Eur J Vasc Endovasc Surg (2019) 58, 13—22

Editor's Choice — A Rotational Thromboelastometry Driven Transfusion Strategy Reduces Allogenic Blood Transfusion During Open Thoraco-abdominal Aortic Aneurysm Repair: A Propensity Score Matched Study

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WHAT THIS PAPER ADDS

While thromboelastometry driven transfusion algorithms have been adopted in several settings, no studies have focused on aortic surgery. The present study proves that a rotational thromboelastometry (ROTEM) driven strategy is safe and effective even in major aortic surgery. A ROTEM transfusion algorithm allowed a decrease in allogenic blood product transfusions, pulmonary complications, and costs.

Objective: Open repair of thoraco-abdominal aortic aneurysm (TAAA) is a challenging procedure, associated with high rates of peri-operative bleeding and blood product transfusions. A large intra-operative volume transfusion has been associated with higher in hospital mortality and prolonged mechanical ventilation. A propensity score matched study was carried out to assess whether the introduction of a rotational thromboelastometry (ROTEM) based transfusion strategy reduces allogenic blood transfusion and affects morbidity in patients undergoing open TAAA repair.

Methods: All patients undergoing open TAAA repair at the San Raffaele Scientific Institute between 2009 and 2017 were included. Until 2016, a protocol based on estimated blood loss and conventional coagulation tests was used. After March 2016 a ROTEM guided transfusion protocol was developed and adopted. To account for selection bias, propensity score matching was performed.

Results: Five hundred and forty-seven consecutive patients were included. After propensity score matching, 77 patients in the ROTEM algorithm group were successfully matched with 77 patients in the standard algorithm group. Patients managed with ROTEM received fewer red blood cells units (3.5 [range 0—11] vs. 4 [range 0—17]; $p = .026$) and a lower volume of fresh frozen plasma (286 ± 496 vs. 2,050 ± 1,120; $p < .001$). In addition, fewer patients received fresh frozen plasma (35% vs. 97%; $p < .001$). Patients in the ROTEM group showed a significant decrease in the occurrence of pulmonary complications (44% vs. 83%; $p = .01$). Cost analysis showed a relevant reduction of per-patient expense after the introduction of ROTEM (€834 ± €577 vs. €1,285 ± €851; $p < .001$)

Conclusion: A ROTEM guided transfusion strategy significantly limited the quantity of transfused blood products during open TAAA repair, improving clinical outcomes while reducing costs, allowing for better resource distribution in a setting where blood loss is relevant.

Keywords: Blood transfusion, Hospital costs, Pulmonary complications, Rotational thromboelastometry, Thoraco-abdominal aortic aneurysm, Transfusion algorithm
Article history: Received 16 November 2018, Accepted 10 February 2019, Available online 8 June 2019

INTRODUCTION

While aortic surgery rapidly proceeds towards an endovascular approach, thoraco-abdominal aortic aneurysms (TAAAs) still need open repair in the vast majority of cases. The extent of the surgical field and the involvement of multiple organs makes this procedure exclusive to highly specialised centres, even though mortality ranges between 5% and 15%.[1—3] Management of bleeding is key to success in this surgery, as both surgical and medical factors, including changes in coagulation patterns and microvascular bleeding, contribute to massive blood loss.[4] However if, on

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1078-5884/
https://doi.org/10.1016/j.ejvs.2019.02.009

the one hand, the loss of large amounts of blood, not promptly replaced, is associated with hypotension and hypoperfusion, on the other hand, transfusion related immune modulation, acute lung injury, and transfusion associated circulatory overload are well known complications of blood transfusions.[5,6] In patients undergoing open TAAA repair, large volume intra-operative transfusions have been associated with higher in hospital mortality and prolonged mechanical ventilation.[7] Transfusion strategy in major aortic surgery has been described as either "reactive",[8] with the administration of blood products in response to the development of a clinical or laboratory evident coagulopathy, or "pre-emptive",[9] based on the administration of blood products in the absence of a clinically detectable coagulopathy. Both approaches lead, ultimately, to a massive use of blood products. A recent review on bleeding management in vascular surgery concluded that haemostasis as far as possible, should be monitored and goal directed.[10] This calls for a different management of bleeding, and the adoption of a transfusion algorithm guided by rotational thromboelastometry (ROTEM) could be an option. As ROTEM use has been validated in only a few settings, including cardiac surgery, further evaluation in acute settings and other patient categories is needed.[11,12]

In the light of this, a propensity score matched study was performed to assess the capacity of a ROTEM based transfusion algorithm to reduce the need for allogenic blood transfusions, complications, and costs in patients undergoing open TAAA repair.

METHODS

Study design and patient population

Patients undergoing elective, urgent, and emergency open TAAA repair at IRCCS San Raffaele Scientific Institute between 2009 and 2017 were included. Up to 2016, a protocol based on estimated blood loss and conventional coagulation tests was used. After March 2016 a ROTEM device (Werfen, Barcelona, Spain) became available and a ROTEM guided transfusion protocol was developed and adopted (Fig. 1). Baseline, procedural and hospitalisation data were collected in a computerised database. All study participants gave written informed consent allowing for scientific data management. Ethical committee approval was waived according to Italian law. The anatomical extent of the aneurysm was defined according to the Crawford classification.[13]

San Raffaele Scientific Institute is a national referral centre for open TAAA repair. Descending thoracic and thoraco-abdominal aortic disease at San Raffaele Institute are treated following the current European Society for Vascular Surgery guidelines.[14] Indications for open repair of TAAA includes aneurysms $>$ 60 mm (less for patients with connective tissue disorders), rapid growth ($>$ 10 mm/year), or symptomatic patients. Patients unfit for open repair were considered for endovascular repair and were therefore excluded from this series. Regarding, isolated descending thoracic aortic aneurysms, open repair was limited to fit patients unsuitable for endovascular repair owing to the absence of adequate arterial access, absence of landing zones, connective tissue disorders in young and healthy patients, high risk of post-procedural neurological deficit, and symptoms related to aneurysm compression.

