

Validation of the European Multicenter Study on Coronary Artery Bypass Grafting (E-CABG) Bleeding Severity Definition

Giovanni Mariscalco, MD, PhD, Riccardo Gherli, MD, Amer B. Ahmed, BMBS, FRCA, Marco Zanobini, MD, PhD, Daniele Maselli, MD, Magnus Dalén, MD, PhD, Gabriele Piffaretti, MD, PhD, Giangiuseppe Cappabianca, MD, Cesare Beghi, MD, and Fausto Biancari, MD, PhD

Department of Cardiovascular Sciences, Clinical Sciences Wing, University of Leicester, Glenfield Hospital, Leicester, United Kingdom; Department of Cardiovascular Science, Cardiac Surgery Unit, S. Camillo-Forlanini Hospital, Rome, Italy; Department of Anaesthesia and Critical Care, Glenfield Hospital, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom; Department of Cardiovascular Sciences, Cardiac Surgery, Centro Cardiologico Monzino IRCCS, University of Milan, Milan, Italy; Department of Cardiovascular Surgery, Cardiac Surgery Unit, S. Anna Hospital Catanzaro, Italy; Department of Cardiothoracic Surgery and Anesthesiology, Karolinska University Hospital, and Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden; Department of Surgical and Morphological Sciences, Vascular Surgery Unit, and Department of Surgical and Morphological Sciences, Cardiac Surgery Unit, Varese University Hospital, University of Insubria, Varese, Italy; and Department of Surgery, University of Oulu, Oulu, Finland

Background. This study evaluated the prognostic significance of a novel bleeding severity classification in adult patients undergoing cardiac operations.

Methods. The European multicenter study on Coronary Artery Bypass Grafting (E-CABG) bleeding severity classification proposes 4 grades of postoperative bleeding: grade 0, no need of blood products with the exception of 1 unit of red blood cells (RBCs); grade 1, transfusion of platelets, plasma, or 2 to 4 units of RBCs, or both; grade 2, transfusion of 5 to 10 units of RBCs or reoperation for bleeding, or both; grade 3, transfusion of more than 10 units of RBCs. This classification was tested in a cohort of 7,491 patients undergoing CABG or valve operations, or combined procedures.

Results. The E-CABG bleeding severity grading method was an independent predictor of in-hospital death, stroke, acute kidney injury, renal replacement therapy, deep sternal wound infection, atrial fibrillation,

intensive care unit stay of 5 days or more, and composite adverse events of death, stroke, renal replacement therapy, and intensive care unit stay of 5 days or more. The area under the receiver operating characteristic curve of the E-CABG bleeding severity grading method for predicting in-hospital death was 0.858 (95% confidence interval, 0.827 to 0.889). E-CABG bleeding severity grades 0 to 3 were associated with in-hospital mortality rates of 0.2%, 1.1%, 7.9%, and 29.0%, respectively ($p < 0.001$), and with composite adverse events of 2.7%, 9.6%, 29.7%, and 75.8%, respectively ($p < 0.001$).

Conclusions. The E-CABG bleeding severity classification seems to be a valuable tool in the assessment of the severity and prognostic effect of perioperative bleeding in cardiac operations.

(Ann Thorac Surg 2016;101:1782–8)

© 2016 by The Society of Thoracic Surgeons

Bleeding is a common and severe condition after cardiac operations associated with increased resource utilization. Severe anemia and use of blood products are recognized as determinants of morbidity and death after cardiac operations [1]. Identification of risk factors for severe bleeding and evaluation of the efficacy of interventions for its prevention and treatment require stratification of the severity of intraoperative and postoperative blood loss. The prognostic effect of blood loss,

use of blood products, and reexploration for excessive bleeding were individually graded by 24 investigators of the European multicenter study on Coronary Artery Bypass Grafting (E-CABG) and pooled to develop a simple method to stratify the severity of bleeding in adult cardiac surgery [2]. The aim of this study was to validate the prognostic significance of the novel E-CABG bleeding severity definition in adult patients undergoing cardiac operations.

Accepted for publication Oct 12, 2015.

Address correspondence to Dr Mariscalco, Department of Cardiovascular Sciences, Clinical Sciences Wing, University of Leicester, Glenfield General Hospital, Groby Rd, Leicester LE3 9QP, UK; email: giovannimariscalco@yahoo.it.

