration rate
POBS-Card	= PeriOperative Bleeding Score in Cardiac surgery
PT	= prothrombin ratio
ROC	= receiver operating characteristic
UDPB	= universal definition for perioperative bleeding

and some are related to the type and the characteristics of the surgery.

Strategies aiming to reduce bleeding are of importance to improve patient outcomes, and guidelines have been published in pursuit of this objective.[5] To identify patients at high risk of bleeding, it is therefore important to implement preventive pre- and intraoperative strategies. Several risk stratification scores have been established.[6-8] However, their performance diagnosis is not discriminant when assessed in others than the initial population study.[9] Several hypotheses may explain this difference: absence of an external validation, progression of cardiopulmonary bypass (CPB) management, exclusive surgery type, and selection of a specific surgical risk patient. Mostly, the common limit that various definitions of bleeding make comparisons difficult.

A standard definition of bleeding has been established as the universal perioperative bleeding definition (UDPB) by the multidisciplinary International Initiative on Haemostasis Management in Cardiac Surgery. It takes in account both the postoperative blood loss and the perioperative transfusion, with a good correlation with major outcomes and mortality.[10] Considering that new standard definition, we hypothesized that the establishment of a new score will be more robust.

To date, the WILL-BLEED is the only score solely based on UDPB. However, this score has only been validated for coronary bypass graft surgery, which places patients at lower risk of bleeding in comparison with more complex surgeries, such as open heart or aortic root/arch surgeries.

Taken together, the current scores suffer from major limitations that we aimed to take in account to improve the performance to predict postoperative bleeding. Notably, we aimed to improve the performance to predict bleeding by using the UDPB criteria of bleeding and by validation of the score on an external cohort to test its robustness.

The aim of the study was to develop a score of bleeding based on the UPDB classification with confirmation of its prediction performance on a validation cohort. The other end point was to compare its prediction performance with current bleeding scores.

METHODS

Study Design and Population Study

We conducted a retrospective cohort study in 2 tertiary university hospitals from January 2016 until March 2019. The study was divided in 2 steps. The first step was dedicated to the identification of preoperative predictive variables of bleeding in a derivation cohort from the center 1 (2016-2018), in the objective of elaborating a predictive score, the PeriOperative Bleeding Score in Cardiac surgery (POBS-Card) score. The second step was dedicated to the validation of this score and its comparison with existing scores during the period immediately following (2019) in center 1 and in an external center (center 2, 2017 period). The selection of an external center during the same period than the derivation cohort and another period from the same center was chosen to strengthen the validation of the score and to limit bias related to change of practices over the time.

Because of the retrospective nature of the study and according to the relevant French law on clinical research, no written consent was required.[11] It was approved by the ethics committee of the French society of anesthesiology (French Society of Anaesthesia, Critical Care and perioperative Medecine; IRB00010254-2023-064, on May 30, 2023). The collection and analyses of data followed the MR-004 protocol from the French commission for data protection (Commission nationale de l'informatique et des libertés). The article was written in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology Statement.[12]

Adult patients were eligible if they benefited from a cardiac surgery with CPB. Exclusion criteria were age younger than 18 years; pregnant or breastfeeding; inherited or acquired coagulation diseases; cardiac surgery for aortic dissection, heart, or lung transplantation; pulmonary artery embolectomy or intracardiac tumor; incomplete medical file; and missing preoperative laboratory tests. Details on patient care and CPB protocols are presented in Appendix E1.

End Points

The main end point was the occurrence of a severe bleeding after surgery, defined by a UDPB score $\geq$2. The UDPB scoring includes items within 12 hours after surgery (see Appendix E1 and Table E1).[10] To summarize, a score of 2 indicates a bleeding of at least 801 mL/12 hours and/or a transfusion of at least 2 packed red blood cells and/or 2 fresh frozen plasma units and/or 1 platelet concentrate and/or administration of fibrinogen concentrates, prothrombin complex concentrates, or recombinant activated factor VII. Because of possible bias related to transfusion, a second analysis of bleeding was performed, including only the chest tube blood loss and the need for surgical re-exploration.

The secondary end points were the duration of invasive mechanical ventilation and intensive care unit (ICU) stay, the occurrence of an acute kidney injury defined, as a maximal Kidney Disease: Improving Global Outcomes score superior or equal to 1, the occurrence of a major complication defined as a shock state (all causes), acute respiratory distress syndrome, any type of infection or an acute kidney injury, and death.

Data Collection

Data were retrospectively collected through the medical ICU software ICCA (Philips Healthcare) and Centricity Critical Care (GE Healthcare). The following potential predictors for bleeding were collected: usual laboratory tests the day before the surgery (blood coagulation tests, including hemoglobin, activated partial thromboplastin time [aPTT], prothrombin ratio [PT], platelet count and fibrinogen; creatinine and associated estimated glomerular filtration rate [eGFR] estimated with the Modification of Diet in

Renal Disease equation); type of surgery (valvular, coronary bypass, combined, ascendant aorta; elective or emergent; redo surgery); and patient characteristics (left ventricular ejection fraction; age; gender; body mass index [BMI], ongoing anticoagulant or antiplatelet treatments). An antiplatelet drug was considered ongoing if the drug was administrated within 3 days before surgery for acetylsalicylic acid, 5 days for clopidogrel and ticagrelor, and 7 days for prasugrel, as recommended by the French group on perioperative hemostasis.[13] An anticoagulant therapy was considered ongoing if the drug was administrated within 3 days before surgery for apixaban and rivaroxaban, 5 days for dabigatran and fluindione, and 7 days for warfarin. Data were also classified according to predetermined thresholds, either according to data from the literature when available, or otherwise to thresholds considered clinically pertinent.

Statistics

Data are presented as medians with first and third quartile [Q1-Q3] for continuous data and as percentages and absolute numbers for discontinuous data. The elaboration of the POBS-Card score was performed according to the Transparent Reporting of multivariable prediction model for Individual Prognosis or Diagnosis guidelines.[14] Statistics were performed using Prism, version 9.0 (GraphPad) and Medcalc, version 14.0 (Medcalc Software Ltd).

Step 1: Elaboration of the POBS-Card Score From the Derivation Cohort

The population was divided in 2 groups according to the severity of the bleeding: insignificant-mild (UDPB 0-1) or moderate-severe (UDPB 2-4). Comparisons of continuous data were performed using the Mann-Whitney *U* test for unpaired values or Student *t* test according to the normality of the population, explored using a D'Agostino test. Discontinuous data were compared using the χ^2 or Fisher exact tests.

Then, we explored the association between the occurrence of a moderate-severe bleeding and different variables of interest. A univariable logistic regression analysis was first performed including the variables: age, gender,