All patients undergoing open TAAA repair underwent a full pre-operative assessment of cardiac, pulmonary, and renal function to evaluate operative risk and plan the best operative strategy. Pre-operative evaluation of the cardiac function consisted of electrocardiography and transthoracic echocardiography at rest in all patients, while coronary computed tomography or coronary angiography was performed in selected patients with a history of coronary disease or abnormal findings on echocardiography or electrocardiography.

Bleeding and transfusion management

The transfusion protocol for open TAAA repair was guided by the estimated blood loss and conventional coagulation tests (international normalised ratio [INR], activated partial thromboplastin time [aPTT], platelet [PLT] count). Briefly, red blood cells (RBCs) and fresh frozen plasma (FFP) were transfused in a 1:1 ratio at a total infusion rate equal to the blood loss. Additional coagulation products were administered with an INR $>$ 1.5 and/or an aPTT $>$ 40 s, while PLT units were transfused when the PLT count was $<$ 100,000/L.

ROTEM is a point of care that identifies specific cascade abnormalities by several activators. In particular, it is able to detect isolated deficits of fibrinogen (FIBTEM) and abnormalities of the intrinsic (INTEM) and extrinsic (EXTEM) pathway.[15] Furthermore, APTEM and HEPTEM provide information, respectively, on hyperfibrinolysis and the presence of heparin in the patient's blood. It requires three mL whole blood collected in a sodium citrate tube.

After ROTEM became available, tests were performed in all patients after heparin reversal with protamine in a 1:1 ratio. As the aim of ROTEM is to treat peri-operative coagulopathy associated with microvascular bleeding, the test was only performed after all surgical sources of bleeding were under control. Meanwhile filtered shed blood from the cell saver and crystalloids were administered to maintain an adequate perfusion pressure. In the event of a haematocrit $<$ 30%, RBC units were transfused in order to achieve a sufficient oxygen delivery.

In the event of a maximum clotting firmness in the EXTEM $<$ 45 mm and in the FIBTEM $<$ 8 mm, two g of fibrinogen were administered. Conversely with a clotting firmness in the FIBTEM $>$ 10 mm, platelets were transfused. After administering fibrinogen and/or platelets, the clotting time (CT) in the EXTEM was considered. If it was $>$ 80 s, FFP (15–20 mL/kg) were administered. Conversely if the EXTEM CT was within the normal range and the INTEM CT was $>$ 240 s, HEPTEM was performed. If HEPTEM CT was at least 20% less than INTEM CT, 50 mg protamine was administered. Otherwise, FFP (15–20 mL/kg) was administered (Fig. 1).