The Supplemental Table can be viewed in the online version of this article [<http://dx.doi.org/10.1016/j.athoracsur.2015.10.028>] on <http://www.annalsthoracic.org>.

Material and Methods

The study protocol was in compliance with the local Institutional Review Boards, and patient consent was waived.

Patient Population

Between July 1999 and December 2011, all patients undergoing CABG or valve operations (with or without concomitant CABG) at 2 university hospitals in Italy—Varese University Hospital (3,267 patients, 52.7% isolated CABG) and Centro Cardiologico Monzino IRCCS (4,224 patients, 50.7% isolated CABG) with complete data on transfused red blood cells (RBCs), fresh frozen plasma, and platelets were reviewed. Elective, urgent, or emergency procedures were included. Patients undergoing thoracic aorta operations were excluded.

The patient population comprised 7,491 patients with complete data on postoperative adverse events as well as other preoperative, perioperative, and postoperative variables. All data were prospectively collected from institutional databases, and information about demographics, comorbidities, medical and surgical history, operative details, and postoperative events during the hospital stay were registered.

Patient Management

Preoperative management, anesthetic, and surgical techniques were standardized for all patients [3]. Antiplatelets and anticoagulation therapies were generally discontinued on the day of hospitalization, whereas other medications were routinely omitted on the day of the operation and restarted after the operation, unless clinically contraindicated. Intravenous heparin (2.5 to 4.0 mg/kg) was administered after sternotomy to maintain an activated clotting time of more than 400 seconds. At the end of the procedure, the circulating heparin was reversed with protamine sulfate (1.5 to 3.0 mg/kg).

The decision to perform an off-pump or on-pump CABG technique was based on individual surgeon preferences. Perioperative need for blood products was determined on a patient-by-patient basis. Homologous red cells were generally given intraoperatively to maintain a hemoglobin concentration exceeding 7 g/dL, or a hematocrit exceeding 20% during cardiopulmonary bypass, or were given postoperatively when hemoglobin was less than 8 g/dL. Additional blood product transfusions were administered at the discretion of the individual surgeon or anesthesiologist. Aprotinin or other hemostatic agents (ie, factor VII) were not used during the study period. At the end of the operation, patients were transferred to a cardiac intensive care unit (ICU).

The amount of blood products transfused refers to those blood-derived products administered intraoperatively as well as during the subsequent in-hospital stay. The types and amount of these products were documented from the blood bank databases.

Outcome End Points and Definitions

The primary outcome end points of this study were in-hospital death, stroke, combined stroke/transient ischemic attack (TIA), renal replacement therapy (RRT), deep sternal wound infection (DSWI), ICU length of stay (as a continuous variable in days or dichotomized as a stay >4 days), and in-hospital length of stay (in days). Postoperative stroke was defined as any new persistent deficit on physical examination, tomography scan, or magnetic resonance imaging, and TIA was defined as any new transient neurologic deficit. Stroke and TIA were confirmed by independent neurologists. Postoperative atrial fibrillation was documented by cardiac telemetry or 12-lead electrocardiogram. DSWI was defined as any infection of the sternal wound, the sternum and mediastinum requiring surgical débridement, and prolonged antibiotic treatment. The decision of reexploration for bleeding was determined by the amount of blood loss, the patient's hemodynamic status, hemoglobin and hematocrit levels, and findings on echocardiography. Postoperative bleeding was generally defined as more than 300 mL during the first hour, more than 250 mL during the second hour, more than 200 mL during the third hour, or 1,000 mL or more during the first 6 hours. The decision for reexploration for bleeding, however, rested with the surgeon on call. Chest tube outputs were used as a measure of bleeding loss, and the present analysis was based on the total volume of loss during the first 24 hours of the patient's stay in the ICU [4]. The composite outcomes measure included any of the following early adverse events: in-hospital death, stroke, DSWI, RRT, ICU stay of 5 days or more.

E-CABG Bleeding Severity Definition

Recently, 24 E-CABG investigators [2] selected a number of interventions for the treatment of postoperative bleeding after cardiac operations, interventions that are believed to indirectly quantify the amount of perioperative bleeding and thus have a prognostic effect on the outcome of these patients. Interventions selected for this purpose were intraoperative and postoperative transfusion of RBCs, platelets, fresh frozen plasma, or solvent- or detergent-treated pooled human plasma, and reexploration for excessive bleeding. Preoperative blood transfusions were not included. The investigators decided to not include here the absolute postoperative blood loss volume as a specific end point because no single time interval may capture the real extent of postoperative bleeding, which indeed may occur at different times postoperatively.

