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Rapid thrombelastography predicts perioperative massive blood transfusion in patients undergoing coronary artery bypass grafting

A retrospective study

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Abstract

Massive blood transfusion (MBT) is a relatively common complication of cardiac surgery, which is independently associated with severe postoperative adverse events. However, the value of using rapid thrombotomography (r-TEG) to predict MBT in perioperative period of cardiac surgery has not been explored. This study aimed to identify the effect of r-TEG in predicting MBT for patients undergoing coronary artery bypass grafting (CABG).

This retrospective study included consecutive patients first time undergoing CABG at the Zhongnan Hospital of Wuhan University between March 2015 and November 2017. All the patients had done r-TEG tests before surgery. The MBT was defined as receiving at least 4 units of red blood cells intra-operatively and 5 units postoperatively (1 unit red blood cells from 200 mL whole blood).

Lower preoperative hemoglobin level ($P = .001$) and longer cardiopulmonary bypass time ($P = .001$) were the independent risk factors for MBT during surgery, and no components of the r-TEG predicted MBT during surgery. Meanwhile, longer activated clotting time ($P < .001$), less autologous blood transfusion ($P = .001$), and older age ($P = .008$) were the independent risk factors for MBT within 24 hours of surgery.

Preoperative r-TEG activated clotting time can predict the increase of postoperative MBT in patients undergoing CABG. We recommend the careful monitoring of coagulation system with r-TEG, which allows rapid diagnosis of coagulation abnormalities even before the start of surgery.

Abbreviations: ABT = autologous blood transfusion, ACT = activated clotting time, CABG = coronary artery bypass grafting, CAD = coronary atherosclerotic heart disease, CPB = cardiopulmonary bypass, Hb = hemoglobin, MA = maximum clot strength, MBT = massive blood transfusion, NYHA = New York Heart Association, RBC = red blood cells, r-TEG = rapid thrombelastography, TEG = thromboelastographic.

Keywords: coronary artery bypass grafting, massive blood transfusion, rapid thrombotomography

1. Introduction

Massive blood loss resulting in multiple units of red blood cells (RBC) transfusion is a relatively common complication of cardiac surgery, which is independently associated with severe postoperative adverse events, such as sepsis, renal failure, acute respiratory distress syndrome, and death.[1–4] Predicting the probability of massive blood transfusion (MBT) in the perioperative period of cardiac surgery is of clinical and research significance. For example, it could limit the use of expensive blood preservation modalities in patients identified as being at low-risk for MBT, such as aprotinin or cell recovery and washing. It could also be used to develop preventive measures to reduce the risk of MBT in those identified as being at high-risk for MBT, such as modifying risk factors or prophylactic administration of coagulation factors or hemostatic agents.[5]

Previous studies have identified several risk factors associated with MBT in perioperative period of cardiac surgery, including female sex, older age, renal dysfunction, lower body mass index, lower preoperative hemoglobin (Hb) and longer cardiopulmonary bypass (CPB), which predicted MBT during cardiac surgery,[6] while body surface area, preoperative Hb concentration, preoperative platelet count, urgency of surgery, surgeon, and type of procedure predicted the MBT within 1 day after surgery.[5] However, the value of using rapid thrombotomography (r-TEG) to predict MBT in perioperative period of cardiac surgery has not been explored.

Compared with conventional coagulation tests, both r-TEG and conventional thromboelastographic (TEG) methods provided substantial time advantages in terms of data collection and interpretation. The r-TEG values are essentially the same as those

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of conventional TEG; however, r-TEG uses tissue factor as activator of the coagulation process, and r-TEG activated clotting time (ACT) replaces the conventional TEG R time, which both reflect the function of soluble coagulation factors.[7] The normal range of the R time in conventional TEG is between 2 and 8 minutes, whereas in r-TEG the normal range of ACT is 86 to 118 seconds. Therefore, the ability to more rapidly analyze critical data on coagulation state is a main advantage of using r-TEG over conventional TEG,[8] especially in the emergency patients.

Since the introduction of r-TEG as a faster TEG method, numerous studies have examined its effectiveness in assessing the coagulation state of trauma patients, considering that r-TEG ACT was predictive of early transfusions.[8–10] Nevertheless, no studies have reported predictive value of r-TEG for MBT in the perioperative phase of cardiac surgery. Consequently, we collected a variety of clinical and laboratory parameters associated with MBT, to identify the value of r-TEG in predicting MBT for patients undergoing coronary artery bypass grafting (CABG).

2. Methods

2.1. Patient population and data collection

This retrospective study included patients with coronary atherosclerotic heart disease who first time underwent CABG involving CPB at the Zhongnan Hospital of Wuhan University between March 2015 and November 2017. Patient data were collected from electronic medical records and were analyzed anonymously. The relevant ethics committees/institutional review boards approved this study, and informed consent was not required due to the retrospective study design.