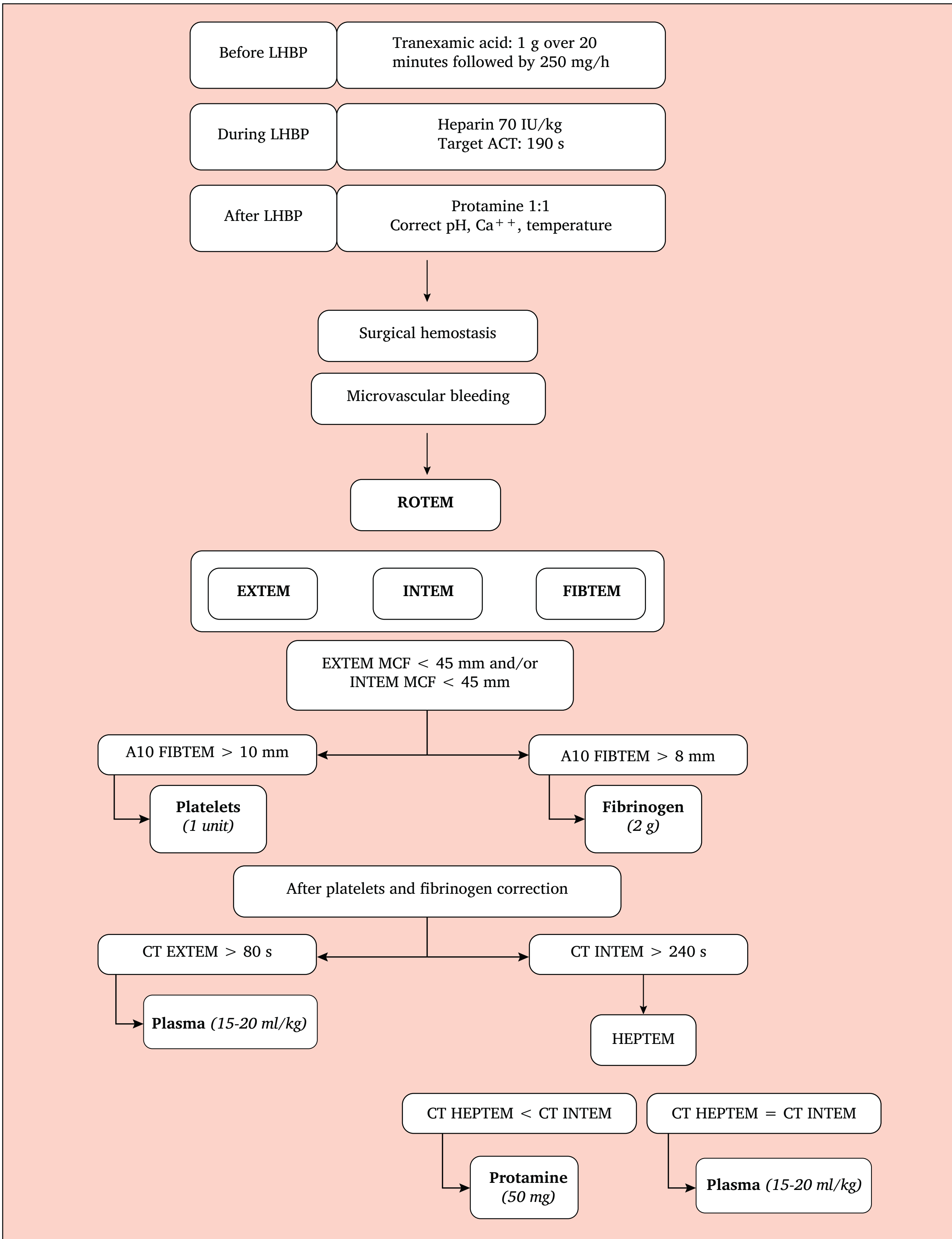

Figure 1. Rotational thromboelastometry (ROTEM) guided transfusion protocol. LHBP = left heart bypass pump; ACT = activated clotting time; MCF = maximum clotting firmness; CT = clotting time; Ca = calcium.

During the study period, all patients received intra-operative infusion of tranexamic acid (1 g over 20 minutes followed by 250 mg/hour) to prevent hyperfibrinolysis according to guidelines. Fibrinogen was introduced into clinical practice in 2014. No other haemostatic products were used during the study period. A Dideco Electa (Sorin Group, Electa, Italy) cellsaver machine was used to process and re-infuse salvaged blood. If needed, left heart bypass was used. The target activated clotting time (ACT) during bypass was > 190 s. Heparin was administrated at a maximum starting dose of 70 IU/kg and reversed at the end of surgery with protamine in a 1:1 ratio. ACT was serially assessed during surgery and additional heparin was administered as necessary. Packed RBCs were transfused if the haematocrit was $< 30\%$. This cut off did not change over the study period.

Anaesthesia, surgery, and post-operative care

Peri-operative management of open TAAA repairs at the authors' institution has been described, in detail, previously.[7] All patients received standardised anaesthetic management. Premedication (morphine 0.1 mg/kg intramuscularly; atropine 0.5 mg intramuscularly; diazepam two mg orally) was administered 30 minutes before surgery. As part of standard monitoring, electrocardiography, pulse oximetry, and non-invasive blood pressure were started as soon as the patient entered the operating room. The right radial artery was then cannulated to monitor arterial blood pressure. When left heart bypass was indicated, the right femoral artery was added for invasive blood pressure monitoring of the lower part of the body. If not contra-indicated, an epidural catheter was inserted between T7 and T8 for post-operative pain control. General anaesthesia was induced with fentanyl (1 μg/kg), propofol (2 mg/kg), and rocuronium 0.6 mg/kg. Single lung ventilation with a left double lumen endotracheal tube was generally performed. Anaesthesia was maintained with propofol 2–4 mg/kg/h and remifentanil 0.05–0.25 μg/kg/minute tailored to clinical response and Bispectral Index. Mannitol (0.5 g/kg) and methylprednisolone (30 mg/kg) were administered at the beginning of surgery to mitigate the effect of renal and spinal cord ischaemia. Owing to the large volume shift during surgery a four lumen central venous catheter (8.5 Fr) and a 12 Fr double lumen short-term haemodialysis catheter were placed in the right internal jugular vein.

A multimodal approach was adopted to decrease the risk of paraplegia. Cerebrospinal fluid drainage was applied if not contraindicated and managed with Liquoguard (Möller Medical GmbH, Fulda, Germany) or a Becker External Drainage System. At least one pair of intercostal arteries were re-implanted whenever possible. The mean arterial pressure was kept > 75 mmHg throughout surgery by administration of norepinephrine when necessary. Since 2015, sensory and motor evoked potentials have become part of standard monitoring during TAAA surgery, allowing early detection of spinal cord ischaemia. As standard practice, no RBCs were administered if the haematocrit was $> 30\%$ to reduce spinal cord injury risk.

When necessary, a standard left heart bypass technique with a 20 Fr mouldable cannula placed in the left atrium via the superior or inferior left pulmonary vein and a 7 cm long inflow cannula in the common femoral artery (14–16 Fr) with a non-occlusive technique was adopted.

Renal perfusion with cold (4 °C) crystalloid solution or Custodiol (Dr Franz-Kohler Chemie GmbH, Bensheim, Germany) were administered through 9 Fr Pruitt perfusion catheters continued until the renal arteries were re-implanted. Selective perfusion of the visceral arteries with normothermic blood was also carried out and continued until circulation was restored.

After surgery, all patients were admitted to the intensive care unit for post-operative monitoring for at least 24 hours and then moved to the surgical ward.

Definitions

Pulmonary complications were defined as need for prolonged mechanical ventilation (> 48 hours), pneumonia or need for non-invasive ventilation, re-intubation, or tracheostomy.