TABLE 1. Preoperative characteristics in the derivation cohort

Variables	Insignificant/mild (n = 1360)	Moderate/severe (n = 344)	*P* value
Age, y	68 [61-74]	69 [62-75]	**.047**
>80 y, % (n)	6.8 (93)	10.5 (36)	**.03**
Male gender, % (n)	74 (1004)	72 (246)	.4
BMI, kg/m^2	28 [24.9-31.7]	26.9 [23.7-30.1]	**<.0001**
<25 kg/m^2, % (n)	25.8 (351)	35.5 (122)	**.0005**
LVEF, %	64 [56-70]	63 [53-70]	.1
Creatinine, μmol/L	85 [71-102]	89 [75-110]	**.0004**
>100 μmol/L, % (n)	25.8 (351)	33.4 (115)	**.006**
eGFR, mL/min/m^2	79 [62-95]	73 [55-89]	**.0001**
<45 mL/min/m^2, % (n)	8.1 (110)	13.1 (45)	**.006**
Redo surgery, % (n)	4.2 (57)	9.0 (31)	**.0009**
Antiplatelet therapy,* % (n)			**.01**
Single	15.0 (204)	18.9 (65)	
Dual	3.7 (50)	6.4 (22)	
Anticoagulant therapy,* % (n)	4.7 (64)	6.1 (21)	.3
Hemoglobin, g/dL	13.9 [12.8-14.8]	13.4 [12.4-14.6]	**<.0001**
<12 g/dL, % (n)	13.6 (185)	19.8 (68)	**.005**
Prothrombin ratio, %	92 [81-100]	86 [74-100]	**<.0001**
<60%, % (n)	5.2 (70)	12.5 (43)	**<.0001**
aPTT ratio	1.05 [0.99-1.13]	1.07 [1.00-1.18]	**<.0001**
>1.2	13.2 (180)	21.5 (74)	**.0002**
Platelets count, g/L	223 [188-264]	206 [168-248]	**<.0001**
<150 g/L, % (n)	7.1 (97)	13.4 (46)	**.0004**
Fibrinogen, g/L	3.46 [2.95-4.07]	3.39 [2.90-4.10]	.3
<3 g/L, % (n)	27.1 (369)	32.6 (112)	.049
Urgent surgery, % (n)	16.2 (220)	18.1 (64)	.4
Type of surgery, % (n)			.005
Coronary bypass	25.9 (378)	20.1 (69)	
Valvular	50.1 (682)	50.6 (174)	
Combined	10.7 (146)	15.4 (53)	
Ascendant aorta	11.3 (154)	13.9 (48)	

Bold refers to $P < .05$. *BMI*, Body mass index; *LVEF*, left ventricular ejection fraction; *eGFR*, estimated Glomerular Filtration Rate using Modification of Diet in Renal Disease formula; *aPTT*, activated partial thromboplastin time. *Antiplatelet and anticoagulant therapy ongoing at the time of the surgery.

BMI, type of surgery, anticoagulant and antiplatelet therapy, preoperative coagulation tests, and eGFR. Variables presenting a $P < .05$ in this first analysis were included in a multivariable logistic regression analysis, with a backward stepwise process, to adjust for confounders (logistic regression full model). *P* values were computed using the Wald method. A Hosmer-Lemeshow test was computed to evaluate the fitness of logistic regression with presented data. To confirm the independency of variables and provide more precise odds ratios, we performed a second logistic regression including only variables with a significant association in the initial full model (logistic regression final model). Results are presented as odds ratio with 95% confidence intervals. The candidate variables for inclusion in the POBS-Card score were those with a $P < .05$ in the final multivariable model.

The elaboration of the predictive POBS-Card score was performed as previously published.[15,16] Variables with a significant association with bleeding ($P < .05$) in the multivariable analysis were eligible for inclusion in the score. The regression coefficients (β parameters) of the included variables were identified from this analysis. The variable with the lowest β parameter was considered as reference. The other coefficients were divided by this reference to obtain a weighted coefficient applied to each variable. We arbitrarily multiplied each weighted coefficient by 5.

The internal validity of the score was explored to confirm its performance in identifying patients at risk of bleeding in this initial cohort. Area under the receiver operating characteristics (ROC) curve (AUC) was computed with its 95% confidence interval.

Step 2: Validation Cohort

The external validity of the score was explored in another retrospective cohort from centers 1 and 2. Comparisons between the centers were performed as described previously. POBS-Card score and other scores previously described were calculated in the whole cohort: TRACK, TRUST,

TABLE 2. Postoperative characteristic and outcomes

Variables	Insignificant/mild (n = 1360)	Moderate/severe (n = 344)	*P* value
Intraoperative period			
CPB duration, min	79 [60-108]	98 [68-137]	<.0001
Tranexamic acid use, % (n)	98.2 (1336)	98.8 (340)	.6
Median dose, mg/kg	0.018 [0.015-0.020]	0.019 [0.016-0.021]	<.0001
Postoperative period			
SAPS-II severity score	34 [27-41]	40 [32-50]	<.0001
Fluid infusion,* mL/kg	7.0 [0.0-15.0]	11.0 [3.2-20.0]	<.0001
Circulatory drugs,* % (n)	32.3 (439)	56.1 (194)	<.0001
Norepinephrine	27.2 (369)	48.3 (167)	
Epinephrine	1.0 (13)	3.8 (13)	
Dobutamine	10.8 (148)	24.6 (84)	
Bleeding,* mL/kg/h	0.3 [0.2-0.5]	0.8 [0.5-1.3]	<.0001
Surgical reintervention, % (n)	0 (0)	13.9 (48)	<.0001
Transfusion*			<.0001
RBC, units	0 [0-0]	1 [0-2]	
FFP, units	0 [0-0]	0 [0-2]	
PLC, units	0 [0-0]	0 [0-1]	
FrC, g	0 [0-0]	0 [0-0]	
rVIIa, % (n)	0 (0)	1.7 (6)	
UDPB classification, % (n)			N/A
Class 0	97.2 (1322)	0 (0)	
Class 1	2.8 (38)	0 (0)	
Class 2	0 (0)	76.1 (262)	
Class 3	0 (0)	23.3 (80)	
Class 4	0 (0)	0.6 (2)	
Troponin,* ng/mL	585 [378-982]	831 [515-1462]	<.0001
Lactate,* mmol/L	1.6 [1.2-2.3]	2.0 [1.5-2.9]	<.0001
pH*	7.35 [7.33-7.39]	7.36 [7.32-7.40]	.1
Invasive ventilation duration, h	6 [4-8]	9 [6-20]	<.0001
KDIGO classification	0 [0-0]	0 [0-0]	<.0001
KDIGO ≥1, % (n)	5.9 (80)	15.1 (52)	<.0001
ICU stay, d	3 [2-5]	4 [3-7]	<.0001
Major complications,† % (n)	30.6 (417)	44.2 (152)	<.0001
Infection, % (n)	10.3 (140)	24.7 (85)	<.0001
Mortality, % (n)	0.7 (10)	2.9 (10)	.003

CPB, Cardiopulmonary bypass; *SAPS-II*, Simplified Acute Physiology Score II; *RBC*, red blood cells; *FFP*, fresh frozen plasma; *PLC*, platelet concentrate; *FrC*, fibrinogen concentrate; *rVIIa*, recombinant activated factor VII; *N/A*, not applicable; *UDPB*, universal definition for postoperative bleeding; *KDIGO*, Kidney Disease: Improving Global Outcomes; *ICU*, intensive care unit. *Within the first 12 hours after surgery. †Composite criteria with at least one among: shock (vasoplegic or cardiogenic); circulatory support with extracorporeal life support; acute respiratory distress syndrome; death.

Papworth, and WILL-BLEED scores.[6-8,17] ROC curves with their respective AUCs were elaborated. Finally, the Youden index for the POBS-Card score was computed to identify optimal combination of sensitivity and specificity.

RESULTS

Step 1: Elaboration of the Predictive Score

Derivation cohort characteristics. In this first cohort, derived from 1 academic hospital from January 2016 until July 2018, 1704 patients were included in the analysis. A total of 344 (20.2%) patients presented a moderate-severe bleeding, defined by a UDPB score ≥2. Preoperative characteristics of interest are presented in Table 1. In brief, patients with a moderate-severe bleeding were slightly older (69 [62-75] years vs 68 [61-74] years, $P = .047$) with a significantly lower BMI (26.9 [23.7-30.1] kg/m^2 vs 28 [24.9-31.7] kg/m^2, $P < .0001$) and eGFR (73 [55-89] mL/min/m^2 vs 79 [62-95] mL/min/m^2, $P < .0001$) and a significantly greater incidence of ongoing antiplatelet drugs. They had significantly more redo surgeries (9.0 vs 4.2%, $P = .0009$) and/or more combined surgery of valve replacement and coronary bypass grafting (15.4 vs 10.7%, $P = .005$). Preoperative laboratory tests were also different, with lower hemoglobin, prothrombin ratio and platelet count, and greater aPTT ratio.