We obtained the following perioperative data: demographics (age, sex, body mass index, history of smoking, and alcohol consumption), preoperative comorbidities (hypertension, diabetes, myocardial infarction, cerebral infarction, hepatic insufficiency, renal dysfunction, hyperlipemia, coronary stenting), heart function classification (New York Heart Association [NYHA] class, American Society of Anesthesiologists grade), history of medications (Angiotensin-Converting Enzyme Inhibitors/angiotensin II receptor blockers, β-adrenergic receptor blockers, calcium channel blockers, nitrates, antiplatelet drugs, anticoagulants, digitoxin, diuretics, lipid-regulating drugs), preoperative laboratory tests (cardiac ultrasonography, routine blood tests, blood biochemistry, coagulation examinations), surgical characteristics (emergency status, duration of operation, CPB duration, concomitant procedure, estimated intraoperative blood loss, autologous blood transfusion (ABT), fresh frozen plasma transfusion, platelet transfusion) and preoperative r-TEG values (ACT, K-time, angle, maximum amplitude). Intraoperative blood loss was estimated by the nurse anesthetist by counting wet swabs and drapes together with suction volume minus volume of any irrigation fluid used.

Inclusion criteria: consecutive patients scheduled for first time CABG were included in the study, who had done rapid thromboelastometry tests before surgery. Exclusion criteria: excluded from the study were patients scheduled for repeated cardiac surgery, patients with missing data that could not be obtained from hospital records, patients who had not had rapid thromboelastometry measurements done before surgery. Flow chart illustrating selection of the study group is presented in Figure 1.

2.2. Surgical procedures and definitions

All the patients were anesthetized, heparinized, undergoing CPB, and surgery was performed according to the existent standard protocol. Before induction of anesthesia and heparinization a sample of blood was removed from a peripheral artery for r-TEG tests. The adequacy of heparin anticoagulation during CPB was monitored by ACT (maintain ACT >480 seconds). At the

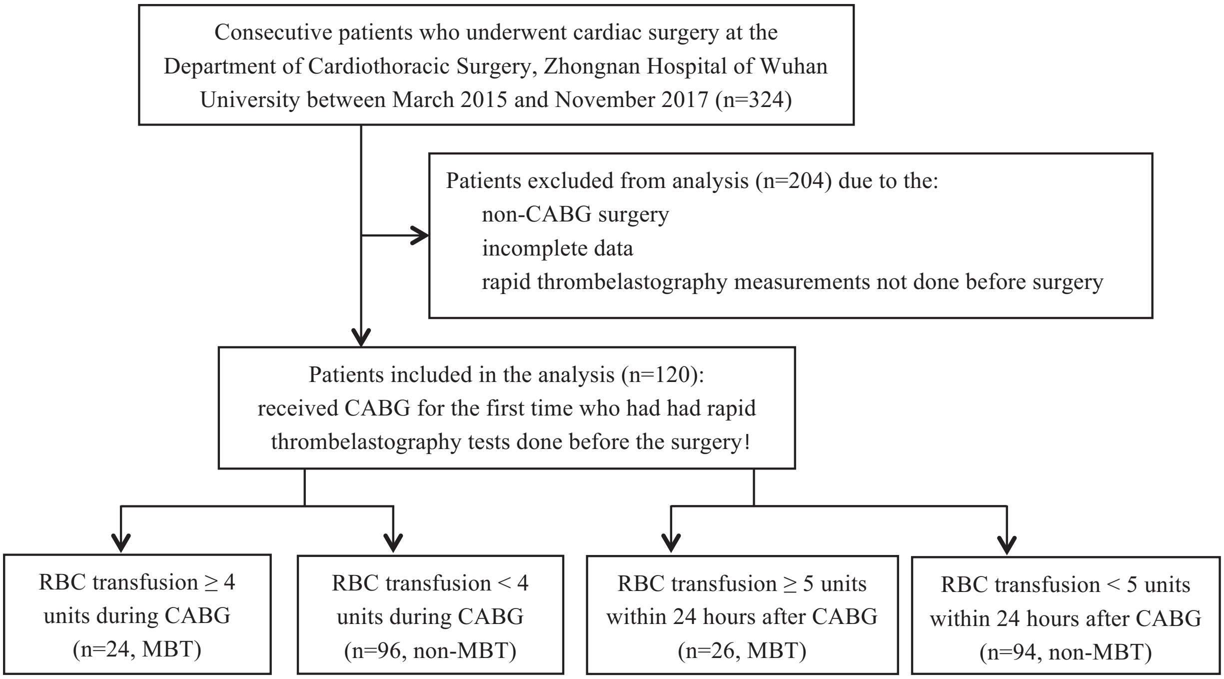

Figure 1. Flow chart illustrating selection of the study groups.

termination of CPB, heparin activity was reversed with protamine in a 1:1 ratio. Additional protamine was administered as needed until ACT returned to the baseline pre-heparin level. After surgery, patients were transferred to the intensive care unit.

In the present study, the definition for MBT during surgery was ≥4 units of RBC transfused. Because beyond this level of intraoperative blood transfusion was associated predominantly with significant increases in postoperative morbidity and mortality.[11,12] The MBT within 1 day of surgery was defined as receiving at least 5 units of RBCs, which was the same as the previous definition of MBT within 24 hours after surgery, and was independently related to the postoperative adverse events.[4,5] (1 unit RBC from 200 mL whole blood)

2.3. Statistical analyses

All analyses were performed using SPSS 22.0. Categorical variables were expressed as frequencies (percentages), and performed using the Chi-square test with Yates correction or Fisher exact test, as appropriate. Normally distributed data were reported as mean ± standard deviation and compared between groups by Student *t* test. Skewed data were expressed as median (interquartile range) and compared between groups by Mann–Whitney *U* test. Variables associated with $P<.05$ in univariate logistic regression were included in regression model. Multivariable logistic regression models were fitted using forward stepwise selection methods, and $P<.05$ was considered statistically significant.