These 24 investigators stratified the severity/estimated the prognostic effect of each of the selected interventions, giving each of them a score from 0 to 10. A score of 10 corresponded to the most severe prognosis (ie, postoperative death). Extrapolating the medians of the investigators' scores, a 0 to 3 grading scale of the severity of intraoperative and postoperative bleeding was constructed according to the type and amount of blood products transfused perioperatively and postoperatively

during the in-hospital stay as well as on the need of reoperation for bleeding (Table 1). An additive score was also constructed based on the sum of rounded medians for each intervention. Further details on the development of the E-CABG bleeding severity definition are reported in the original article [2].

Statistical Analysis

Statistical analysis was computed using SPSS 22.0 software (IBM Corp, Armonk, NY). Missing values were not replaced. Group differences were evaluated by the Mann-Whitney, Kruskal-Wallis, Pearson χ^2 , and Fisher exact tests. Correlation between continuous variables was evaluated by the Spearman test. Receiver operating characteristic (ROC) curve analysis was used to estimate the ability of the E-CABG bleeding severity score to predict adverse end points. Logistic regression was used to adjust the effect of baseline and operative covariates (all covariates listed in Table 2) on postoperative adverse events. Multinomial regression analysis (including all covariates listed in Table 2) was used to estimate the multiple propensity scores of being assigned to 1 of the 4 E-CABG bleeding severity grades, with E-CABG bleeding severity grade 0 set as the reference category. The 4 propensity scores were used as covariates for adjusted analysis in logistic regression. In this analysis, the E-CABG bleeding severity grade was considered as a continuous variable. In addition, the E-CABG grades were adjusted for baseline hemoglobin and additive European System for Cardiac Operative Risk Evaluation. All tests were two-sided, with the α level set at 0.05 for statistical significance.

Results

Baseline and operative characteristics of 7,491 patients are presented in Table 2. Hospital death occurred in 307

Table 1. The European Coronary Artery Bypass Grafting Grading and Additive Score for Classification of Severity of Intraoperative and Postoperative Bleeding After Adult Cardiac Surgery^a

Grades	Intervention for Treatment of Bleeding	Additive Score
Grade 0	No use of blood products with the exception of 1 unit of RBCs	0
Grade 1	Transfusion of platelets	2
	Transfusion of fresh frozen plasma or prothrombin complex concentrate	3
	Transfusion of 2-4 units of RBCs	3
Grade 2	Transfusion of 5-10 units of RBCs	5
	Reoperation for bleeding	5
Grade 3	Transfusion of >10 units of RBCs	7

^a This classification included any transfusion of RBCs, platelets, and fresh frozen plasma that occurred during the operation and postoperatively during the same in-hospital stay. Preoperative transfusions are not included in this classification.

RBCs = red blood cells.

patients (2.1%), stroke in 104 (1.4%), combined stroke/TIA in 149 (2.0%), RRT in 116 (1.5%), atrial fibrillation in 2,471 (33.0%), DSWI in 54 (1.7% of 3,267 patients with available data on this outcome end point), ICU stay was 5 days or more in 580 patients (7.7%), and the composite adverse events end point in 744 (9.9%). Data on transfusion of blood products, reexploration for bleeding, and blood loss are summarized in Table 3.

Among 460 patients who underwent reexploration for bleeding, 166 (36.1%) received 5 to 10 units of RBCs, 77 (16.7%) received more than 10 units of RBCs, 374 (81.3%) received fresh frozen plasma, and 247 (53.7%) received platelets transfusion.

Blood loss was significantly associated with the E-CABG bleeding severity score ($\rho = 0.317$, $p < 0.001$) and grades ($\rho = 0.266$, $p < 0.001$). Mean blood loss in each E-CABG bleeding severity grade was 552 ± 254 mL in grade 0, 643 ± 359 mL grade 1, $1,052 \pm 716$ mL in grade 2, and $1,774 \pm 1,368$ mL grade 3 ($p < 0.001$).