The main outcomes are presented in Table 2. The moderate-severe bleeding group had more significant adverse outcomes and a greater mortality rate. The main outcomes according only to the chest tube blood loss and/or surgical re-exploration are mostly similar and are presented in Tables E2-E4.

Risk factors for bleeding: Uni- and multivariable analyses. Results for the univariable and multivariable analyses are presented in Table 3. Fourteen variables were analyzed using a logistic regression model: age, gender, BMI, eGFR, characteristics of surgery (redo, urgent, type), antiplatelet and anticoagulation therapy, and preoperative laboratory tests (aPTT, PT, platelet count, fibrinogen, hemoglobin).

Among these variables, gender, presence of a preoperative anticoagulation therapy, and the urgency of the surgery were not considered in the multivariable logistic regression model because of $P > .05$. Eight variables were significantly and independently associated with a severe bleeding in the final model: BMI, characteristics of surgery (redo and type), antiplatelet therapy, aPTTr >1.2, PT ratio <60%, platelet count <150 g/L, and fibrinogen <3 g/L. The Hosmer-Lemeshow test presented a P of .99, assuming the logistical regression model satisfactorily fitted with data.

Score elaboration. On the basis of these findings, β parameters of the 8 final variables were computed from the final logistical regression model. The lowest value was fibrinogen preoperative value and was considered as the reference to weight the other variables, with the presence

TABLE 3. Associations between preoperative factors and moderate-severe bleeding

Variables	Univariable analysis		Logistic regression full model*		Logistic regression final model†	
	OR [95% CI]	*P* value	OR [95% CI]	*P* value	OR [95% CI]	*P* value
Age >80 y	**1.53 [1.00-2.27]**	**.04**	1.37 [0.89-2.08]	.1		
Male gender	0.89 [0.67-1.16]	.4				
BMI <25 kg/m^2	**1.58 [1.23-2.03]**	**.0004**	**1.48 [1.14-1.92]**	**.003**	**1.48 [1.14-1.93]**	**.003**
eGFR <45 mL/min/m^2	**1.71 [1.17-2.46]**	**.004**	1.46 [0.97-2.18]	.06		
Redo surgery	**2.26 [1.42-3.54]**	**.004**	**1.70 [1.03-2.75]**	**.03**	**1.76 [1.07-2.82]**	**.02**
Antiplatelet drugs						
Single	1.37 [0.99-1.86]	.05	**1.51 [1.09-2.07]**	**.01**	**1.50 [1.09-2.05]**	**.01**
Dual	**1.89 [1.11-3.14]**	**.02**	**1.93 [1.11-3.26]**	**.02**	**2.00 [1.15-3.37]**	**.01**
Anticoagulant therapy	1.32 [0.78-2.15]	.3				
Hemoglobin <12 g/dL	**1.57 [1.15-2.12]**	**.004**	1.22 [0.86-1.72]	.3		
Prothrombin ratio <60%	**2.63 [1.75-3.91]**	**<.0001**	**1.76 [1.11-2.76]**	**.02**	**1.91 [1.21-2.97]**	**.005**
aPTTr >1.2	**1.78 [1.32-2.42]**	**.0001**	**1.40 [1.00-1.95]**	**.046**	**1.44 [1.03-1.99]**	**.03**
Platelets <150 G/L	**2.01 [1.37-2.90]**	**.0002**	**1.72 [1.15-2.55]**	**.007**	**1.74 [1.17-2.57]**	**.006**
Fibrinogen <3 g/L	**1.30 [1.00-1.67]**	**.046**	**1.37 [1.04-1.79]**	**.02**	**1.33 [1.02-1.73]**	**.04**
Urgent surgery	1.18 [0.87-1.60]	.3				
Type of surgery*						
Valvular	**1.40 [1.03-1.91]**	**.03**	1.23 [0.92-1.73]	.1	1.29 [0.94-1.77]	.1
Combined†	**1.99 [1.32-2.98]**	**.0009**	**1.78 [1.13-2.61]**	**.01**	**1.81 [1.19-2.74]**	**.005**
Ascendant aorta‡	**1.71 [1.26-2.58]**	**.01**	**1.59 [1.04-2.43]**	**.03**	**1.56 [1.02-2.38]**	**.04**

OR, Odds ratio; *CI*, confidence interval; *BMI*, body mass index; *eGFR*, estimated glomerular filtration rate using Modification of Diet in Renal Disease formula; *aPTTr*, activated partial thromboplastin time ratio. *With coronary bypass grafting surgery as reference. †Valvular and coronary surgery. ‡Ascendant aorta with or without valve replacement. Bold variables are included in the full model for logistic regression* and, if significant, in the final model with a backward stepwise process.†

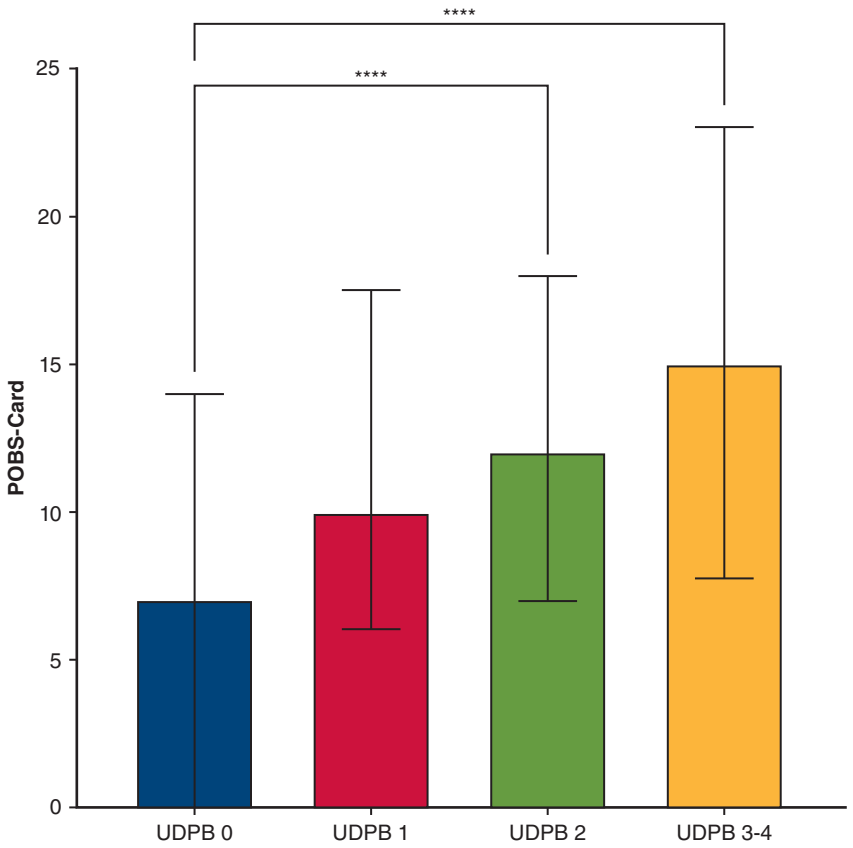

FIGURE 1. POBS-Card values among the postoperative bleeding categories, according to the universal definition for perioperative bleeding (*UDPB*). ****$P < .0001$. *POBS-Card*, PeriOperative Bleeding Score in Cardiac surgery.

of a dual antiplatelet therapy presenting the greatest value (Table E5). The sum of the weight associated with variables resulted in a final score from 0 to 86. As expected, patients with moderate-severe bleeding presented greater POBS-Card scores (13 [7-19] vs 7 [0-14], $P < .0001$). We observed an incremental increase in the median scores according to the UDPB classification (Figure 1). Finally, the AUC under ROC curve to predict a UDPB $\geq$2 was 0.643 [0.610-0.676].