3. Results

3.1. Patients' characteristics

A total of 324 adult patients with cardiac disease who underwent cardiac surgery were screened. Out of these, 204 patients were excluded because they didn't undergo CABG; their medical records were incomplete; or they did not do the rapid thrombelastography measurements before surgery. In the end, 120 patients were included in the analysis, of whom 24 (20.0%) underwent MBT during surgery, and 26 (21.7%) received MBT within 24 hours after surgery (Fig. 1).

Demographic variables of the patients were given in detailed in Table 1. The average age of patients was 61.6 ± 7.6 years (range of 48–82), including 92 male and 28 female. Hypertension (71.7%) was the most common comorbidity. All chronic medications were recorded and had no effect on MBT no matter during or after surgery (Tables 2 and 4). No patient in our study received preoperative RBC transfusion. During surgery, 58 (48.3%) patients did not receive any transfusion, while the remaining 62 (51.7%) received a total of 215 RBC units, with each patient receiving an average of 3.5 units. Within 1 day after surgery, 56 (46.7%) patients did not receive any transfusion, while the remaining 64 (53.3%) received a total of 316 RBC units, with each patient receiving an average of 4.9 units.

Table 1

Demographic variables of the patients and perioperative transfusion of blood products.

Patient characteristics	
Age (yr)	61.6 ± 7.6
Female, n (%)	28 (23.3)
Body mass index (kg/m^2)	23.5 ± 2.8
Smoking, n (%)	44 (36.7)
Alcohol consumption, n (%)	26 (21.7)
Comorbidities, n (%)	
Hypertension	86 (71.7)
Diabetes	38 (31.7)
Myocardial infarction	16 (13.3)
Cerebral infarction	14 (11.7)
Hepatic insufficiency	9 (7.5)
Renal dysfunction	34 (28.3)
Hyperlipemia	48 (40.0)
Coronary stenting	12 (10.0)
Medications, n (%)	
ACEI/ARB	44 (36.7)
β-adrenergic receptor blockers	92 (76.7)
Calcium channel blockers	50 (41.7)
Nitrates	86 (71.7)
Antiplatelet drugs	30 (25.0)
Anticoagulants	104 (86.7)
Digitoxin	12 (10.0)
Diuretics	40 (33.3)
Lipid-regulating drugs	98 (81.7)
Surgical factors	
Estimated intraoperative blood loss (mL)	500 (287.5, 600)
Transfusion	
Autologous blood transfusion (mL)	500 (250, 512.5)
Red blood cells (U)	2 (0, 3)
Fresh frozen plasma (mL)	250 (0, 412.5)
Platelet (U)	0 (0,1)

ACEI = angiotensin converting enzyme inhibitor, ARB = angiotensin II receptor blockers.

3.2. Influencing factors of MBT during CABG

According to the univariate analysis (Table 2), the factors associated with MBT during surgery were female ($P=.001$), smoking ($P=.023$), diabetes ($P=.031$), lower preoperative Hb level ($P=.001$), longer CPB time ($P=.003$), and higher maximum clot strength (MA) level ($P=.001$). Multivariate logistic regression analysis (Table 3) demonstrated that lower preoperative Hb level ($P=.001$) and longer CPB time ($P=.001$) were the independent risk factors for MBT during surgery. No components of the r-TEG predicted MBT during surgery.

MBT incidence increased with decreasing preoperative Hb level (Fig. 2A). Incidence was 10.7% among patients with Hb ≥130 g/L, but it increased sharply from 23.1% at Hb ≥110 g/L, to 50.0% at Hb <110 g/L. Longer CPB was associated with increased MBT risk (Fig. 2B). Each 20-minute prolongation of CPB increased MBT incidence by 0.5 to 1 time. When CPB duration exceeded 100 minutes, the incidence of MBT increased sharply from 12.5% to 25.0%. When it exceeded 120 minutes, the incidence of MBT increased most, from 25.0% to 38.5%.

3.3. Influencing factors of MBT within 24 hours of CABG

Univariate analysis (Table 4) showed that the factors associated with MBT within 24 hours of surgery were older age ($P=.016$), female ($P=.039$), lower preoperative Hb level ($P<.001$), lower preoperative hematocrit level ($P=.002$), longer thrombin time ($P=.047$), less ABT ($P<.001$), longer ACT ($P<.001$), and longer k-time (speed of clot formation) ($P=.007$). Multivariate logistic regression analysis (Table 5) indicated that longer ACT ($P<.001$), less ABT ($P=.001$), and older age ($P=.008$) were the independent risk factors for MBT within 24 hours of surgery.

MBT incidence generally increased with increasing ACT (Fig. 3C). No MBT event occurred among patients with ACT <90 seconds, but it increased sharply from 12.9% at ACT <110

Table 2

Univariate analysis of massive blood transfusion (MBT) during CABG.

