Interactive CardioVascular and Thoracic Surgery 24 (2017) 196–202
doi:10.1093/icvts/ivw339 Advance Access publication 17 October 2016

ORIGINAL ARTICLE

Cite this article as: Ranucci M, Baryshnikova E, Pistuddi V, Menicanti L, Frigiola A for the Surgical and Clinical Outcome REsearch (SCORE) Group. The effectiveness of 10 years of interventions to control postoperative bleeding in adult cardiac surgery. Interact CardioVasc Thorac Surg 2017;24:196–202.

The effectiveness of 10 years of interventions to control postoperative bleeding in adult cardiac surgery

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Received 19 May 2016; received in revised form 1 August 2016; accepted 5 September 2016

Abstract

OBJECTIVES: Postoperative bleeding in cardiac surgery remains an important complication, leading to increased morbidity and mortality. Different interventions are possible to prevent/treat postoperative bleeding. The present study aims to investigate the effectiveness of these interventions in a real-world scenario.

METHODS: This is a retrospective study based on 19 670 consecutive adult cardiac surgery patients operated from 2000 to 2015. During the study period, the following interventions have been applied and tested for effectiveness with a before versus after analysis: thromboelastography (TEG)-based diagnosis and treatment in actively bleeding patients; platelet function tests (PFTs); timing of surgery based on PFTs; fresh frozen plasma (FFP)-free strategy using prothrombin complex concentrate and fibrinogen concentrate.

RESULTS: TEG-based diagnostic and therapeutic approach resulted in a significant ($P = 0.006$) reduction of postoperative bleeding and significant ($P = 0.001$) increase in platelet concentrate transfusion rate. Timing of surgery based on PFTs resulted in a significant reduction of postoperative bleeding ($P = 0.001$), surgical re-exploration rate ($P = 0.002$), FFP ($P = 0.001$) and platelet concentrate ($P = 0.016$) transfusion rate. FFP-free strategy was associated with a significant decrease in postoperative bleeding ($P = 0.005$) and FFP transfusions ($P = 0.001$). The combination of all the interventions was associated with a significant ($P = 0.001$) reduction in postoperative bleeding, surgical re-exploration rate and FFP transfusions, whereas platelet concentrate transfusion rate was significantly ($P = 0.001$) higher.

CONCLUSIONS: Despite a continuous increase in the bleeding risk profile, the application of a bundle of interventions is effective in controlling postoperative bleeding and related complications. Platelet transfusions remain unreplaceable in the present scenario.

Keywords: Cardiac surgical procedures • Haemorrhage • Blood transfusions

INTRODUCTION

Postoperative bleeding following cardiac surgery remains a clinically relevant problem. Severe bleeding is associated with increased morbidity and mortality [1], and is the main reason leading to allogeneic blood products use. When a surgical re-exploration is required to control bleeding, the mortality rate is increased by two to three times [2–4].

The factors leading to excessive postoperative bleeding are multifactorial, and include the effects of preoperative drugs (anticoagulants and antiplatelet), consumption of soluble coagulation factors and fibrinogen, hyperfibrinolysis, residual heparin effects and surgical sources [5]. Each of these factors may be prevented or treated with different strategies [6], constituting an important pillar of the concept of patient's blood management [7].

The efficacy of any of these strategies to control postoperative bleeding has been tested in numerous randomized controlled trials, but still there is little evidence on their real-world effectiveness in limiting the phenomenon, and the surgical re-exploration rate remains as high as 5% in many reports.

At our Institution, during the last 10 years we have progressively introduced a number of interventions to prevent/control postoperative bleeding. The present study is a retrospective analysis of the effectiveness of each strategy in limiting postoperative bleeding and related surgical re-exploration rate and use of allogeneic blood products.

METHODS

Retrospective study was based on prospectively collected data. The study was approved by the Local Ethics Committee, and the need for an informed consent was waived. All the patients gave a written consent for the use of their clinical data in an anonymous form and for scientific purposes.

Patients

The patient population was selected from our institutional cardiac surgery database which is active since the year 2000. From 2000 to 2015, 19 670 adult (≥18 years) patients undergoing cardiac surgery were identified and constituted our study population. For each patient demographics, co-morbidities, surgical details and outcome data were available for the analysis.