The E-CABG investigators assigned a median score of 0.5 to transfusion of 1 unit of RBCs because most of them assumed that it would not affect the outcome of these patients [2]. In the total data set, 3,587 received none (3,408 patients) or 1 unit (179 patients) of RBCs. Logistic regression adjusted for all baseline and operative covariates showed that transfusion of 1 unit of RBCs was not associated with increased risk of in-hospital death

Table 2. Baseline and Operative Characteristics

Baseline Characteristics	No. (%) or Mean \pm SD
Age, y	67.4 \pm 10.7
Body mass index, kg/m ²	26.2 \pm 4.1
Female gender	2,270 (30.3)
Hypertension	4,976 (66.4)
Diabetes	1,790 (23.9)
Pulmonary disease	638 (8.5)
Peripheral vascular disease	1,074 (14.3)
Cerebrovascular disease	507 (6.8)
Prior myocardial infarction	2,307 (30.8)
Prior cardiac operation	461 (6.2)
Atrial fibrillation	799 (10.7)
eGFR, mL/min/1.73 m ²	70.9 \pm 20.4
Dialysis	44 (0.6)
Emergency	459 (6.1)
Preoperative IABP	98 (1.3)
Left ventricular ejection fraction	
0.30-0.50	1,908 (25.5)
<0.30	185 (2.5)
Type of operation	
Isolated CABG	3,865 (51.6)
Isolated valve procedure	2,525 (33.7)
Combined CABG/valve procedure	1,101 (14.7)
Off-pump coronary operation	582 (7.8)

CABG = coronary artery bypass grafting; eGFR = estimated glomerular filtration rate according to the Modification of Diet in Renal Disease formula; IABP = intraaortic balloon pump; SD = standard deviation.

Table 3. Postoperative Bleeding, Resternotomy for Bleeding, Use of Blood Products, and European Coronary Artery Bypass Grafting Grades and Score

Variable	No. (%) or Mean ± SD
Resternotomy for bleeding	460 (6.1)
Blood losses, mL	669 ± 466
Any blood product transfusion	4,177 (55.8)
RBC transfusion	4,083 (54.5)
Units transfused	1.9 ± 2.9
Fresh frozen plasma transfusion	2,269 (30.3)
Units transfused	1.1 ± 2.5
Platelets transfusion	811 (10.8)
Units transfused	0.4 ± 1.6
E-CABG bleeding severity grades	
Grade 0	3,411 (44.5)
Grade 1	3,074 (41.0)
Grade 2	882 (11.8)
Grade 3	124 (1.7)
E-CABG bleeding severity score	3.2 ± 3.9

E-CABG = European Coronary Artery Bypass Grafting; RBC = red blood cell; SD = standard deviation.

($p = 0.994$), stroke ($p = 0.995$), stroke/TIA ($p = 0.338$), acute kidney injury ($p = 0.566$), RRT ($p = 0.792$), atrial fibrillation ($p = 0.824$), ICU stay 5 days or more ($p = 0.071$), or the composite adverse event end point ($p = 0.403$). However, transfusion of 1 unit of RBCs was associated with an increased risk of DSWI (odds ratio [OR], 7.65; 95% confidence interval [CI], 1.63 to 35.89; $p = 0.010$).

Univariate Analysis

Univariate analysis showed that the E-CABG bleeding severity grading and additive scoring methods were both predictive of early adverse events after cardiac operations

(Tables 4 and 5). The additive scoring method showed a rather large area under the ROC curve (>0.7) in predicting in-hospital death, acute kidney injury, RRT, prolonged ICU stay, and the composite adverse events end point (Table 5). The largest areas under the ROC curve of the E-CABG additive scoring method were observed for in-hospital death (0.857; 95% CI, 0.827 to 0.888) and RRT (0.828; 95% CI, 0.787 to 0.870). Similar areas under the ROC curve were observed also with the E-CABG bleeding severity grading method for in-hospital death (0.858; 95% CI, 0.827 to 0.889).

Adjusted Analyses

Multiple propensity score-adjusted analysis showed that increasing E-CABG bleeding severity grades were associated with increased risk of all studied early adverse events (Table 6). In the center with available data on DSWI, the risk of this complication was significantly increased only in patients with E-CABG bleeding severity grade 2 (ie, in patients with 5 to 10 RBCs transfusion or reexploration for bleeding, or both).