Feature	MBT (n=24)	No MBT (n=96)	*P*-value
Demographics:			
Age (yr)	61.0±5.0	61.7±8.1	.589
Female, n (%)	12 (50.0)	16 (16.7)	.001
Body mass index (kg/m^2)	22.7±3.5	23.7±2.7	.124
Smoking	4 (16.7)	40 (41.7)	.023
Alcohol consumption	4 (16.7)	22 (22.9)	.506
Clinical Characteristics:			
Comorbidities, n (%)			
Hypertension	16 (66.7)	70 (72.9)	.543
Diabetes	12 (50.0)	26 (27.1)	.031
Myocardial infarction	2 (8.3)	14 (14.6)	.523
Cerebral infarction	2 (8.3)	12 (12.5)	.733
Hepatic insufficiency	1 (4.2)	8 (8.3)	.685
Renal dysfunction	10 (41.7)	24 (25.0)	.105
Hyperlipemia	12 (50.0)	36 (37.5)	.264
Coronary stenting	2 (8.3)	10 (10.4)	>.99
Diameter of left atrium (mm)	35.6±6.2	35.6±5.4	.974
Left ventricular ejection fraction (%)	53.7±12.7	56.3±12.6	.352
NYHA class III-IV, n (%)	20 (83.3)	64 (66.7)	.111
ASA III-V, n (%)	22 (91.7)	78 (81.3)	.358
Medications, n (%)			
ACET/ARB	12 (50.0)	32 (33.3)	.130
β-adrenergic receptor blockers	18 (75.0)	74 (77.1)	.829
Calcium channel blockers	8 (33.3)	42 (43.8)	.355
Nitrates	18 (75.0)	68 (70.8)	.685
Antiplatelet drugs	4 (16.7)	26 (27.1)	.292
Anticoagulants	22 (91.7)	82 (85.4)	.523
Digitoxin	4 (16.7)	8 (8.3)	.255
Diuretics	10 (41.7)	30 (31.3)	.333
Lipid-regulating drugs	22 (91.7)	76 (79.2)	.239
Laboratory data:			
Haemoglobin (g/L)	119.1±17.5	131.0±15.3	.001
Platelets count (× 10^9/L)	182.2±56.5	181.4±42.9	.938
Hematocrit (%)	37.1±4.5	38.8±5.0	.129
Prothrombin time (s)	11.4 (10.4, 11.9)	10.9 (10.6, 11.5)	.520
Abnormal INR, n (%)	4 (16.7)	12 (12.5)	.737
Activated partial thrombokinase time (s)	32.8 (30.2, 37.7)	33.0 (30.0, 34.3)	.306
Thrombin time (s)	13.7 (13.1, 14.9)	13.6 (12.7, 14.2)	.176
Fibrinogen (mg/mL)	387.7±102.2	342.7±71.7	.072
Surgical factors			
Emergency status, n (%)	4 (16.7)	10 (10.4)	.476
Duration of operation (min)	485.4±57.2	482.5±54.7	.645
Cardiopulmonary bypass (min)	115±21.3	96.6±27.3	.003
Concomitant procedure, n (%)	4 (16.7)	16 (16.7)	>.99
Autologous blood transfusion (mL)	470 (187.5, 637.5)	500 (250, 500)	.851
Preoperative r-TEG			
ACT (s)	105.0 (105.0, 122.8)	105.0 (97.0, 121.0)	.155
K-time (min)	0.8 (0.8, 1.1)	0.8 (0.8, 1.1)	.700
Angle (deg)	78.7 (78.1, 81.2)	78.7 (76.1, 79.8)	.185
MA (mm)	75.9 (73.2, 77.6)	72.1 (70.0, 74.0)	.001

Where applicable, results are expressed as median (range). Other values in parentheses are percentages.

ACEI=angiotensin converting enzyme inhibitor, ACT=activated clotting time, ARB=angiotensin II receptor blockers, ASA=American Society of Anesthesiologists grade, INR=international normalized ratio, MA=maximum clot strength, NYHA=New York Heart Association.

Table 3

Multivariate analysis of massive blood transfusion (MBT) during CABG.

Factors	Regression coefficient (B)	*P*-value	OR	95% CI
CPB duration, per 10 min	0.387	.001	1.473	1.178–1.841
Hemoglobin, per 10 g/L	−0.680	.001	0.507	0.345–0.745

CI = confidence interval, CPB=cardiopulmonary bypass, OR = odds ratio.

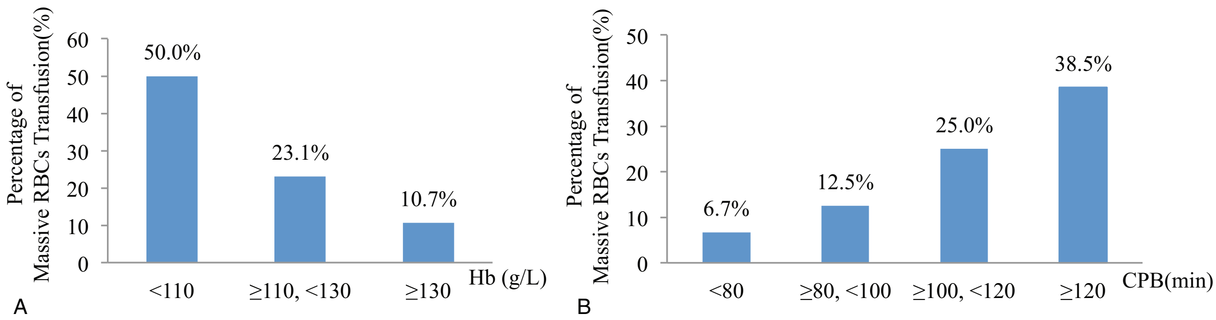

Figure 2. Effect of risk factors on massive RBCs transfusion during CABG. Lower preoperative hemoglobin (Hb) level (A), and longer cardiopulmonary bypass (CPB) time (B). CABG = coronary artery bypass grafting, RBCs = red blood cells.