Data collection and definitions

For each patient, the following data were collected: Preoperative: demographics; left ventricular ejection fraction (%); preoperative haematocrit (%); recent (within 30 days prior to surgery) myocardial infarction; congestive heart failure; active endocarditis; unstable angina; preoperative use of intra-aortic balloon pump; serum creatinine value (mg/dl); chronic dialysis; chronic obstructive pulmonary disease; diabetes (on medication); previous cerebrovascular accident; previous cardiac surgery; urgent/emergent procedure. Operative: type of operation; cardiopulmonary bypass (CPB) duration (minutes); nadir haematocrit on CPB. Complex surgery was defined as coronary + valve surgery, left ventricle aneurysm repair, two or three valve surgery, ascending aorta surgery. Postoperative: postoperative bleeding (drain blood collected in the first 12 postoperative hours); allogeneic blood products transfusion rate; surgical re-exploration rate.

To investigate the preoperative bleeding risk, we have used the Papworth Bleeding Score [8] which is based on the selection of the above-listed variables (surgery priority, surgery type, aortic valve surgery, body mass index and age).

Surgery

CPB was generally conducted under moderate (32–34°C) hypothermia and alpha-stat management, unless for specific operations. The priming volume consisted of a mixture of 80% gelatine and 20% tromethamine solution.

The surgical staff remained quite stable in the study period, with the great majority of the patients operated by the same senior surgeons. The cardioplegic arrest was achieved with antegrade administration of cold crystalloid cardioplegia and, in a minority of the cases, with antegrade cold blood cardioplegia.

Interventions

Throughout the whole observation period, we have used tranexamic acid (15 mg/kg after the induction of anaesthesia, and 15 mg/kg after heparin reversal) intraoperatively; aprotinin was never used. Anticoagulation was achieved with unfractionated heparin according to our standard protocol to reach and maintain an activated clotting time of 450–480 s, and heparin reversal was achieved with adequate doses of protamine sulphate at an initial ratio of 1:1 with the heparin loading dose.

No specific additional interventions were applied until the year 2006, when we started using thromboelastography (TEG, Hemoscope, Niles, IL, USA) in all the patients in whom an active bleeding was observed after heparin reversal with protamine.

At the end of 2009, we started using platelet function tests (PFTs, Multiplate, Roche Diagnostics GmbH, Mannheim, Germany) to test platelet function before surgery in patients who received platelet inhibitors of the receptor P_2Y_{12} (ticlopidine, clopidogrel, prasugrel, ticagrelor) within 7 days from the planned date of surgery. From the year 2011, we started planning the date of surgery based on cut-off values of PFTs as described in previous studies [9, 10].

At the end of 2011, we introduced, in our clinical practice, the use of thromboelastometry (TEM, TEM International, Munich, Germany) basically for the point-of-care assessment of the fibrinogen contribution to clot firmness with the specific FIBTEM test, and in 2012 we started a policy aimed to limit/avoid the use of fresh frozen plasma (FFP) to replace coagulation factors and fibrinogen, conversely using prothrombin complex concentrates (PCCs) and/or fibrinogen concentrate guided by TEG and FIBTEM values (FFP-free strategy).

The effectiveness of the different strategies applied to prevent/control postoperative bleeding was analysed according to a 'before and after' approach having as outcome measures (i) the amount of chest drain blood loss during the first 12 postoperative hours; (ii) the rate of surgical re-exploration; and (iii) the rate of exposure to allogeneic blood products used to treat bleeding patients (FFP and platelets).

The red blood cells (RBCs) transfusion rate was not considered as a marker of effectiveness of the different strategies because two major confounders were anticipated: (i) the impact of preoperative anaemia as a bleeding-independent determinant of transfusions, and (ii) the changes in the RBC transfusion protocol applied during the study period.

To investigate the effectiveness of the different strategies applied avoiding overlapping of the effects of two or more strategies, the following periods have been considered for each strategy:

(1) TEG-based diagnosis and treatment of bleeding patients: before (2004–2005, 3165 patients) versus after (2006–2008, 3166 patients).
(2) Preoperative assessment of platelet function: before (2009, 1197 patients) versus after (2010, 1133 patients).
(3) Timing of surgery based on PFT: before (2006–2010, 5496 patients) versus after (2011–2015, 5447 patients).
(4) FFP-free strategy: before (2011, 1151 patients) versus after (2012–2015, 3154 patients).

Additionally, a comparative analysis was performed between the no-interventions era (2000–2005, 8727 patients) and the all-interventions era (2012–2015, 4296 patients).