Step 2: External Validation

We included 597 patients, 297 patients from center 1 (same center as for the elaboration of the score) between October 2018 and March 2019, and 300 patients from center 2 between November 2016 and March 2017 (same period as the derivation cohort, but in a different hospital). The main characteristics of these cohorts are presented in the Table E6, and comparisons of ROC for the different scores of interests are presented in Table 4 and Figure E1. The ROC curve for POBS-Card score was similar as observed in the elaboration with an AUC of 0.645 [0.605-0.683] and was greater than the AUC of the other scores, which all were inferior to 0.6. The Youden index identified a POBS-Card score >14 with a specificity of 73% and a sensitivity of 50% for prediction of moderate-severe bleeding (Figure 2). Finally, we didn't

TABLE 4. Receiver operating curves of the different scores for prediction of a moderate-severe bleeding

	Whole cohort		Center 1		Center 2	
Score	AUC	95% CI	AUC	95% CI	AUC	95% CI
Papworth	0.553	[0.512-0.593]	0.560	[0.481-0.640]	0.547	[0.489-0.605]
Track	0.597	[0.557-0.637]	0.580	[0.501-0.659]	0.616	[0.558-0.671]
Trust	0.569	[0.528-0.609]	0.566	[0.490-0.643]	0.572	[0.514-0.629]
WILL-BLEED	0.579	[0.538-0.619]	0.546	[0.462-0.630]	0.620	[0.562-0.675]
POBS-Card	0.645	[0.605-0.683]	0.631	[0.554-0.708]	0.659	[0.603-0.713]

Scores are compared in the whole bicentric validation cohort and in the two different centers. The POBS-Card score was elaborated in the center 1 (derivation cohort, 2016-2018) and then validated (validation cohorts) in the center 1 (2018-2019) and center 2 (external center, 2016-2017). *AUC*, Area under the curve; *CI*, confidence interval; *POBS-Card*, PeriOperative Bleeding Score in Cardiac surgery.

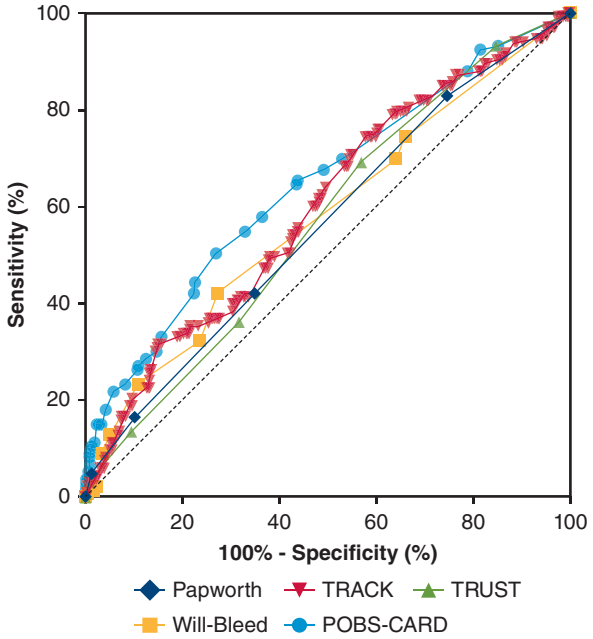

FIGURE 2. Receiver operating characteristic curve of the POBS-Card score for prediction of moderate-severe bleeding in the validation cohort. *POBS-Card*, PeriOperative Bleeding Score in Cardiac surgery.

observe a meaningful variation of bleeding over the time in the center, suggesting the occurrence of a severe bleeding was stable over this period (Figure E2).

DISCUSSION

Our main findings are as follows: (1) POBS-Card score is more robust than other scores in predicting severe bleeding after cardiac surgery and (2) POBS-Card score diagnosis performance is not enough discriminant to a routine clinical use to predict severe bleeding.

Definition of Bleeding

Because bleeding and transfusion are sources of morbidity, mortality, and significantly increases in health care costs, early identification of at-risk patients is a challenge for health care systems.[10,18-20] We believe our score takes in account the limits of current scores we described previously. Indeed, with the exception of the WILL-BLEED score, most current scores are based on nonconsensual definitions of bleeding, with a definition based either on blood product administration (TRACK and TRUST scores) or on bleeding amount through chest drains (Papworth score). These differing definitions of bleeding present limits related to a center's habits and protocols. Indeed, despite guidelines on blood management in cardiac surgery, a recent survey highlighted the sustained heterogeneity in practice regarding transfusion during bleeding.[21-23] Moreover, one half of the centers surveyed didn't have an institutional transfusion protocol.[23] Thus, definitions only based on blood product transfusion may lead to a misdiagnosis on bleeding. Similarly, relying only on drain loss seems inaccurate. Indeed, fluid production is not necessarily related to bleeding but might represent plasma or even lymph production, and its amount may be influenced by the modalities of draining (active tube clearance, number of drains, vacuum, etc).[24,25] The combination of transfusion, drain quantification, and need for reoperation may be a good compromise, as described for the UDPB definition.[10] This definition has been challenged by other modern definitions, such as the European Multicenter Study on Coronary Artery Bypass Grafting or Bleeding Academic Research Consortium definition, with similar performances.[26,27] Because it seems to us more ubiquitous and simpler, we chose the UDPB definition. In our cohort, patients with a UDPB $\geq$2 bleeding presented a much greater rate of major complications, with a more frequent use of intensive care unit therapies (norepinephrine, fluid infusion, invasive mechanical ventilation), a greater plasma level of troponin, a longer intensive care unit stay and ultimately a 3-fold greater mortality. These poor outcomes comforted the relevance of the UDPB classification in our cohort.

Only the WILL-BLEED score explored the prediction of bleeding using the UDPB classification.[8] Nevertheless, this score was elaborated in a population of patients undergoing coronary bypass graft, whereas the type of surgery influences the risk of bleeding, limiting the generalization of data.[28]

Preoperative Risk Factors for Bleeding

We observed several risk factors of excessive bleeding that have been previously described: lower BMI, preoperative impairment in hemostasis, redo surgery, and antiplatelet therapy.[29-31] Among them, antiplatelet therapy seemed to be the most important factor, with an odds ratio of 1.50 [1.09-2.50] for single therapy (ie, acetylsalicylic acid) and 2.00 [1.15-3.37] for dual therapy (ie, clopidogrel or ticagrelor). The 2018 European Association for Cardio-Thoracic Surgery guidelines, and its 2017 focus on dual antiplatelet therapy in coronary disease, recommended the maintenance of acetylsalicylic acid (ie, single therapy) in the perioperative period of cardiac surgery.[32,33] Indeed, despite a slight increase risk of bleeding, several randomized controlled trials demonstrated a reduction in myocardial infarction.[34] In contrast, the use of P2Y12 inhibitors, such as clopidogrel, ticagrelor, or prasugrel, is associated with an increased risk of bleeding after coronary artery bypass grafting, without a clear benefit on other outcomes in comparison with acetylsalicylic acid alone.[35,36] Thus, discontinuation of P2Y12 must be achieved before surgery when possible and be resumed as soon as possible after surgery.[33] In case of emergent surgeries, some strategies are suggested to try to reduce bleeding. Platelet transfusion can restore platelet aggregation in patients treated with acetylsalicylic acid or clopidogrel but not with ticagrelor.[13] For the latter,