Similarly, logistic regression showed that, when adjusted for all of the baseline and operative covariates listed in Table 2, the E-CABG bleeding severity additive scoring method was predictive of all early adverse events (Table 5). This score had a slightly higher OR in predicting in-hospital death and RRT compared with the other adverse events.

When adjusted for additive European System for Cardiac Operative Risk Evaluation, increasing E-CABG bleeding severity grades were associated with increased risk of in-hospital death ($p < 0.0001$), stroke ($p < 0.001$), stroke/TIA ($p < 0.001$), RRT ($p < 0.001$), DSWI ($p = 0.050$), atrial fibrillation ($p < 0.001$), ICU stay of 5 days or more ($p < 0.001$), and the composite adverse end point ($p < 0.001$).

Data on baseline hemoglobin were available only for 3,267 patients operated on at one of the participating

Table 4. Unadjusted Analysis of the Effect of Increasing European Coronary Artery Bypass Grafting Bleeding Severity Grades on the Risk of Early Postoperative Adverse Events After Cardiac Operation

Outcome End Points ^a	E-CABG Bleeding Severity Grades				p Value
	Grade 0	Grade 1	Grade 2	Grade 3	
In-hospital death	6 (0.2)	34 (1.1)	70 (7.9)	36 (29.0)	<0.0001
Stroke	23 (0.7)	45 (1.5)	23 (2.6)	13 (10.5)	<0.0001
Stroke/TIA	32 (0.9)	67 (2.2)	32 (3.6)	18 (14.5)	<0.0001
RRT	9 (0.3)	32 (1.0)	43 (4.9)	32 (25.8)	<0.0001
Atrial fibrillation ^b	778 (24.9)	916 (34.0)	301 (40.3)	54 (52.4)	<0.0001
DSWI ^c	13 (0.9)	26 (1.9)	14 (3.4)	1 (1.9)	0.006
ICU stay, h	45 ± 27	59 ± 48	94 ± 10	3,250 ± 321	<0.0001
ICU stay ≥5 days	64 (1.9)	241 (7.8)	204 (23.1)	71 (57.3)	<0.0001
Composite end point ^d	92 (2.7)	296 (9.6)	262 (29.7)	94 (75.8)	<0.0001

^a Categorical variables are reported as counts (percentages), and continuous variables are reported as the mean ± standard deviation. ^b Patients with preoperative atrial fibrillation were excluded from the analysis (6,669 patients available for this analysis). ^c Data were available only from 1 center (3,267 patients included in the analysis). ^d Composite end point includes any of the following early major adverse events: in-hospital death, stroke, RRT, ICU stay ≥5 days.

DSWI = deep sternal wound infection; E-CABG = European Coronary Artery Bypass Grafting; ICU = intensive care unit; RRT = renal replacement therapy; TIA = transient ischemic attack.

Table 5. C Statistics of the European Coronary Artery Bypass Grafting Bleeding Severity Grades and Additive Score

Outcome end points	E-CABG grades 0-3 C statistic ^a (95% CI)	E-CABG additive score C statistic ^a (95% CI)
In-hospital mortality	0.858 (0.827-0.889)	0.857 (0.827-0.888)
Stroke	0.667 (0.612-0.722)	0.686 (0.630-0.742)
Stroke/TIA	0.668 (0.622-0.713)	0.683 (0.637-0.729)
RRT	0.821 (0.779-0.863)	0.828 (0.787-0.870)
Atrial fibrillation ^b	0.574 (0.559-0.589)	0.565 (0.550-0.580)
DSWI ^c	0.621 (0.546-0.696)	0.609 (0.536-0.682)
ICU stay ≥5 days	0.767 (0.746-0.787)	0.771 (0.751-0.791)
Composite end point ^d	0.768 (0.750-0.787)	0.771 (0.753-0.790)

^a The C statistic is a measure of the area under the receiver operating characteristic curve. ^b Patients with preoperative atrial fibrillation were excluded from the analysis (6,669 patients available for this analysis). ^c Data were available only from 1 center (3,267 patients included in the analysis). ^d Composite end point includes any of the following early major adverse events: in-hospital death, stroke, RRT, ICU stay ≥5 days.

CI = confidence interval; DSWI = deep sternal wound infection; E-CABG = European Coronary Artery Bypass Grafting; ICU = intensive care unit; RRT = renal replacement therapy; TIA = transient ischemic attack.

centers. The effect of the E-CABG bleeding severity classification, as adjusted by baseline hemoglobin, was significant for each of the main outcome end points, but not for DSWI (Supplemental Table 1). However, grade 2 was associated with a significantly higher risk of DSWI (OR, 2.40; 95% CI, 1.05 to 5.48), likely due to the specific effect of chest reopening on wound infection.