Statistics

The patient population was analysed comprehensively and separately by the year of surgery. All data are presented as number with percentage for categorical variables, and mean with standard deviation for continuous, normally distributed variables. Non-normally distributed variables are expressed as median and interquartile range. Normality of distribution was checked with the Hosmer–Lemeshow test. Differences between the year-based periods of observation were investigated using an analysis of variance with *post hoc* Tukey's test and adjustment for multiple comparisons, and with a Pearson's χ^2 test for categorical variables. Before versus after interventions differences were analysed using the Student's *t*-test for continuous, normally distributed variables

and non-parametric tests for continuous, non-normally distributed variables, and Pearson's χ^2 for categorical variables.

An analysis of the time-related changes in the bleeding risk and in the postoperative blood loss was performed with a polynomial regression analysis.

All tests were two-sided. A *P*-value of <0.05 was considered to be significant for all statistical tests. Statistical calculations were performed using computerized statistical programs (SPSS 13.0, Chicago, IL, USA and GraphPad Prism 6, San Diego, CA, USA).

RESULTS

The general characteristics of the patient population are reported in Table 1. Table 2 describes the bleeding-related characteristics of the population separately for each year of observation. Overall, the bleeding risk profile has been increasing over time, mainly due to an increased surgical complexity, with a significantly higher rate of redo, non-elective, complex cases, with a significantly longer CPB duration. As a result, the bleeding risk score in the last years is 60% higher than what found in the first years of observation. Preoperative use of antiplatelet agents was stable around 25% for salicylates that are not routinely withdrawn before surgery and 1–2% for warfarin. Low-molecular weight heparin was more commonly used in the first period (2000–2007) at a rate of 25–30%; subsequently, the rate declined to reach a value around 10% in the last years. Clopidogrel and other P2Y12 platelet inhibitors were usually discontinued 5 days before surgery until 2011, when we started using PFT to settle the timing of surgery.

Table 1: Patient characteristics and surgical details of the patient population (*N* = 19 670)

Variables	Value
Age (years)	67 (58–74)
Gender male	13 279 (67.5)
Weight (kg)	72 (64–81)
Congestive heart failure	1193 (6.1)
Recent (30 days) myocardial infarction	2343 (11.9)
Ejection fraction	0.54 (0.46–0.60)
Active endocarditis	261 (1.3)
Diabetes	2874 (14.6)
Chronic obstructive pulmonary disease	1355 (6.9)
Serum creatinine (mg/dl)	1.0 (0.8–1.3)
Serum bilirubin (mg/dl)	0.50 (0.4–0.8)
Previous cerebrovascular accident	782 (4.0)
Haematocrit (%)	39.2 (36–42)
Antiplatelet drugs	3469 (17.6)
Warfarin	288 (1.5)
Low-molecular weight heparin	4144 (21.1)
Redo surgery	1362 (6.9)
Elective surgery	18 188 (92.5)
Type of surgery	
Isolated coronary revascularization	8375 (42.5)
Isolated valve	4446 (22.6)
Others (single surgery)	664 (3.5)
Others (complex surgery)	6185 (31.4)
Bleeding risk score	1 (1–2)
Cardiopulmonary bypass time (min)	70 (53–94)
Nadir haematocrit on cardiopulmonary bypass	27 (24–30)
Nadir temperature (°C) on cardiopulmonary bypass	32 (31–32.8)

Continuous data are presented as median (interquartile range); categorical data as number (%).

Figures 1–4 are showing the behaviour of our four bleeding-related outcome variables (postoperative bleeding, surgical re-exploration rate, rate of exposure to FFP or platelet concentrates).

Postoperative bleeding (Fig. 1) had a peak value in the year 2004, progressively decreasing after that time and stabilizing after the year 2008. Surgical re-exploration rate (Fig. 2) peaked in 2005 progressively decreasing and stabilizing around 2% from 2008. The rate of FFP transfusions (Fig. 3) progressively increased from 2000 to 2005–2006, when the peak level of 24% was reached; subsequently, there was a progressive decrease and since 2012 the value has been stable around 5–6%. Finally, the rate of platelet concentrate transfusions (Fig. 4) remained low until 2003 (2–3%), and then started climbing up to 12% in 2010. Subsequently, there was a decrease, and the value stabilized around 8% in the last 4 years.