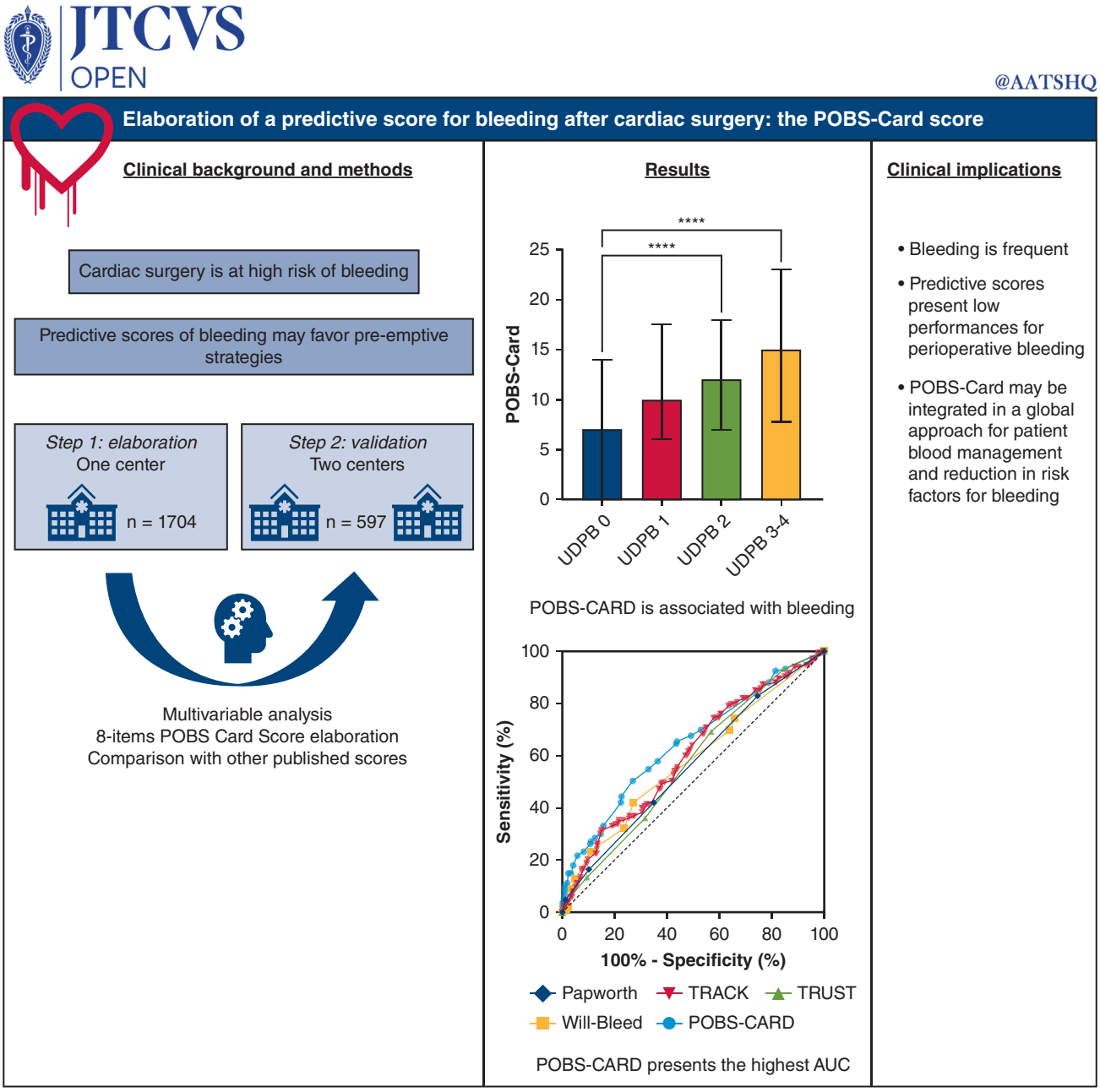

FIGURE 3. Graphical abstract. *POBS-Card*, PeriOperative Bleeding Score in Cardiac surgery.

no strategy has definitively proved its efficiency. High volume of platelet transfusion, recombinant activated factor VII, or adsorption with Cytosorb may be suggested but will necessitate further investigation.[13,37]

Interest and Limits of the New POBS-Card Score

Our score presented the highest performance in predicting bleeding. Nevertheless, the AUC was still modest, with a value inferior to 0.7, whereas the other scores presented an AUC under 0.6. Salsano and colleagues[9] observed in a multicenter cohort study similar modest results for predictive scores, with the greatest AUC of 0.658 [0.600-0.716] for the WILL-BLEED score. This highlights the difficulty of a priori predicting the risk of bleeding in a surgery as complex and sometimes unpredictable as cardiac surgery, with many intra- and postoperative factors that can influence bleeding independently of the preoperative risk factors. For example, a post hoc analysis of the FIBrinogen REplenishment in Surgery (FIBRES) trial observed that duration of CPB $\geq$120 minutes was associated with at least a 2-fold increase in the amount of bleeding and greater proportion of UDPB score $\geq$2.[38] If the duration of CPB may be

anticipated according to the type of surgery, surgical complications may be unpredictable and may explain the inaccuracy of predictive scores. In our cohort, patients with severe bleeding presented with a greater duration of CPB, and despite a greater proportion of complex surgeries, we cannot rule out the possibility of surgical hazards that are difficult to identify retrospectively.

The retrospective nature of the study exposes to the risk of bias, which may also explain the low predictive value of scores. We cannot exclude that some transfusions were performed for prophylactic rather than therapeutic purposes. Nevertheless, bleeding and outcomes are quite similar to other studies. We observed 20% of UDPB score $\geq$2/4 versus 33.8% in the study by Dyke and colleagues.[10] Similarly, Brascia and colleagues.[39] in the prospective European Multicenter Study on Coronary Artery Bypass Grafting registry, showed a significant increase in mortality when UDPB $\geq$2, as did we. Thus, it seems to us that biases are fairly limited and comparable with the literature, and the use of UDPB remains relevant. In the same way, patients with bleeding had more comorbidities (advanced age, low BMI, renal failure, need for complex surgery), and we were unable to differentiate between worsening prognosis caused by the bleeding or to the patient's comorbidities, the 2 being closely linked, as demonstrated in the multivariable analysis.

The incidence of bleeding may vary between centers, which may limit the generalization of our results and the interest of predictive score elaborated in a particular center.[3] We included another center in the validation cohort, and indeed the UDPB score and the amount of bleeding varied between the 2 centers, but the POBS-Card performance score remained similar in the 2 centers. This suggests its possible application in different cardiac surgery centers. Of course, many other intraoperative factors may influence bleeding, such as the intraoperative use of surgical suction, use of autologous transfusion devices, and body and cardioplegia temperature, etc, whose standardization must be integrated into protocols of patient blood management, according to current guidelines.[40]

Despite the aforementioned limitations, our score also presents strengths that can make it useful in a global transfusion-sparing approach. First, it's one of the only scores that considers an ongoing antiplatelet therapy, even though it is the most important factor in our score. Second, despite a low sensitivity, a cut-off value of 14 reached a specificity of 73%, which can help practitioner in identifying patients at greater risk of bleeding and ultimately in planning specific strategies for hemorrhage-sparing. The 2021 Society of Thoracic Surgeons/Society of Cardiovascular Anesthesiologists/American Society of Extracorporeal Technology/Society for the Advancement of Blood Management guidelines provide key elements to reduce the risk of bleeding, comprising 4 major tenets of patient blood management: managing anemia, optimizing coagulation, interdisciplinary blood conservation, and patient-centered decision-making. As examples, reduction in cardiotomy surgical suction, reduction in the volume of CPB priming, maintenance of normothermia after weaning from CPB, enhanced use of antifibrinolytic drugs, preoperative anemia optimization, routine use of red cell salvage with centrifugation, use of modified ultrafiltration during CPB, and other suggestions may enhance patient safety. Moreover, among these recommendations the preoperative identification of patients at high-risk of bleeding is recommended with a class I.[41] This is where our score may be helpful. On the basis of these guidelines, the elaboration of a patient blood management turnkey order set may be of interest to protocolized and standardized practices.[42]

CONCLUSIONS

The elaboration of the new preoperative POBS-Card score presented the best predictive value for postoperative bleeding. Nevertheless, its performance remains limited. This emphasizes the difficulty of predicting bleeding reliably in a surgery as complex as cardiac surgery. However, the use of such scores should not be neglected but integrated into a global approach for bleeding risk reduction, including preoperative identification of patients and a rigorous optimization of intra- and postoperative factors (Figure 3).