Predictors of Severe Bleeding (E-CABG Bleeding Severity Grade 2 or 3)

Logistic regression showed a number of independent factors were associated with severe bleeding, defined as any condition fulfilling the criteria of E-CABG bleeding

severity grade 2 or 3 (Table 7). Among these predictive factors, a prior cardiac operation (OR, 3.15; 95% CI, 2.52 to 3.95), emergency operation (OR, 2.14; 95% CI, 1.65 to 2.77), preoperative insertion of an intraaortic balloon pump (OR, 2.00; 95% CI, 1.22 to 3.30), and valve operation combined with CABG (OR, 2.52; 95% CI, 2.08 to 3.04) were most predictive of severe postoperative bleeding as defined by E-CABG bleeding severity grade 2 or 3. When body mass index was dichotomized according to a cutoff of 25 kg/m², patients above this threshold had a significantly lower risk of severe bleeding than patients beneath this threshold (adjusted analysis: OR, 0.68; 95% CI, 0.59 to 0.78).

When baseline hemoglobin (data available on 3,267 patients operated on at one of the participating centers) was included in this regression model, this variable (OR, 0.77; 95% CI, 0.72 to 0.81) was an independent predictor of bleeding severity grades 2 to 3 along with body mass index (OR, 0.93; 95% CI, 0.91 to 0.96), emergency procedure (OR, 2.11; 95% CI, 1.56 to 2.87), preoperative intra-aortic balloon pump (OR, 3.18; 95% CI, 1.86 to 5.45), prior cardiac operation (OR, 2.22; 95% CI, 1.54 to 3.19), peripheral vascular disease (OR, 1.31; 95% CI, 1.00 to 1.73), estimated glomerular filtration rate (OR, 0.99; 95% CI, 0.98 to 0.99), and type of operation with CABG as reference category (isolated valve surgery: OR, 1.40; 95% CI, 1.07 to 1.83; valve operation combined with CABG: OR, 2.43; 95% CI, 1.85 to 3.19).

Comment

The need of a grading system of postoperative complications has been recognized in surgery as a measure and a means to improve the quality of health care delivery [5]. Therefore, ranking methods have been developed for the assessment of quality of surgical treatment [5, 6]. There are objective difficulties in ranking postoperative complications after cardiac operations because these adverse events may be related to the preoperative comorbidity burden

Table 6. Multiple Propensity Score-Adjusted Analysis of the Effect of the European Coronary Artery Bypass Grafting Bleeding Severity Grades on the Risk of Early Postoperative Adverse Events After Cardiac Operation

Outcome End Points	E-CABG Bleeding Severity Grades				p Value
	Grade 0 OR (95% CI)	Grade 1 OR (95% CI)	Grade 2 OR (95% CI)	Grade 3 OR (95% CI)	
In-hospital death	Reference	3.66 (1.50-8.92)	21.92 (9.19-52.23)	76.58 (29.99-195.58)	<0.0001
Stroke	Reference	1.49 (0.87-2.56)	2.46 (1.31-4.62)	9.49 (4.33-20.79)	<0.0001
Stroke/TIA	Reference	1.79 (1.14-2.81)	2.77 (1.62-4.72)	11.66 (5.96-22.81)	<0.0001
RRT	Reference	3.07 (1.42-6.61)	12.67 (5.90-27.23)	65.28 (28.35-150.34)	<0.0001
Atrial fibrillation ^a	Reference	1.20 (1.06-1.36)	1.53 (1.28-1.84)	2.34 (1.55-3.54)	<0.0001
DSWI ^b	Reference	1.87 (0.92-3.80)	3.41 (1.47-7.87)	1.31 (0.15-11.82)	0.037
ICU stay ≥5 days	Reference	2.79 (2.08-3.76)	8.02 (5.87-10.98)	28.70 (17.98-45.80)	<0.0001
Composite end point ^c	Reference	2.36 (1.08-3.05)	7.74 (5.89-10.16)	47.55 (29.17-77.50)	<0.0001

^a Patients with preoperative atrial fibrillation were excluded from the analysis (6,669 patients available for this analysis). ^b Data available only from 1 center (3,267 patients included in the analysis). ^c Composite end point includes any of the following early major adverse events: in-hospital death, stroke, RRT, ICU stay ≥5 days.