seconds, to 33.3% at ACT ≥110 g/L. Among patients with ACT ≥150 seconds, 60% received MBT. More ABT was associated with lower MBT risk (Fig. 3D). When ABT <200 mL, the incidence of MBT was as high as 50%. MBT decreased sharply from 36.4% to 8.1% when ABT exceeded 400 mL. Moreover, increasing age was associated with increased MBT incidence (Fig. 3E). Incidence was 14.3% among patients under the age of 60, but it increased sharply from 21.2% among patients aged 60 to 69 to 50.0% among those at least 70 years old.

4. Discussion

Based on the average transfusion of 3.5 and 4.9 units respectively in patients who received transfusion during surgery and within 1 day after surgery, intraoperative MBT was defined as at least 4 units of RBCs transfusion, and postoperative MBT was defined as at least 5 units, which was consistent with the thresholds in previous reports,[4,5,11,12] and the results were worthy for reference. In our study, 20% of patients received MBT and accounted for 55.8% of the total units of allogeneic RBCs consumed during surgery, meanwhile 21.7% of patients received MBT and accounted for 67.1% of the total units of allogeneic RBCs consumed within 1 day of surgery. These findings also provided strong support for the view that reducing MBT can significantly reduce the overall demand for blood products.[6] In order to evaluate the utility of r-TEG to predict MBT in patients undergoing CABG more definitely, we analyzed the risk factors of MBT in different time periods.

Results showed that all components of the r-TEG failed to predict MBT during surgery. Although preoperative MA was an independent predictor in the linear regression model, it did not remain so in the final logistic regression model. Perhaps, because increased MA indicated a hypercoagulable state, which was related to the severity of coronary atherosclerotic heart disease (CAD) and may increase the difficulty and duration of surgery, but the effect on MBT was indirect, so it did not independently contribute to the model of massive transfusion more than did CPB time alone. Similar to the previous study,[13] we considered that preoperative r-TEG did not appear to be useful in predicting the MBT during CABG.

Lower preoperative Hb level and longer CPB were associated with an increased incidence of MBT during surgery, which have been reported previously.[6,14] In our research, MBT risk increased 1-fold for each 10 g/L decrease in Hb level. When the level of Hb was lower than that of 110 g/L, the MBT incidence increased sharply from 23.1% to 50.0%. Huang et al[6] also believed that a large jump in MBT incidence occurred when Hb level decreased to <110 g/L. Therefore, reducing RBC consumption substantially will require increasing preoperative Hb levels, preferably above 110 g/L.[15] Besides, MBT risk increased by 47% for each 10-minute prolongation of CPB, even higher than the 15% increase reported previously.[6] We observed sharp increases in MBT incidence for CPB lasting longer than 110 or 120 minutes. In contrast, only 6.7% of patients with CPB shorter than 80 minutes required MBT. Our findings suggest that CPB should be as short as possible, preferably within 100 minutes.

In our study, r-TEG ACT was associated with an increased incidence of MBT within 1 day after surgery. We found a 1.5-fold increase in MBT risk for each 10-minute prolongation of ACT, and it increased sharply from 12.9% to 33.3% when ACT reached over 110 s. The ACT was increased with factor deficiency or severe hemodilution.[10] On the basis of previous histological assessment of atherosclerotic lesions with microthrombosis,[16–19] greater consumption of coagulation factors was likely to lead to a decrease in concentrations seen in patients with more severe CAD.[20] Additionally, coagulation factors were further reduced owing to hemodilution and consumption after cardiac surgery with CPB.[21,22] We had reason to believe that low concentration of coagulation factors was the possible cause of postoperative MBT. Waldemar et al[23] confirmed that preoperative extrinsically activated test, especially clotting time, was useful in predicting an increased likelihood of postoperative bleeding in patients undergoing CABG. Likewise, we suggested that r-TEG ACT can predict the MBT in the early postoperative period of CABG. And supplementation of plasma or coagulation factors was necessary to reduce ACT, preferably within 110 seconds. In addition, we assessed interaction by logistic regression model, and use NYHA class to represent the severity of CAD. The results showed that there was no interaction between ACT and severity of CAD (ACT by NYHA class, $P = .562$), and no interaction between ACT and CPB time (ACT by CPB time, $P = .281$).

Previous studies[24,25] have determined that ABT can reduce blood loss and allogeneic blood transfusion. Its application in surgeries could moderately improve early postoperative Hb levels and tissue oxygenation.[26,27] We found that ABT decreased risk of postoperative MBT by approximately 30% with each 100 mL increase. In agreement with earlier reports,[28] intraoperative blood salvage was an effective method to reduce the postoperative MBT. Older age has also been demonstrated to be associated

Table 4

Univariate analysis of massive blood transfusion (MBT) within 24 h after CABG.