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: cardiac surgical procedures, hemorrhage, risk assessment, risk factors

APPENDIX E1. PATIENT CARE

In this section, we detail the main lines of patient care management in the 2 centers. Most of practices presented similarities, but because of the retrospective nature of the study, we cannot affirm that all procedures perfectly matched with these protocols.

Anesthesia and monitoring were performed according to current guidelines for cardiac surgery with cardiopulmonary bypass (CPB).[E1] After induction of anesthesia, patients received a bolus of tranexamic acid (doses between 1 and 2 g as a single bolus). Aprotinin was not available during the study period. After anticoagulation using heparin (10,000 IU/m^2 based on body surface area of the patient in center 1, and 300 UI/kg in center 2), the inferior vena cava and the aorta were cannulated. An activated clotting time (ACT) >400 seconds was mandatory before CPB (Hemochron signature Elite; Werfen) and additional heparin may be administrated to maintain an ACT >350 seconds during CPB. After weaning from CPB, heparin was antagonized using protamine (center 1: full dose with 1 IU for 1 IU of heparin if CPB duration <60 minutes, reduced dose with 0.6 IU for 1 IU of heparin if CPB ≥60 minutes; center 2: full dose with 1 IU for 1 IU of heparin regardless of CPB duration). No viscoelastic testing was available for the intraoperative period in the 2 centers. TEG 6S was available in center 1 after admission in the intensive care unit in case of a significant bleeding, and its realization was at the discretion of the intensivist. Because of the need for a specific teaching on this technology, less than one third of practitioner used TEG 6S during the study period. The interpretation of viscoelastic testing results followed the protocol of the IMOTEC trial.[E2] To summarize in brief, in cases of delayed clotting time after kaolin activation corrected by heparinase (Citrated Kaolin reaction time/Citrated Kaolin reaction time with heparinase >2), protamine was administrated; in cases of citrated rapid TEG maximal amplitude <48 mm and citrated functional fibrinogen maximal amplitude >16 mm, platelet was administrated; in cases of citrated functional fibrinogen maximal amplitude <17 mm and citrated rapid TEG maximal amplitude >47 mm, fibrinogen concentrates were administrated; in cases of normal viscoelastic testing, activated factor VII or re exploration were suggested.

CPB was managed according to current guidelines. To summarize in brief, CPB was conducted with heart-lung machines (Stockert S5; LivaNova) using roller pumps for aspirating wound blood, venting cardiac chamber, cardioplegia, and systemic circulation (occlusive pump with an objective of 2.4-2.8 L/min/m^2 of blood flow, according to mean arterial pressure and arterial delivery of oxygen). Mean arterial pressure was maintained at >65 mm Hg off CPB and between 50 and 80 mm Hg on CPB. No centrifugal pump was used. Reservoirs and oxygenators were coated with phosphorylcholine (Inspire S6 or S8; LivaNova) or with biocompatible amphiphilic polymer surface (CAPIOX FX15; Terumo). Reperfusion of autologous blood was provided by Cellsaver, Cell Saver Elite Plus (Haemonetics) or CATSmart (Fresenius Kabi). Despite our concern to minimize the length of the circuit's lines, our practices were not part of a minimal invasive extracorporeal circulation protocol. One surgeon in center 1 occasionally practiced minimal invasive extracorporeal circulation with a centrifugal pump (no reservoir) in a small number of patients benefiting from coronary artery bypass grafting. Priming of CPB consisted in Gelofusine 4% in center 1 and Gelofusine 4%/Ringer's lactate/4.2% sodium bicarbonate in center 2. Maximal infusion of Gelofusine was limited to 33 mL/kg on the operative day. Retrograde autologous priming was not routinely used.

Bleeding management in the operating room was left at the discretion of the anesthetist-surgeon team. In brief, the surgeon checked the different zones at risk of bleeding (operative and CPB sites, mediastinum, chest wall, sternum), and transfusion was guided according to conventional laboratory testing (platelet concentrate if platelet count <100 g/L, fibrinogen concentrate if fibrinogen plasma level <2 g/L, fresh frozen plasma if prothrombin ratio <40%). Protamine was readministrated if initial heparin-protamine ratio was <1 or ACT >100 seconds or antiXa activity >0.1 unit/mL. Red blood cells were administrated after CPB if hemoglobin was <8 g/dL or rapidly decreasing (administration because of low arterial oxygen delivery during CPB or because of correction of a low preoperative hemoglobin before CPB was not considered for UDPB calculation).

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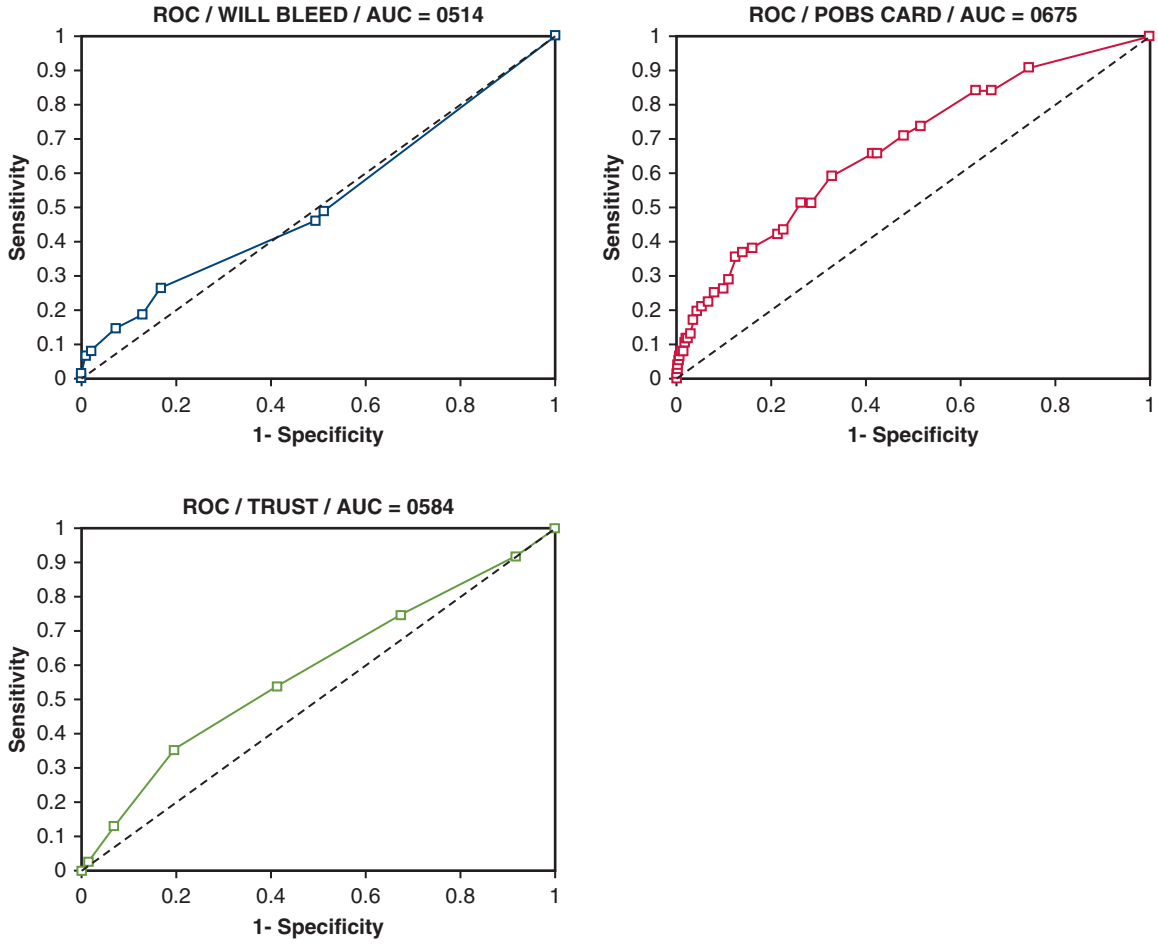