CI = confidence interval; DSWI = deep sternal wound infection; E-CABG = European Coronary Artery Bypass Grafting; ICU = intensive care unit; OR = odds ratio; RRT = renal replacement therapy; TIA = transient ischemic attack.

Table 7. Independent Predictors of European Coronary Artery Bypass Grafting Bleeding Severity Grades 2 to 3

Variables	OR (95% CI)
Female gender	1.26 (1.08–1.47)
Body mass index	0.95 (0.94–0.97)
Peripheral vascular disease	1.34 (1.11–1.62)
Prior cardiac surgery	3.15 (2.52–3.95)
eGFR	0.99 (0.98–0.99)
Emergency	2.14 (1.65–2.77)
Preoperative IABP	2.00 (1.22–3.30)
Left ventricular ejection fraction	
0.30–0.50	1.04 (0.88–1.22)
<0.30	1.64 (1.12–2.39)
Type of operation	
Isolated CABG	
Isolated valve procedure	1.33 (1.11–1.60)
Combined CABG/valve procedure	2.52 (2.08–3.04)
Use of cardiopulmonary bypass	1.47 (1.05–2.07)

CABG = coronary artery bypass grafting; CI = confidence interval; eGFR = estimated glomerular filtration rate according to the Modification of Diet in Renal Disease formula; IABP = intraaortic balloon pump; OR = odds ratio.

and perioperative treatment methods. Furthermore, data are lacking for a proper weighting of the prognostic effect of postoperative complications. Indeed, ranking methods of postoperative complications are usually not derived from statistical analyses of clinical data sets but are rather proposed by a few experienced clinicians and researchers based on the current knowledge of the clinical effect of the specific postoperative complication.

Severe bleeding and use of blood products after cardiac operations are recognized as important determinants of outcome after cardiac interventions [1]. This prompted a panel of experts to propose a grading system for the severity of perioperative bleeding, the Universal Definition of Perioperative Bleeding (UDPB) classification [7]. The UDPB classification is based on the amount of bleeding, use of blood products, administration of prothrombotic drugs, and the need of reexploration for surgical hemostasis. The UDPB classification is scientifically sound and based on current evidence of the adverse events associated with all factors taken into account. However, the complexity of the UDPB classification could make its use in clinical and research activities difficult and impractical; for example, the UDPB classification includes blood loss 12 hours after the operation as a variable for defining the severity of bleeding [5]. One can argue, however, that the severity of perioperative bleeding should also include perioperative blood loss as well as blood loss beyond 12 hours after the operation. In fact, severe anemia may occur 2 to 4 days after the operation even in absence of clear signs of major bleeding or significant hemodilution.

Because there is no reliable method to measure perioperative blood loss, it may be more accurate to indirectly measure the severity of total bleeding by quantifying the amount of blood products administered to correct anemia

and prevent further blood loss. Beside the use of blood products, reexploration for excessive bleeding is per se an important variable in the evaluation of the severity of bleeding.

The E-CABG investigators assigned specific prognostic severity scores for the bleeding-related interventions as transfusion of blood products and reexploration for bleeding [2]. The median of the investigators' scores was used to stratify the severity and prognostic effect of these factors (Table 1). The investigators did not grade the amount of blood loss for reasons explained above, which is worth noting. Furthermore, transfusion of 1 unit of RBCs was not considered as a marker of significant bleeding of any prognostic importance. This was confirmed in a subanalysis of this subset of patients, in whom transfusion of only 1 unit of RBCs was not associated with any adverse events apart from DSWI.

The E-CABG bleeding severity grading method was an independent predictor of early adverse events after adult cardiac operations, particularly for in-hospital death, RRT, and prolonged ICU stay (Tables 4 and 5). These findings were confirmed by multiple propensity score-adjusted analyses and support the validity of the E-CABG bleeding severity definition, which strength resides in its simplicity and straightforward clinical significance. Importantly, the E-CABG bleeding severity grading method showed similar predictive ability compared with the E-CABG bleeding severity additive score; hence, the simpler grading method could be used instead of the more complex additive scoring method.