Mechanical ventilation was discontinued when the following criteria were met: satisfactory spontaneous breathing trial for 10 minutes minimum with adequate gas exchange; haemodynamic stability and no excessive bleeding; normothermia; satisfactory neurological status; and adequate pain control.[16]

The criteria for non-invasive ventilation (NIV) were respiratory frequency > 22 breaths/minute, peripheral oxygen saturation $< 92\%$, and clinical signs of major respiratory distress (dyspnoea, use of accessory respiratory muscles, paradoxical movement of the thoraco-abdominal wall) not corrected by oxygen.[17]

Major adverse cardiac events were defined as peri-operative myocardial infarction (appearance of Q wave ≥ 40 milliseconds or the loss of R wave amplitude in two continuous leads of the same vascular territory), atrial fibrillation, and occurrence of intra-operative or post-operative low cardiac output syndrome secondary to systolic ventricular dysfunction (need for inotropic support to avoid metabolic acidosis and urine output < 0.5 mL/kg/hour). Sepsis was defined as an organ dysfunction, identified as an acute change in total sequential organ failure assessment score ≥ 2 points as a result of infection.

Intensive care unit discharge to the ward was performed as soon as all these criteria were met: collaborating patient, stable haemodynamics with no inotropic support, spontaneous breathing without clinical signs of respiratory distress, $SpO_2 > 94\%$ on room air, bleeding under control, and urinary output > 1 mL/kg/hour.

Statistical analysis

To account for selection bias between patients managed with ROTEM transfusion algorithm and those managed with a standard protocol, propensity score matching was performed. Propensity score matching was obtained from a multivariable logistic regression for patients receiving transfusions guided by a ROTEM algorithm, including pre- and intra-operative variables potentially associated with intra-operative transfusions or outcome. Thus, all pre- and intra-operative variables included in Table 1 were included in the propensity score as covariates. Nearest neighbour matching with a 1:1 ratio and a calliper of 0.20 were applied. Baseline and post-propensity score matching balance between covariates were assessed by means of standardised mean differences; a standardised mean difference < 0.10 was considered to represent good adjustment between groups (Fig. 2).[18] After patient matching, the McNemar test for categorical variables and paired *t* test for continuous variables were used to assess the effect of the ROTEM transfusion algorithm on post-operative outcomes.

A *p* value $< .05$ was considered to be significant statistically. Continuous variables are presented as mean $\pm$ SD and compared with the *t* test. Categorical variables are presented as frequency (percentages) and compared using the chi-square test or Fisher's exact test when indicated. Statistical analysis was performed with SPSS 23 (IBM, Armonk, NY, USA) and R software version 2.12. The R package of MatchIt was used for the propensity score analysis.

Cost analysis

To perform cost analysis, the price for each blood component was considered and the final per-patient expense was compared. RBCs were priced at €181 per unit, FFP at €172 per 250 mL unit, and PLT pools at €97. The total expense of ROTEM was €45 per test.

RESULTS

The pre-operative characteristics of all 547 consecutive patients (ROTEM algorithm, $n = 106$; standard algorithm, $n = 441$) undergoing open TAAA repair during the study period before and after propensity score matching are reported in Table 1. After propensity score matching, 77 patients in the ROTEM group were successfully matched with 77 patients in the standard algorithm group.

Patients in the ROTEM group had a reduction in transfusion blood products (RBC and FFP) and there was a reduction in the number of patients transfused both before and after propensity matching, with the effects being more pronounced in the intra-operative period (Table 2).

Intra-operatively, both the number of patients transfused with RBC and the number of RBC units were significantly lower after the introduction of the ROTEM algorithm (65% vs. 89% [$p < .001$] and 1 [range 0—5] units vs. 3 [range 0—10] units [$p < .001$], respectively). The same findings applied to FFP administration (27% vs. 95% [$p < .001$] and 0 $\pm$ 600 mL vs. 1,600 $\pm$ 900 mL [$p < .001$], respectively). Notably, the use of fibrinogen was increased in the ROTEM group (44% vs. 1%; $p < .001$).

During the first 48 hours, both the number of patients transfused with RBC and the number of units of RBC were significantly lower after the introduction of the ROTEM algorithm (12% vs. 35% [$p = .001$] and 0 [range 0—4] units vs. 0 [range 0—6] units, respectively [$p = .004$]). After 48 hours, 42% of patients in the standard algorithm group and 69% in the ROTEM algorithm group had received RBCs ($p < .001$).

Overall, a similar number of patients in both groups received RBCs (95% vs. 91%; $p = .50$), but a greater number of RBC units were administered in the standard algorithm group (4 [range 0—17] units vs. 3.5 [range 0—11] units; $p = .026$) (Fig. 3A). These differences were also observed in the overall population. Eighty patients received more than four RBC transfusions during their hospital stay: 42 in the standard group and 38 in the ROTEM group. As for FFP, 92% of patients in the standard group received $>$ 1,000 mL FFP vs. 14% in the standard group. Haemoglobin level at the end of surgery did not differ between the groups (11.4 $\pm$ 1.48 mg/dL vs. 11.3 $\pm$ 1.42 mg/dL; $p = .87$). The overall number of patients transfused with FFP and total FFP volume administered (Fig. 3B) was significantly lower in the ROTEM algorithm group compared with the standard algorithm group (96% vs. 34% [$p < .001$] and 2,050 $\pm$ 1,120 mL vs. 286 $\pm$ 496 mL [$p < .001$]). With regard to the total number of patients transfused with PLT and overall number of PLT units administered (Fig. 3C), the two groups were similar.

The effect of introduction of the ROTEM protocol on clinically relevant outcomes is reported in Table 3. Patients who underwent open TAAA repair after the introduction of the ROTEM protocol showed a significant decrease in pulmonary complications (44% vs. 83%; $p = .01$).

No significant difference was found for in hospital mortality (8% vs. 4%; $p = .50$).

Since the introduction of ROTEM, a significant decrease in total transfusion cost per patient has been shown (€834 $\pm$ 577 vs. €1,285 $\pm$ 851; $p < .001$) (Table 4).