Feature	MBT (n=26)	No MBT (n=94)	*P*-value
Demographics:			
Age (yr)	64.8±6.8	60.7±7.6	.016
Female, n (%)	10 (38.5)	18 (19.1)	.039
Body mass index (kg/m^2)	22.8±3.0	23.7±2.8	.133
Smoking	6 (23.1)	38 (40.4)	.104
Alcohol consumption	4 (15.4)	22 (23.4)	.380
Clinical Characteristics:			
Comorbidities, n (%)			
Hypertension	18 (69.2)	68 (72.3)	.755
Diabetes	10 (38.5)	28 (29.8)	.400
Myocardial infarction	4 (15.4)	12 (12.8)	.728
Cerebral infarction	6 (23.1)	8 (8.5)	.077
Hepatic insufficiency	4 (15.4)	5 (4.3)	.101
Renal dysfunction	4 (15.4)	30 (31.9)	.098
Hyperlipemia	8 (23.1)	40 (44.7)	.278
Coronary stenting	4 (15.4)	8 (8.5)	.289
Diameter of left atrium (mm)	34.5±6.5	35.9±5.2	.225
Left ventricular ejection fraction (%)	52.3±15.4	56.8±11.8	.108
NYHA class III-IV, n (%)	20 (76.9)	64 (68,1)	.384
ASA III-V, n (%)	22 (84.6)	78 (83.0)	>.99
Medications, n (%)			
ACEI/ARB	12 (46.2)	32 (34.0)	.257
β-adrenergic receptor blockers	22 (84.6)	70 (74.5)	.279
Calcium channel blockers	14 (53.8)	36 (38.3)	.155
Nitrates	18 (69.2)	68 (72.3)	.755
Antiplatelet drugs	8 (30.8)	22 (23.4)	.443
Anticoagulants	24 (92.3)	80 (85.1)	.518
Digitoxin	2 (7.7)	10 (10.6)	>.99
Diuretics	8 (30.8)	32 (34.0)	.754
Lipid-regulating drugs	24 (92.3)	74 (78.7)	.155
Laboratory Data:			
Haemoglobin (g/L)	122.1±7.4	130.5±17.7	<.001
Platelets count (× 10^9/L)	170.2±47.3	184.6±44.9	.151
Hematocrit (%)	35.9±4.7	39.2±4.8	.002
Prothrombin time (s)	11.2 (10.5, 12.2)	11.0 (10.6, 11.6)	.575
Abnormal INR, n (%)	6 (23.1)	10 (10.6)	.111
Activated partial thrombokinase time (s)	32.9 (30.0, 36.5)	32.9 (30.0, 34.5)	.524
Thrombin time (s)	14.1 (13.7, 14.7)	13.3 (12.7, 14.4)	.047
Fibrinogen (mg/mL)	388.2±68.8	355.4±82.9	.329
Surgical factors			
Emergency status, n (%)	4 (15.4)	10 (10.6)	.500
Duration of operation (min)	489.2±65.6	481.4±52.1	.518
Cardiopulmonary bypass (min)	103.8±24.0	99.3±28.0	.463
Concomitant procedure, n (%)	4 (15.4)	16 (17.0)	>.99
Estimated intraoperative blood loss (mL)	500 (300, 600)	500 (212.5, 600)	.290
Autologous blood transfusion (mL)	250 (0, 350)	500 (325, 575)	<.001
Red blood cells (U)	2 (0, 3)	0 (0, 3)	.334
Fresh frozen plasma (mL)	300 (0, 650)	200 (0, 400)	.214
Platelet (U)	0 (0, 1)	0 (0, 1)	.308
Preoperative r-TEG			
ACT (s)	128.0 (105.0, 144.0)	105.0 (97.0, 109.0)	<.001
K-time (min)	0.9 (0.8, 1.5)	0.8 (0.8, 1.1)	.007
Angle (deg)	78.6 (76.7, 80.6)	78.8 (75.7, 79.8)	.721
MA (mm)	74.0 (68.1, 74.8)	72.1 (68.9, 74.7)	.400

Where applicable, results are expressed as median (range). Other values in parentheses are percentages.

ACEI=angiotensin converting enzyme inhibitor, ACT=activated clotting time, ARB=angiotensin II receptor blockers, ASA=American Society of Anesthesiologists grade, INR=international normalized ratio, MA=maximum clot strength, NYHA=New York Heart Association.

with more postoperative blood transfusion, which may be related to a greater likelihood of complications.[29] In our sample, the incidence of MBT was as high as 50% among patients at least 70 years old, which was about 3-fold higher than that among younger patients. Accordingly, it was of high importance to optimize perioperative care, particularly in the elderly.

As shown in our results, the failure to predict the perioperative MBT during surgery using r-TEG components could be

Table 5

Multivariate analysis of massive blood transfusion (MBT) within 24 h after CABG.

Factors	Regression coefficient (B)	*P*-value	OR	95% CI
ACT, per 10 s	0.405	<.001	1.499	1.199–1.875
ABT, per 100 mL	−0.383	.001	0.682	0.549–0.847
Age, per 10 yr	1.108	.008	3.029	1.343–6.832

ABT = autologous blood transfusion, ACT = activated clotting time, CI = confidence interval, OR = odds ratio.