Table 3 reports the effectiveness of the four interventions, in terms of the four outcomes considered.

The routine use of TEG isolated by the other interventions was associated with a significant ($P = 0.001$) reduction of postoperative bleeding and a non-significant reduction of surgical re-exploration rate (0.6% difference). The rate of patients receiving platelet concentrates significantly ($P = 0.001$) increased with the TEG-based intervention.

PFTs in patients under dual antiplatelet therapy resulted in only a significant reduction in postoperative bleeding, without effects on the other outcomes. However, when the timing of surgery was decided based on specific cut-off values of preoperative PFTs, this resulted in a significant reduction in surgical re-exploration rate, use of FFP, and use of platelet concentrates.

The FFP-free strategy, based on FFP replacement with PCCs and/or fibrinogen concentrate, resulted in a significant reduction in postoperative bleeding and significant abatement of FFP transfusions. Finally, the comprehensive application of all the interventions with respect to no-intervention produced a significant reduction of postoperative blood loss, surgical re-exploration rate and FFP transfusions. Conversely, platelet transfusion rate was significantly higher.

Concerning RBC transfusion rate, the value was stable ~40–45% in 2000–2003, than there was a progressive rise up to a peak of 66% in 2005; subsequently, there was a progressive decrease with a stabilization around 36–37% in the last years.

Figure 5 shows a regression analysis (third-degree equation) of the postoperative bleeding and the bleeding risk score in the study period. The analysis shows a significant ($P = 0.001$) association between the time of surgery (on a day-by-day basis) and both the bleeding risk score and the postoperative bleeding. The years 2000–2005 were characterized by concomitant increase in bleeding risk and observed postoperative bleeding. During the following years, despite a continuous increase in the bleeding risk, the observed postoperative bleeding declined and stabilized in the last 3 years.

DISCUSSION

A historical perspective

The early period: 2000–2002. These years were characterized by a patient population at low–medium bleeding risk (low rate of

Table 2: Bleeding risk profile of the patient population in the different years

Period (number of patients)	Age (years)	BMI	Non-elective surgery (%)	Redo (%)	Complex surgery (%)	Aortic surgery (%)	CPB time (min)	Bleeding risk score
2000 (962)	65 (58–71)	25.4 (23.4–27.7)	28 (2.9)	66 (6.9)	247 (26)	181 (19)	62 (45–80)	1.07 (0.98)
2001 (1795)	66 (58–72)	25.7 (23.5–28)	36 (2.0)	50 (1.8)	476 (26)	389 (22)	64 (49–87)	1.08 (1.01)
2002 (1019)	67 (59–72)	25.9 (23.7–28.6)	15 (1.5)	33 (3.2)	296 (29)	227 (22)	63 (49–85)	1.11 (0.99)
2003 (1786)	67 (58–74)	25.7 (23.3–28.4)	94 (5.3)	120 (6.7)	566 (32)	441 (25)	63 (49–84)	1.27 (1.06)
2004 (1706)	68 (59–74)	25.6 (23.3–28.3)	101 (5.9)	98 (5.7)	499 (29)	399 (23)	66 (50–88)	1.26 (1.02)
2005 (1459)	68 (59–75)	25.4 (23.1–28.3)	93 (6.4)	98 (6.7)	396 (27)	382 (26)	69 (50–92)	1.30 (1.05)
2006 (1308)	68 (59–74)	25.4 (23.3–28.5)	60 (4.6)	105 (8.0)	389 (30)	359 (27)	74 (55–98)	1.30 (1.06)
2007 (1130)	68 (59–75)	25.7 (23.4–28.4)	44 (3.9)	81 (7.2)	296 (26)	300 (26)	68 (54–95)	1.24 (1.06)
2008 (728)	67 (58–73)	25.8 (23.4–28.4)	14 (1.9)	45 (6.2)	219 (30)	226 (31)	70 (55–94)	1.25 (1.06)
2009 (1197)	68 (59–75)	25.9 (23.5–29)	43 (3.6)	88 (7.4)	393 (33)	432 (36)	75 (58–100)	1.41 (1.07)
2010 (1133)	68 (58–75)	25.7 (23.3–28.4)	41 (3.6)	84 (7.4)	358 (32)	405 (36)	75 (58–98)	1.41 (1.07)
2011 (1151)	68 (58–75)	25.7 (23.4–28.6)	40 (3.5)	87 (7.6)	424 (37)	458 (40)	77 (59–106)	1.47 (1.16)
2012 (1142)	68 (58–75)	25.6 (23.2–28.4)	32 (2.8)	112 (9.8)	437 (38)	431 (38)	76 (58–102)	1.49 (1.07)
2013 (1091)	68 (57–75)	25.4 (22.8–28.3)	228 (20.8)	102 (9.3)	402 (37)	407 (37)	75 (56–100)	1.76 (1.08)
2014 (1072)	69 (58–76)	25.7 (23–28.6)	223 (20.8)	112 (10.4)	408 (38)	415 (39)	75 (56–103)	1.77 (1.13)
2015 (991)	69 (59–76)	25.5 (23–28.3)	195 (19.7)	81 (8.2)	379 (38)	394 (40)	75 (58–104)	1.74 (1.11)
P-value (between years)[a]	0.145	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Data expressed as median (interquartile range) or mean (standard deviation) or number (percentage).
BMI: body mass index; CPB: cardiopulmonary bypass.
[a]Analysis of variance or Pearson's χ^2.