DISCUSSION

In the present cohort of consecutive patients undergoing open TAAA repair, the application of a ROTEM driven transfusion protocol significantly decreased the intra- and post-operative use of blood products. This was associated with a considerably lower risk of developing post-operative pulmonary complications, which are common after massive allogenic transfusions.[19]

To the authors' knowledge, TAAA patients are a population relatively neglected by previous studies, which have concentrated mainly on cardiac surgery.[20,21] For example Weber *et al.*,[21] in a randomised control trial, showed that the introduction of a viscoelastic test based algorithm resulted in a significant reduction in the volume of blood products transfused, and a shorter length of ICU and hospital stay after cardiac surgery.[21] These results were confirmed in a recent Cochrane review.[22] Although there is no literature regarding standardised ROTEM guided transfusion protocols during TAAA, several transfusion strategies have been developed.[9,23] These protocols generally follow the principles of empiric resuscitation, sometimes referred

Table 1. Baseline clinical characteristics and intra-operative data

	Overall population (n = 547)			Propensity score matched population (n = 154)		
	Standard algorithm (n = 441)	ROTEM algorithm (n = 106)	p	Standard algorithm (n = 77)	ROTEM algorithm (n = 77)	p
Mean ± SD age (y)	65.5 ± 10.3	65 ± 10.6	.50	66.7 ± 7.8	65.5 ± 9.8	.43
Male	115 (26)	36 (34)	.10	28 (36)	28 (36)	.99
Mean ± SD body mass index (kg/m^2)	25.6 ± 4.0	26.0 ± 4.6	.35	25.7 ± 3.35	26.0 ± 5.0	.63
Hypertension	326 (74)	91 (86)	.01	66 (86)	66 (86)	.99
Dyslipidaemia	109 (25)	50 (47)	< .001	33 (43)	33 (43)	.99
Diabetes	28 (6)	15 (14)	.07	7 (9)	6 (8)	.77
COPD	73 (17)	23 (22)	.19	14 (18)	15 (19)	.84
Current smoker	179 (41)	45 (42)	.72	31 (40)	29 (38)	.74
Chronic renal failure	119 (27)	24 (23)	.36	15 (19)	17 (22)	.69
Coronary artery disease	82 (19)	27 (25)	.11	15 (19)	14 (18)	.83
Myocardial infarction	29 (7)	11 (10)	.18	5 (6)	6 (8)	.75
Arrhythmia	38 (9)	8 (7)	.72	4 (5)	5 (6)	.73
Previous percutaneous transluminal coronary angioplasty/coronary artery bypass grafting	58 (13)	17 (16)	.43	11 (14)	10 (13)	.81
Previous cardiac surgery	72 (16)	29 (27)	.01	16 (21)	19 (25)	.56
Previous major vascular surgery	135 (31)	44 (42)	.32	26 (34)	28 (36)	.74
Previous aortic surgery	160 (36)	37 (35)	.79	25 (32)	28 (36)	.61
Marfan syndrome	18 (4)	5 (5)	.77	1 (1)	3 (4)	.31
Cerebrovascular disease	13 (3)	4 (4)	.75	4 (5)	2 (3)	.4
Pre-operative lab results (mean ± SD)						
Haemoglobin (g/dL)	12.5 ± 1.9	12.4 ± 2.6	.56	12.5 ± 1.8	12.4 ± 2.5	.81
Platelets (× 10^9/dL)	198.4 ± 66.6	218.7 ± 71.8	.01	214 ± 78.7	215 ± 69.7	.89
International normalised ratio	1.3 ± 4.6	1.1 ± 0.2	.57	1.05 ± 0.06	1.08 ± 0.17	.16
Activated partial thromboplastin time ratio	1.05 ± 0.2	2.2 ± 10.1	.29	1.03 ± 0.16	1.02 ± 0.24	.97
Pre-operative therapy						
Aspirin	194 (44)	63 (59)	.04	42 (55)	44 (57)	.75
Other platelet inhibitors	53 (12)	11 (10)	.60	10 (13)	8 (10)	.62
Oral anticoagulant	29 (7)	4 (4)	.26	0	3 (4)	.08
β blockers	247 (56)	65 (61)	.32	47 (61)	47 (61)	.99
Diuretics	127 (29)	37 (35)	.23	28 (36)	29 (38)	.87
Angiotensin converting enzyme inhibitors/angiotensin II receptor blockers	238 (54)	57 (54)	.91	33 (43)	43 (56)	.11
Calcium channel blockers	160 (36)	32 (30)	.22	29 (38)	25 (32)	.50
Statins	154 (35)	45 (42)	.14	35 (45)	31 (40)	.50
Elective surgery	404 (92)	90 (85)	.04	67 (87)	69 (90)	.61
TAAA type			.78			.92
I	93 (21)	25 (24)		18 (23)	17 (22)	
II	128 (29)	30 (28)		21 (27)	24 (31)	
III	114 (26)	29 (27)		25 (32)	25 (32)	
IV	96 (22)	18 (17)		11 (14)	8 (10)	
V	10 (2)	4 (4)		2 (3)	3 (4)	
Use of left heart bypass	325 (74)	89 (84)	.03	67 (87)	69 (90)	.62
Mean ± SD aortic cross clamp time (min)	49.9 ± 25.6	54.8 ± 27.7	.09	51.7 ± 24.7	52.3 ± 21.3	.69
Intra-operative fluid balance (mean ± SD)						
Blood losses (mL)	5,270 ± 3,800	5,300 ± 2,960	.92	4,400 ± 3,200	5,300 ± 2,800	.07
Crystalloids (mL)	4,900 ± 1,700	6,800 ± 11,300	.09	4,900 ± 1,470	7,200 ± 13,000	.12
Colloids (mL)	420 ± 620	350 ± 420	.14	410 ± 550	340 ± 410	.38
Albumin (mL)	155 ± 120	156 ± 121	.94	140 ± 93	160 ± 110	.15
Salvaged blood (mL)	1,700 ± 1,400	2,100 ± 1,400	.01	1,400 ± 1,000	2,200 ± 1,600	< .001
Diuresis (mL)	1,440 ± 920	1,300 ± 650	.03	1,600 ± 1,100	1,400 ± 670	.14

Data are n (%) unless otherwise indicated. ROTEM = rotational thromboelastometry; TAAA = thoraco-abdominal aortic aneurysm; COPD = chronic obstructive pulmonary disease; SD = standard deviation.