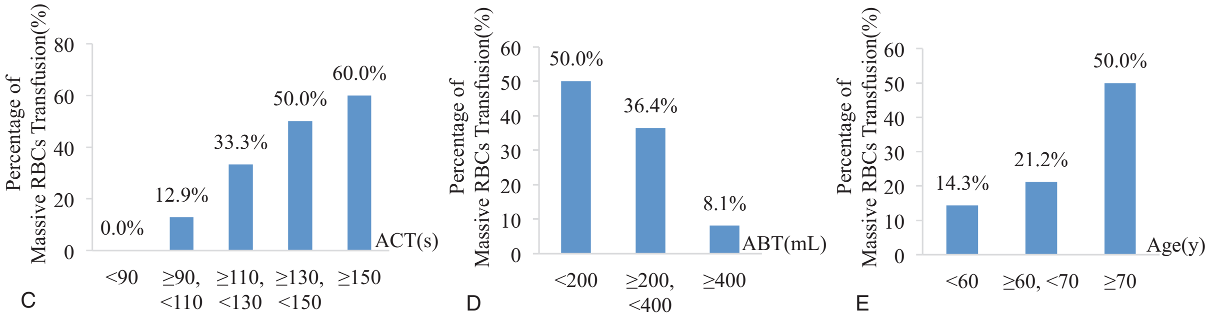

Figure 3. Effect of risk factors on massive RBCs transfusion within 24 h after CABG. Longer activated clotting time (ACT) (C), less autologous blood transfusion (ABT) (D), and older age (E). CABG = coronary artery bypass grafting, RBCs = red blood cells.

attributed to the following factors. According to our data, the median ACT was 128 seconds in patients with postoperative MBT, and was 105 seconds in patients without postoperative MBT. We found that 8 patients with ACT >128 seconds did not receive postoperative MBT. These patients had a mean age of 60.8 years, and all of them received ABT more than 500 mL. The lower age levels and larger ABT may be the reasons why patients with longer ACT did not need MBT. Besides, 4 patients with ACT <105 seconds received postoperative MBT, with an average age of 76.5 years and an average ABT volume of 250 mL. The older age and less ABT may be the reasons why patients with shorter ACT need MBT. Therefore, we should integrate multiple factors comprehensively to evaluate the requirements for MBT. Besides, preoperative K-time and angle which mainly reflected the fibrinogen level showed no significant correlation with postoperative MBT. The level of fibrinogen was also reduced during CPB secondary to dilution, but the transformation of fibrinogen to fibrin was typically not impaired, suggesting that fibrinogen was not usually a significant problem.[30] Previous studies have indicated that patients with coronary heart disease were in a state of hypercoagulability, with high platelet count and platelet function.[31] In our research, the median of preoperative MA in patients with postoperative MBT (74.0 mm) was even higher than that without postoperative MBT (72.1 mm). Thus, the higher MA may be associated with the increased blood clotting, but would not cause postoperative MBT. In addition, all components of the r-TEG failed to predict MBT during surgery. The possible reason may be that surgery-related factors (such as CPB, surgical damage, etc) were the most direct cause of intraoperative MBT, while r-TEG 's prediction of intraoperative MBT was indirect, so the correlation between components of the r-TEG and intraoperative MBT was not significant.

There are several study limitations, one of them being that it was retrospective in nature, which may have led to biased selection of patients. Besides, the number of participants was quite low, and further studies were needed to investigate our observation in a larger group of patients. As well as the study population was also heterogeneous, for instance, gender ratio was mismatched. However, these results were from a consecutive series of cases and so male dominance was unpredictable. In addition, this study only applied to pre-operative r-TEG and not intraoperative r-TEG or postoperative r-TEG. The effect of intraoperative and postoperative r-TEG should be explored and discussed in further studies. Moreover, the findings of r-TEG cannot be applied to ROTEM. Finally, if the thromboelastometry tests could be performed before and during CABG, there will be additional costs to cover reagents and maintenance, and this economic factor might be difficult to accept in some centers.

5. Conclusions

Based on the analysis of the presented results, preoperative r-TEG ACT can predict the increase of postoperative MBT in patients undergoing CABG. We recommend the careful monitoring of coagulation system with r-TEG, which allows rapid diagnosis of coagulation abnormalities even before the start of surgery.

Author contributions

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References

[1] Unsworth-White MJ, Herriot A, Valencia O, et al. Resternotomy for bleeding after cardiac operation: a marker for increased morbidity and mortality. Ann Thorac Surg 1995;59:664–7.

[2] Moulton MJ, Creswell LL, Mackey ME, et al. Reexploration for bleeding is a risk factor for adverse outcomes after cardiac operations. J Thorac Cardiovasc Surg 1996;111:1037–46.

[3] Crabtree TD, Codd JE, Fraser VJ, et al. Multivariate analysis of risk factors for deep and superficial sternal infection after coronary artery bypass grafting at a tertiary care medical center. Semin Thorac Cardiovasc Surg 2004;16:53–61.

[4] Karkouti K, Wijeysundera DN, Yau TM, et al. The independent association of massive blood loss with mortality in cardiac surgery. Transfusion 2004;44:1453–62.