FIGURE E1. ROC curves for prediction of bleeding of the WILL-BLEED, TRUST, and POBS-Card scores. *ROC*, Receiver operating characteristic; *POBS-Card*, PeriOperative Bleeding Score in Cardiac surgery; *UDPB*, universal definition for postoperative bleeding.

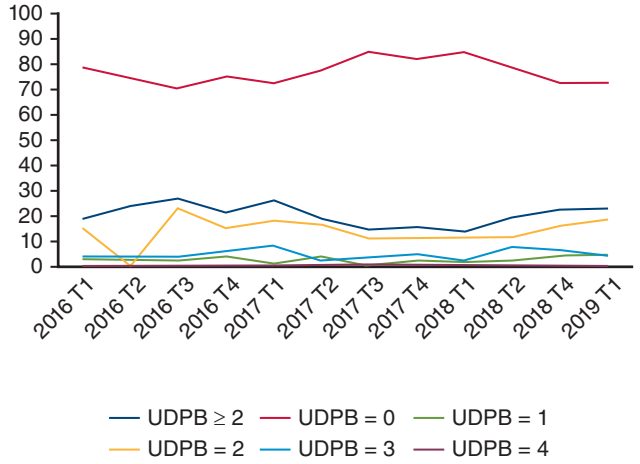

FIGURE E2. Percentages of bleeding according to the UDPB in center 1 between 2016 and mid-2019. UDPB is graded from 0 to 4. Grade ≧2 was considered as moderate-severe bleeding. The time period is divided into trimesters. The third trimester of 2018 was not collected because of a technical issue. *UDPB*, Universal definition for postoperative bleeding.

TABLE E1. Universal definition of perioperative bleeding (UDPB)

Bleeding category	Postoperative blood loss through chest drains within 12 h, mL	PRBCs, units	FFP, units	PLC, units	Fibrinogen concentrates	PCC	rVIIa	Reexploration/ tamponnade
0	<600	0	0	0	No	No	No	No
1	601-800	1	1	0	No	No	No	No
2	801-1000	2-5	2-5	Yes	Yes	Yes	No	No
3	1001-2000	5-10	5-10	N/A	N/A	N/A	No	Yes
4	>2000	>10	>10	N/A	N/A	N/A	Yes	No

Adapted from Dyke and colleagues.[10] *PRBCs*, Packed red blood cells; *FFP*, fresh frozen plasma; *PLC*, platelet concentrates; *PPC*, prothrombin complex concentrate; *rFVIIa*, recombinant activated factor VII.

TABLE E2. Preoperative characteristics in the derivation cohort

Variables	Bleeding ≤800 mL (n = 1628)	Bleeding >800 mL or surgical reintervention (n = 76)	*P* value
Age, y	69 [62-71]	66 [59-74]	.2
>80 y, % (n)	7.5 (122)	9.2 (7)	.5
Male gender, % (n)	73.4 (1195)	71.4 (22)	.7
BMI, kg/m^2	27.8 [24.7-31.3]	26.6 [22.7-29.7]	**.006**
<25 kg/m^2, % (n)	27.2 (442)	40.8 (31)	**.01**
LVEF in %	64 [55-70]	62 [55-70]	.5
Creatinine, μmol/L	87 [71-103]	92 [78-116]	**.03**
>100 μmol/L, % (n)	26.8 (437)	38.2 (29)	**.04**
eGFR, mL/min/m^2	78 [61-94]	72 [55-89]	**.03**
<45 mL/min/m^2, % (n)	9.8 (145)	17.1 (13)	**.02**
Redo surgery, % (n)	4.9 (80)	10.5 (8)	.055
Antiplatelet therapy,* % (n)			.6
Single	15.6 (257)	15.8 (12)	
Double	4.1 (67)	6.6 (5)	
Anticoagulant therapy,* % (n)	4.6 (75)	13.2 (10)	**.003**
Hb, g/dL	13.9 [12.7-14.8]	13.5 [11.9-14.7]	.1
<12 g/dL	14.3 (233)	26.3 (20)	**.008**
Prothrombin ratio, %	91 [81-100]	85 [69-100]	**.004**
<60%, % (n)	6.1 (99)	18.4 (14)	**.003**
aPTT ratio	1.05 [0.99-1.14]	1.06 [1.01-1.18]	.2
>1.2	14.6 (237)	22.4 (17)	.07
Platelets count, g/L	220 [185-263]	200 [160-236]	**.003**
<150 g/L, % (n)	8.2 (133)	13.2 (10)	.1
Fibrinogen, g/L	3.5 [3.0-4.1]	3.2 [2.6-4.1]	.06
<3 g/L	27.5 (447)	44.7 (34)	**.002**
Urgent surgery, % (n)	16.2 (264)	26.3 (20)	**.03**
Type of surgery, % (n)			**<.0001**
Coronary bypass	27.1 (441)	7.9 (6)	
Valvular	50.1 (816)	52.6 (40)	
Combined	11.4 (185)	18.4 (14)	
Ascendant aorta	11.4 (185)	21.1 (16)	

BMI, Body mass index; *LVEF*, left ventricular ejection fraction; *eGFR*, estimated glomerular filtration rate using Modification of Diet in Renal Disease formula; *aPTT*, activated partial thromboplastin time. *Antiplatelet and anticoagulant therapy ongoing at the time of the surgery.

TABLE E3. Postoperative characteristic and outcomes in the derivation cohort

Variables	Bleeding ≤800 mL (n = 1628)	Bleeding >800 mL or surgical reintervention (n = 76)	*P* value
Intraoperative period			
CPB duration, min	81 [60-112]	122 [79-159]	<.0001
Tranexamic acid use, % (n)	98.3 (1600)	100 (76)	.6
Median dose, mg/kg	0.018 [0.016-0.020]	0.019 [0.016-0.22]	**.002**
Postoperative period			
SAPS-II severity score	38 [32-50]	45 [36-56]	**<.0001**
Fluid infusi on,* mL/kg	7.7 [0-15.6]	12.9 [6.2-23.5]	**<.0001**
Circulatory drugs,* % (n)	36.1 (587)	65.8 (50)	**<.0001**
Norepinephirine	30.2 (492)	57.9 (44)	
Epinephrine	1.1 (19)	10.5 (8)	
Dobutamine	13.0 (211)	26.3 (20)	
Bleeding,* mL/kg/h	0.36 [0.23-0.56]	1.76 [1.26-2.32]	**<.0001**
Surgical reintervention, % (n)	0 (0)	63.2 (48)	**<.0001**
Transfusion*			
RBC, units	0 [0-0]	2 [0-3]	**<.0001**
FFP, units	0 [0-0]	0 [0-3]	**<.0001**
PLC, units	0 [0-0]	0 [0-1]	**<.0001**
FrC, g	0 [0-0]	0 [0-0]	**<.0001**
rVIIa, % (n)	0 (0)	7.9 (6)	**<.0001**
Troponin,* ng/mL	608 [387-1039]	976 [666-1875]	**<.0001**
Lactate,* mmol/L	1.7 [1.2-2.4]	2.3 [1.7-4.0]	**<.0001**
pH*	7.36 [7.33-7.39]	7.36 [7.30-7.39]	.3
Invasive ventilation duration, h	6 [5-9]	21 [13-105]	**<.0001**
KDIGO classification	0 [0-0]	0 [0-0]	**<.0001**
KDIGO ≥1, % (n)	7.2 (117)	19.7 (15)	**.0005**
ICU stay, d	3 [2-5]	6 [4-9]	**<.0001**
Major complications,† % (n)	34.3 (559)	65.8 (50)	**<.0001**
Infection, % (n)	11.9 (194)	40.8 (31)	**<.0001**
Mortality, % (n)	0.9 (15)	6.6 (5)	**<.0001**