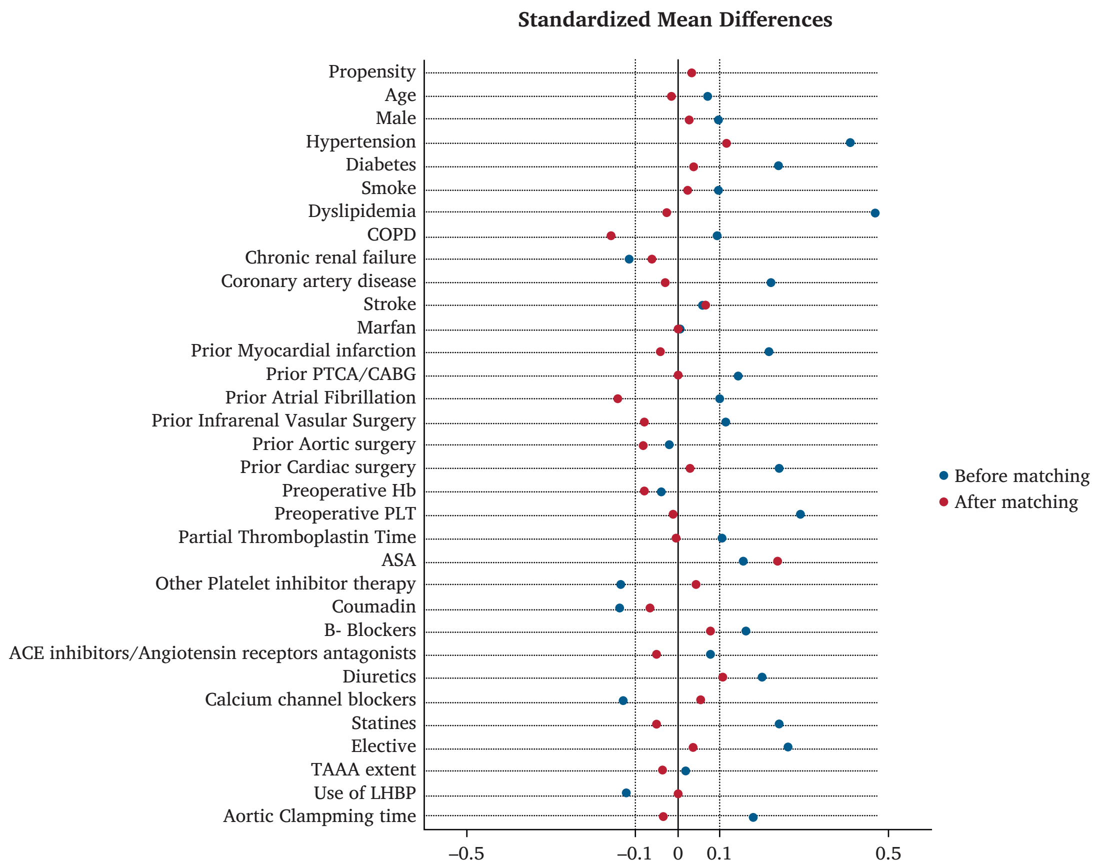

Figure 2. Baseline and post-propensity score matching balance between covariates. COPD = chronic obstructive pulmonary disease; PTCA = Percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass graft; PLT = platelets; ASA = acetylsalicylic acid; ACE = angiotensin converting enzyme; TAAA = thoraco-abdominal aortic aneurysm; LHBP = left heart bypass.

to as "damage control resuscitation". Cinà *et al.* described a pre-emptive strategy in which transfusion of RBCs and FFP in a 1:1 fashion is applied to administer a total infusion rate equal to the estimated blood loss, reporting an average transfusion of allogeneic blood products of 50—60 units.[9] Similarly, Svensson *et al.* observed in their TAAA series the intra-operative use of an average of 51 units of blood products.[24] The rationale for these approaches is to minimise dilutional and consumptive coagulopathy, avoiding delay in blood product replacement during ongoing blood loss. However, empiric resuscitation is not universally accepted, even during open TAAA repair. Godet *et al.* reported the use of a reactive transfusion strategy with the administration of blood products only when the haematocrit fell below 30% and/or clinical or laboratory evidence of coagulopathy development.[8] Nevertheless, the transfusion rate remained high, with a mean intra-operative blood product transfusion of 29 units.

The present series reports a much lower transfusion rate: 14 units were used on average before the introduction of ROTEM, and only four units were administered in the ROTEM group. These findings highlight the unsuitability of standard coagulation tests to guide transfusion protocols in modern era high bleeding risk settings This may be due to the fact that standard coagulation tests are not readily available as point of care, and they are assessed on plasma rather than on whole blood; therefore, they do not assess the platelet contribution to haemostasis.