This study has some limitations that must be acknowledged. Although the data of the 2 institutional registries were prospectively collected, the present analysis was not planned at the time of data collection, and a number of important variables were not collected. Indeed, we do not have data on all variables included in the UDPB classification, and this prevents a comparison of these two scoring methods. The lack of data on preoperative hemoglobin levels from 1 center prevented us from evaluating its effect in the overall data set. However, restraining the analysis to the subgroup of patients with available preoperative hemoglobin data confirmed that our classification maintains its prognostic value also when adjusted for it.

In conclusion, the E-CABG bleeding severity grades and additive score were independently associated with early adverse events after cardiac operations. This simple bleeding severity classification can be a valuable tool in the assessment of the severity and prognostic effect of perioperative bleeding in adult cardiac surgery.

The authors wish to thank the Fondazione Cesare Bartorelli and Fondazione Italiana per il Cuore (Milan, Italy) for their support.

References

1. Loor G, Rajeswaran J, Li L, et al. The least of 3 evils: exposure to red blood cell transfusion, anemia, or both? *J Thorac Cardiovasc Surg* 2013;146:1480–7.

2. Biancari F, Ruggieri VG, Perrotti A, et al. European multi-center study on coronary artery bypass grafting (E-CABG registry): study protocol for a prospective clinical registry and proposal of classification of postoperative complications. *J Cardiothorac Surg* 2015;10:90.
3. Mariscalco G, Biancari F, Zanobini M, et al. Bedside tool for predicting the risk of postoperative atrial fibrillation after cardiac surgery: the POAF score. *J Am Heart Assoc* 2014;3:e000752.
4. Mariscalco G, Bruno VD, Cottini M, et al. Optimal timing of discontinuation of clopidogrel and risk of blood transfusion after coronary surgery. Propensity score analysis. *Circ J* 2011;75:2805-12.
5. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-13.
6. Strasberg SM, Linehan DC, Hawkins WG. The Accordion severity grading system of surgical complications. *Ann Surg* 2009;250:177-86.
7. Dyke C, Aronson S, Dietrich W, et al. Universal definition of perioperative bleeding in adult cardiac surgery. *J Thorac Cardiovasc Surg* 2014;147:1458-63.

Fifty-Third Annual Meeting of The Society of Thoracic Surgeons, Call for Abstracts

The 53rd Annual Meeting of The Society of Thoracic Surgeons (STS) will be held at the George R. Brown Convention Center in Houston, Texas, January 21-25, 2017.

CALL FOR ABSTRACTS AND SURGICAL VIDEOS

Electronic Submission Deadline: June 10, 2016, at 11:59 PM Central Time

Oral presentation, scientific poster, and surgical video abstracts will soon be accepted for the 2017 STS 53rd Annual Meeting. Only electronic abstracts submitted using the online system will be reviewed. Visit www.sts.org/abstracts for complete details about submitting abstracts, including instructions and policies.

Abstract Awards

The Society will once again offer the President's Award, which will be selected from abstracts submitted by residents or young investigators (who have completed training in the last 5 years) in cardiothoracic surgery. These abstracts will be assessed based on quality and potential impact on the field of cardiothoracic surgery. The President's Award will be announced at the STS Award Presentations on Tuesday, January 24, 2017.

The Thoracic Surgery Directors Association (TSDA) will once again offer the Benson R. Wilcox Resident Award. Potential award abstracts must represent original work by a cardiothoracic surgery resident enrolled in a

U.S. ACGME-accredited cardiothoracic surgery residency program at the time the research was conducted. General surgery residents are not eligible. The resident must be the first author and presenter. Those interested in consideration for this award should check the designated box when applying through the online abstract submission system. Poster abstracts and surgical video submissions are not eligible for the Wilcox Award. The Wilcox Award recipient will be recognized at the TSDA General Session and the STS Award Presentations.

In discussion of papers, the Society encourages a healthy spirit of constructive critical review and rebuttal comments pertinent to the paper's content. Presentation of discussion in the form of "secondary papers" will not be welcomed.

Keith S. Naunheim, MD
Secretary

Joseph F. Sabik III, MD
Secretary-Elect

The Society of Thoracic Surgeons
633 N Saint Clair St, 23rd Floor
Chicago, IL 60611-3658
Telephone: (312) 202-5800
Fax: (312) 202-5801
Email: sts@sts.org
Website: www.sts.org