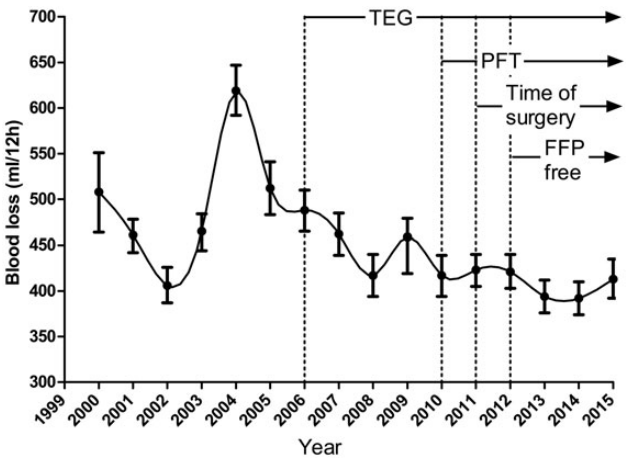

Figure 1: Time course of postoperative blood loss. Data are median with 95% confidence interval. FFP: fresh frozen plasma; PFT: platelet function test; TEG: thromboelastography.

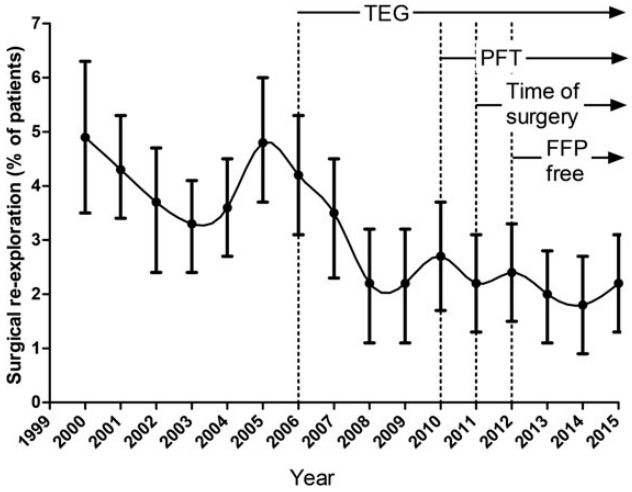

Figure 2: Time course of surgical re-exploration rate. Data are percentage with 95% confidence interval. FFP: fresh frozen plasma; PFT: platelet function test; TEG: thromboelastography.

complex, non-elective and aortic surgery), with correspondent low postoperative blood loss, low FFP and platelet concentrate transfusion rate, and a surgical re-exploration rate of 3–4%.

Double antiplatelet therapy and patients' quality deterioration: 2003–2005. During this period, we could observe a significant deterioration in the patients' risk profile, and namely in bleeding risk, with an increase in the bleeding risk score of ~25% with respect to the previous period. This was basically due to an older age, a higher rate of non-elective operations and complex surgery. Additionally, this is the historical period when the practice of double antiplatelet therapy entered the clinical scenario and became very well established.

It is not doubtful that we were unprepared to tackle this rapidly changing scenario. Postoperative blood loss peaked in 2004, and the surgical re-exploration rate reached 5% in 2005. As a result, FFP transfusions nearly doubled and platelet concentrate transfusions tripled. To match the need for an adequate patient blood management, at the end of 2005 we started introducing new technologies to control postoperative bleeding and related complications.