Similar findings have been reported in patients undergoing cardiac surgery,[11,12] liver transplant,[25] trauma patients,[26,27] and postpartum haemorrhage.[28] Interestingly, intra-operative blood loss and the salvaged blood re-infused were higher in the ROTEM algorithm group but similar to what has been reported in a previous study.[9]

As described previously, transfusion related acute lung injury and transfusion associated circulatory overload are commonly observed after massive blood product administration in patients experiencing bleeding and shock.[5,6] All these conditions are usually met during open TAAA repair. Therefore, the reduction of adverse pulmonary events in the current study may be directly related to a lower transfusion rate.

Moreover, the ROTEM guided transfusion strategy also revealed a positive impact on costs: while in the standard algorithm group the mean cost per-patient was estimated to be €1,285 ± 851, the mean cost was only €834 ± 577 per patient in the ROTEM algorithm group, allowing for a better resource allocation and a reduction in healthcare costs.

Interestingly, while less plasma was administered in the ROTEM group, no difference for RBC administration was

Table 2. Intra-operative, post-operative, and overall use of blood products

	Overall population (n = 547)			Propensity score matched population (n = 154)		
	Standard algorithm (n = 441)	ROTEM algorithm (n = 106)	p	Standard algorithm (n = 77)	ROTEM algorithm (n = 77)	p
Intra-operative						
Red blood cells (RBC)						
No. of patients	384 (87)	68 (64)	< .001	69 (90)	50 (65)	< .001
Median (interquartile range [IQR]) no. of units	3 (0–11)	1 (0–10)	< .001	3 (0–10)	1 (0–5)	< .001
Fresh frozen plasma (FFP)						
No. of patients	424 (96)	30 (28)	< .001	73 (95)	21 (27)	< .001
Mean ± SD mL	1,800 ± 870	240 ± 466	< .001	1,600 ± 900	1 ± 600	< .001
Platelets						
No. of patients	113 (26)	26 (24)	.82	17 (22)	17 (22)	.99
Median (IQR) no. of units	0 (0–2)	0 (0–2)	.97	0 (0–1)	0 (0–1)	.99
Fibrinogen						
No. of patients	26 (6)	47 (44)	< .001	1 (1)	34 (44)	< .001
Mean ± SD g	0.23 ± 1.2	1.7 ± 2	< .001	0 ± 0.1	1.6 ± 1.9	< .001
From end of surgery to 48 h after surgery						
RBC						
No. of patients	63 (14)	36 (34)	< .001	9 (12)	27 (35)	<.001
Median (IQR) no. of units	0 (0–2)	0 (0–6)	.07	0 (0–4)	0 (0–6)	.004
FFP						
No. of patients	46 (10)	7 (7)	.23	4 (5)	5 (6)	.73
Mean ± SD mL	175 ± 600	46 ± 220	< .001	108 ± 480	43 ± 200	.22
Platelets						
No. of patients	37 (8)	7 (7)	.54	6 (8)	5 (6)	.75
Median (IQR) number of units	0 (0–1)	0 (0–1)	.16	0 (0–2)	0 (0–2)	.56
From 48 h after surgery to hospital discharge						
RBC						
No. of patients	187 (42)	71 (67)	< .001	32 (42)	53 (69)	.001
Median (IQR) no. of units	0 (0–19)	0 (0–6)	.09	0 (0–10)	0 (0–6)	.036
FFP						
No. of patients	34 (8)	4 (4)	.15	5 (6)	3 (4)	.46
Mean ± SD mL	100 ± 460	12 ± 100	< .001	105 ± 486	16 ± 118	.13
Platelets						
No. of patients	41 (9)	11 (10)	.73	4 (5)	8 (10)	.23
Median (IQR) no. of units	0 (0–4)	0 (0–3)	0.92	0.08 (0.36)	0.13 (0.47)	.45
Overall transfusions						
RBC						
No. of patients	412 (93)	96 (91)	.30	73 (95)	70 (91)	.50
Median (IQR) no. of units	4 (0–44)	3.5 (0–13)	.01	4 (0–17)	3.5 (0–11)	.026
FFP						
No. of patients	428 (97)	37 (35)	< .001	74 (96)	26 (34)	< .001
Mean ± SD mL	2,100 ± 1,200	300 ± 510	< .001	2,050 ± 1,120	286 ± 496	< .001
Platelets						
No. of patients	147 (33)	34 (32)	.80	22 (29)	24 (31)	.72
Median (IQR) no. of units	0 (0–6)	0 (0–5)	.64	0 (0–4)	0 (0–5)	.83

Data are n (%) unless otherwise indicated. ROTEM = rotational thromboelastometry; RBC = red blood cells; IQR = interquartile range; FFP = fresh frozen plasma; SD = standard deviation.

detected. In fact, while ROTEM allows for proper coagulation treatment reducing unnecessary administration of FFP, the probability of receiving RBCs in the post-operative remains, even if the patient does not bleed (i.e., anaemia secondary to acute kidney injury, need to increase the delivery of oxygen).

Open surgical TAAA repair represents a unique scenario in which to assess the performance of ROTEM. The combination of pre-existing coagulopathy due to aneurysm/dissection, consumptive coagulopathy, haemodilution, liver and gut ischaemia, and heparin administration act together leading to bleeding and massive transfusion.