[5] Karkouti K, O'Farrell R, Yau TM, et al. Prediction of massive blood transfusion in cardiac surgery. Can J Anaesth 2006;53:781–94.

[6] Huang D, Chen C, Ming Y, et al. Risk of massive blood product requirement in cardiac surgery: a large retrospective study from 2 heart centers. Medicine (Baltimore) 2019;98:e14219.

[7] Gonzalez E, Pieracci FM, Moore EE, et al. Coagulation abnormalities in the trauma patient: the role of point-of-care thromboelastography. Semin Thromb Hemost 2010;36:723–37.

[8] Lee TH, McCully BH, Underwood SJ, et al. Correlation of conventional thrombelastography and rapid thrombelastography in trauma. Am J Surg 2013;205:521–7.

[9] Jeger V, Zimmermann H, Exadaktylos AK. Can rapid TEG accelerate the search for coagulopathies in the patient with multiple injuries? J Trauma 2009;66:1253–7.

[10] Cotton BA, Faz G, Hatch QM, et al. Rapid thrombelastography delivers real-time results that predict transfusion within 1 hour of admission. J Trauma 2011;71:407–14.

[11] Goudie R, Sterne JA, Verheyden V, et al. Risk scores to facilitate preoperative prediction of transfusion and large volume blood transfusion associated with adult cardiac surgery. Br J Anaesth 2015;114:757–66.

[12] Leal-Noval SR, Rincon-Ferrari MD, Garcia-Curiel A, et al. Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery. Chest 2001;119:1461–8.

[13] Dorman BH, Spinale FG, Bailey MK, et al. Identification of patients at risk for excessive blood loss during coronary artery bypass surgery: thromboelastography versus coagulation screen. Anesth Analg 1993;76:694–700.

[14] Karkouti K, Wijeysundera DN, Beattie WS, et al. Variability and predictability of large-volume red blood cell transfusion in cardiac surgery: a multicenter study. Transfusion 2007;47:2081–8.

[15] Craver C, Belk KW, Myers GJ. Measurement of total hemoglobin reduces red cell transfusion in hospitalized patients undergoing cardiac surgery: a retrospective database analysis. Perfusion 2018;33:44–52.

[16] Spurlock BO, Chandler AB. Adherent platelets and surface microthrombi of the human aorta and left coronary artery: a scanning electron microscopy feasibility study. Scanning Microsc 1987;1:1359–65.

[17] Bini A, Fenoglio JJJr, Mesa-Tejada R, et al. Identification and distribution of fibrinogen, fibrin, and fibrin (ogen) degradation products in atherosclerosis. Use of monoclonal antibodies. Arteriosclerosis 1989;9:109–21.

[18] Ip JH, Fuster V, Chesebro JH. Exploration of the atherosclerotic plaque. Biomed Pharmacother 1990;44:343–52.

[19] Crawley J, Lupu F, Westmuckett AD, et al. Expression, localization, and activity of tissue factor pathway inhibitor in normal and atherosclerotic human vessels. Arterioscler Thromb Vasc Biol 2000;20:1362–73.

[20] Brummel-Ziedins KE, Lam PH, Gissel M, et al. Depletion of systemic concentrations of coagulation factors in blood from patients with atherosclerotic vascular disease. Coron Artery Dis 2013;24:468–74.

[21] Coakley M, Hall JE, Evans C, et al. Assessment of thrombin generation measured before and after cardiopulmonary bypass surgery and its association with postoperative bleeding. J Thromb Haemost 2011;9:282–92.

[22] Bevan DH. Cardiac bypass haemostasis: putting blood through the mill. Br J Haematol 1999;104:208–19.

[23] Gozdzik W, Adamik B, Wysoczanski G, et al. Preoperative thromboelastometry for the prediction of increased chest tube output in cardiac surgery: a retrospective study. Medicine (Baltimore) 2017;96:e7669.

[24] Zhou J. A review of the application of autologous blood transfusion. Braz J Med Biol Res 2016;49:e5493.

[25] Ashworth A, Klein AA. Cell salvage as part of a blood conservation strategy in anaesthesia. Br J Anaesth 2010;105:401–16.

[26] Colwell CWJr, Beutler E, West C, et al. Erythrocyte viability in blood salvaged during total joint arthroplasty with cement. J Bone Joint Surg Am 2002;84:23–5.

[27] Hovav T, Yedgar S, Manny N, et al. Alteration of red cell aggregability and shape during blood storage. Transfusion 1999;39:277–81.

[28] Ferraris VA, Ferraris SP, Saha SP, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg 2007;83(5 Suppl):S27–86.

[29] Ad N, Massimiano PS, Burton NA, et al. Effect of patient age on blood product transfusion after cardiac surgery. J Thorac Cardiovasc Surg 2015;150:209–14.

[30] McKenna R, Bachmann F, Whittaker B, et al. The hemostatic mechanism after open-heart surgery. II. Frequency of abnormal platelet functions during and after extracorporeal circulation. J Thorac Cardiovasc Surg 1975;70:298–308.

[31] Walter T, Szabo S, Kazmaier S, et al. Investigation of platelet adhesiveness in patients with coronary artery disease and acute myocardial infarction using the platelet adhesion assay (PADA). Clin Lab 2011;57:315–20.