CPB, Cardiopulmonary bypass; *SAPS-II*, Simplified Acute Physiology Score II; *RBC*, red blood cells; *FFP*, fresh frozen plasma; *PLC*, platelet concentrate; *FrC*, fibrinogen concentrate; *rVIIa*, recombinant activated factor VII; *UDPB*, universal definition for postoperative bleeding; *KDIGO*, Kidney Disease: Improving Global Outcomes; *ICU*, intensive care unit. *Within the first 12 hours after surgery. †Composite criteria with at least one among: shock (vasoplegic or cardiogenic); circulatory support with ECLS; acute respiratory distress syndrome; death.

TABLE E4. Predictive scores for bleeding in the derivation cohort

Variables	Bleeding ≤800 mL (n = 1628)	Bleeding >800 mL or surgical reintervention (n = 76)	*P* value	AUC for prediction of bleeding
WILL-BLEED	1 [0-2]	0 [0-3]	.7	0.514 [0.446-0.582]
TRUST	2 [1-3]	3 [2-4]	**.01**	0.584 [0.514-0.653]
POBS-Card	8 [0-15]	15 [7-22]	**<.0001**	0.675 [0.612-0.739]

POBS-Card, PeriOperative Bleeding Score in Cardiac surgery.

TABLE E5. Preoperative variables included in the POBS-Card score

Variable	β	95% CI	Weighted score
BMI <25 kg/m^2	0.39	[0.13-0.66]	7
Redo surgery	0.56	[0.07-1.04]	10
PT ratio <60%	0.65	[0.19-1.09]	11
aPTTr >1.2	0.36	[0.03-0.69]	6
Platelets <150 g/L	0.56	[0.15-0.94]	10
Fibrinogen <3 g/L	0.29_{ref}	[0.03-0.55]	5
Combined surgery	0.59	[0.18-1.01]	10
Ascendant aorta surgery	0.45	[0.02-0.87]	8
Antiplatelet therapy—single	0.40	[0.08-0.72]	7
Antiplatelet therapy—dual	0.69	[0.14-1.22]	12

Each variable is weighted by dividing its β parameter by 0.29 (β-parameter of fibrinogen) and multiplying by 5. The sum of the weighted variables equals to the POBS-Card score, from 0 to 86. Constant intercept β −2.15, multivariable regression model $r^2 = 0.05$, and Hosmer-Lemeshow 1.56, $P = .99$. *CI*, Confidence interval; *BMI*, body mass index; *PT*, prothrombin time; *aPTTr*, activated partial thromboplastin time ratio; *POBS-Card*, PeriOperative Bleeding Score in Cardiac surgery.

TABLE E6. Demographic characteristics of the validation cohort in whole cohort and in the 2 centers: center 1, where the score was elaborated but in the 2018-2019 period; center 2, another university hospital during the 2016-2017 period

	Whole cohort (n = 597)	Center 1 2019-2020 (n = 297)	Center 2 2016-2017 (n = 300)	*P* value
Age, y	68 [61-74]	68 [60-74]	69 [62-75]	.4
Male gender, % (n)	71 (423)	70 (210)	71.7 (213)	.7
BMI, kg/m^2	27.6 [24.3-31.1]	27.4 [24.1-31.2]	27.7 [24.3-31.2]	.9
<25 kg/m^2, % (n)	29.8 (178)	29.7 (89)	29.9 (89)	1
LVEF in %	62 [55-68]	60 [54-67]	63 [55-69]	.04
Creatinine, μmol/L	79 [69-96]	79 [68-97]	79 [69-94]	.5
>100 μmol/L, % (n)	19.6 (118)	21.6 (64)	18.0 (54)	.3
eGFR, mL/min/m^2	80 [66-95]	80 [64-94]	80 [66-96]	.6
Redo surgery, % (n)	6 (33)	7.4 (22)	3.7 (11)	.049
Antiplatelet therapy,* % (n)				.3
Single	41 (243)	42.1 (125)	46.7 (140)	
Dual	7 (42)	4.4 (13)	2.3 (7)	
Hemoglobin, g/dL	13.6 [12.4-14.6]	13.9 [12.5-14.9]	13.4 [12.3-14.4]	.03
<12 g/dL, % (n)	16 (95)	15.7 (47)	16.2 (48)	.9
Prothrombin ratio, %	92 [83-100]	93 [83-100]	92 [81-100]	.4
<60%, % (n)	6 (33)	5.4 (16)	5.7 (17)	1
aPTT ratio	1.03 [0.97-1.12]	1.06 [1.00-1.16]	1.00 [0.97-1.07]	<.0001
>1.2	13 (80)	17.2 (51)	9.7 (29)	.008
Platelet, g/L	216 [179-261]	219 [184-265]	212 [175-258]	.1
<150 g/L, % (n)	11 (68)	9.4 (28)	13.3 (40)	.2
Fibrinogen, g/L	3.6 [3.0-4.3]	3.6 [3.0-4.3]	3.6 [3.1-4.2]	1
<3 g/L, % (n)	21 (126)	22.9 (68)	19.3 (58)	.3
Urgent surgery, % (n)	15 (91)	22 (64)	9 (27)	<.0001
Type of surgery, % (n)				.009
Coronary bypass	27 (160)	26.9 (80)	26.7 (80)	
Valvular	50 (298)	52.8 (157)	47 (141)	
Combined	12 (71)	13.2 (39)	10.7 (32)	
Ascendant aorta	11 (68)	7.1 (21)	15.6 (47)	
Postoperative bleeding				
Drain volume, mL/12 h	320 [220-470]	260 [170-375]	410 [280-590]	<.0001
UDPB classification	0 [0-2]	0 [0-1]	0 [0-2]	.002
UDPB ≥2, n (%)	27 (164)	22.6 (67)	32.3 (97)	.008
Surgical reintervention	4 (25)	5.4 (16)	3.0 (9)	.2
Red blood cells, units	0 [0-0]	0 [0-0]	0 [0-2]	<.0001
Platelet units, units	0 [0-0]	0 [0-0]	0 [0-0]	.009
Fresh frozen plasma, units	0 [0-0]	0 [0-0]	0 [0-0]	.02
Fibrinogen concentrate, g	0 [0-0]	0 [0-0]	0 [0-0]	.06
Activated FVII, μg/kg	0 [0-0]	0 [0-0]	0 [0-0]	1

BMI, Body mass index; *LVEF*, left ventricular ejection fraction; *eGFR*, estimated glomerular filtration rate using Modification of Diet in Renal Disease formula; *aPTT*, activated partial thromboplastin time; *UDPB*, universal definition for postoperative bleeding; *FVII*, factor VII. *Antiplatelet therapy ongoing the day of the surgery.