In the present study, patients were not divided into groups according to the amount of intra-operative blood loss. The division was not performed because of the lack of threshold identifying high volume blood loss, but owing to the fact that all surgical TAAA patients should be considered high blood loss patients. Owing to the ease of use, cost

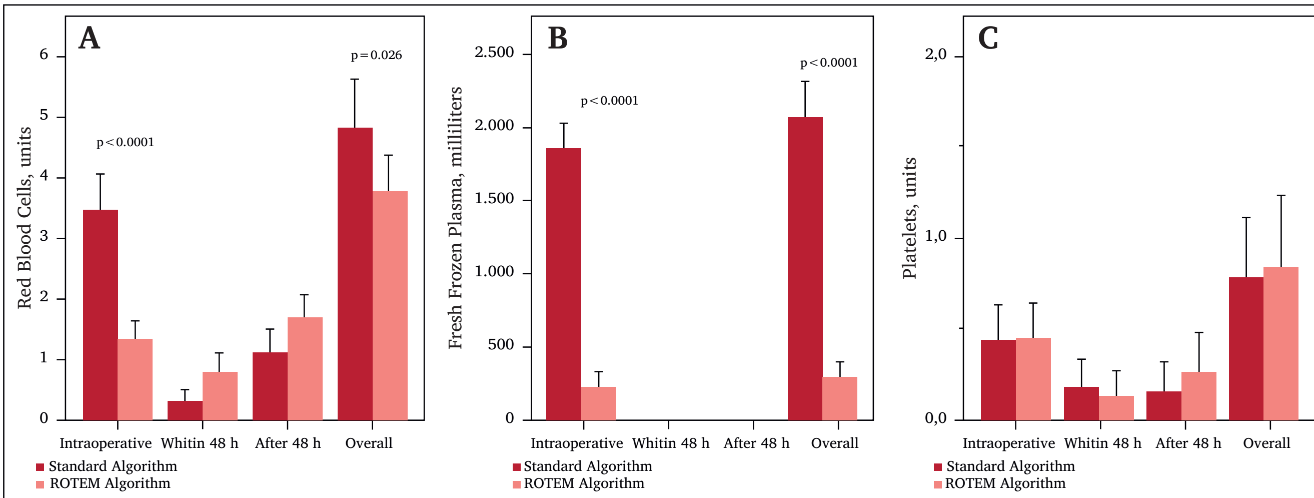

Figure 3. Intra-operative and post-operative administration of blood products. ROTEM = rotational thromboelastometry.

effectiveness, and availability of ROTEM, it is believed that the algorithm needs to be applied to all patients in this setting.

This study has some limitations and several strengths. Although its retrospective nature may be considered a source of intrinsic risk of confounding bias, the use of propensity score matching has led to reliable and relevant results, efficiently balancing the main pre- and intra-operative variables.[29] Also, the use of a cell saver may have affected the number of allogenic blood products transfused during the study period. However, as the use of a cell saver is standard practice at the authors' centre, it is reasonable that allogenic blood transfusions were equally decreased in both groups. As the study was conducted over a relative long period of time, improving surgical techniques and a learning curve effect may have progressively improved the outcome. However, the centre has been a national referral centre for almost 20 years and open TAAA repairs were performed before 2009, by the same surgical staff. The role of fibrinogen administration should also be discussed: coagulopathy during open TAAA repair is associated with a reduction in clotting factor activity, D-dimer increase, and thrombin generation.[30] The intense thrombin generation leads to a decrease in serum fibrinogen levels. Taking into account the above considerations, the use of fibrinogen seems reasonable even more so when the ROTEM (FIBTEM) allows a quick detection of intra-operative hypofibrinogenaemia.

In conclusion, the results of the present study may provide new insight into the transfusion management of patients undergoing open TAAA repair, decreasing the number of blood products assigned and used, making resources available to other patients, and reducing hospital costs. It seems evident that in the modern era ROTEM is an essential tool with which to guide transfusions, allowing a rapid diagnosis and goal directed correction of specific components of haemostasis in operative procedures at high risk of massive bleeding.

Table 3. **Clinical outcomes**

	Overall population (n = 547)			Propensity score matched population (n = 154)		
	Standard algorithm (n = 441)	ROTEM algorithm (n = 106)	p	Standard algorithm (n = 77)	ROTEM algorithm (n = 77)	p
Pulmonary complications	242 (55)	52 (49)	.28	64 (83)	34 (44)	.01
Re-operation for bleeding	28 (6)	1 (1)	.03	1 (1)	1 (1)	.99
Sepsis	16 (4)	4 (4)	.94	3 (4)	3 (4)	.99
Major adverse cardiovascular event	66 (15)	25 (24)	.03	12 (16)	18 (23)	.32
Permanent dialysis	12 (3)	5 (5)	.29	2 (3)	5 (6)	.45
In hospital mortality	31 (7)	7 (7)	.88	3 (4)	6 (8)	.50
Median (IQR) hospital stay (d)	8 (0–90)	9 (0–50)	.78	8 (5–43)	9 (2–50)	.70
Median (IQR) intensive care unit stay (h)	23 (2–1,643)	23 (10–864)	.69	21 (6–644)	23 (12–864)	.56

Data are n (%) unless otherwise indicated. ROTEM = rotational thromboelastometry; IQR = interquartile range; d = days; h = hours.

Table 4. Cost analysis for blood components per patient in the propensity score matched population ($n = 154$)

	Standard algorithm ($n = 77$)	ROTEM algorithm ($n = 77$)	p
Red blood cells (€)	894 ± 660	701 ± 478	.039
Fresh frozen plasma (€)	354 ± 191	49 ± 85	< .001
Platelets (€)	37 ± 69	40 ± 82	.81
ROTEM essays (€)	0	54 ± 18	
Total transfusion costs (€)	1,285 ± 851	834 ± 577	< .001

Data are mean ± SD (standard deviation). ROTEM = rotational thromboelastometry.

CONFLICTS OF INTEREST

None.

FUNDING

The study was supported by departmental funds.

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