The thromboelastography-based approach to the bleeding patient: 2006–2008. During this period, the TEG use in our institution was basically focused on the diagnostic and therapeutic aspects of the bleeding patient. TEG with and without heparinase was routinely performed in the operating room in patients with the evidence of microvascular bleeding after protamine administration, and in the intensive care unit in patients with

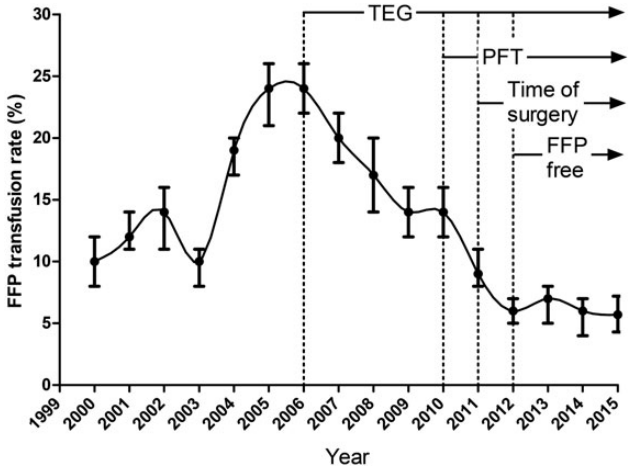

Figure 3: Time course of fresh frozen plasma rate. Data are percentage with 95% confidence interval. FFP: fresh frozen plasma; PFT: platelet function test; TEG: thromboelastography.

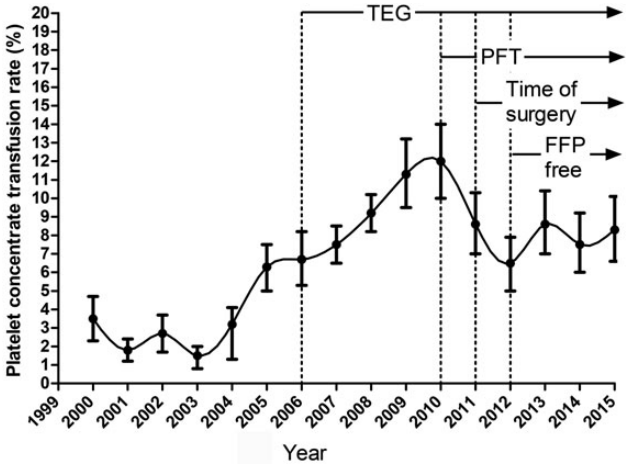

Figure 4: Time course of platelet concentrate transfusion rate. Data are percentage with 95% confidence interval. FFP: fresh frozen plasma; PFT: platelet function test; TEG: thromboelastography.

excessive chest drain blood loss. The routine application of TEG-based diagnostic and therapeutic algorithms resulted in an improvement in some of our bleeding-related outcome variables (postoperative chest drain blood loss), but others remained unchanged (surgical re-exploration rate and FFP transfusion rate) or even worsened (platelet concentrate transfusion rate). However, it must be recognized that these limited results were obtained in the presence of a concomitant increase in the bleeding risk score; consequently, the TEG-based strategy was probably effective in at least stabilizing the trend towards more bleeding, surgical re-exploration and transfusions.

Additionally, it should be remembered that in 2006–2008 some misconceptions about the diagnostic properties of the TEG were quite diffused. The TEG patent (issued in 2004) describes an algorithm based on the concepts of (i) the α-angle defined as a measure of 'the rapidity of fibrin build-up and cross-linking (clot kinetics)' and (ii) the maximum amplitude (MA) defined as 'a direct function of the maximum dynamic properties of fibrin and platelet bonding via GPIIb/IIIa' [11]. As a consequence, the existing algorithms incorporated the concepts of cryoprecipitate/fibrinogen concentrate administration based on the alpha-angle and of platelet administration based on the MA [12–14].

Nowadays, it is very well known that the α-angle is inadequate to detect fibrinogen deficiency [15], and specific viscoelastic tests have been developed to address this issue (functional fibrinogen and FIBTEM); additionally, it is now accepted that the MA is inadequate to assess platelet function in the presence of P_2Y_{12} platelet receptor inhibitors and that even in terms of platelet count its role is limited [16]. Again, specific PFTs are presently available to address this issue.

Given these considerations, it is likely that the early years of use of the TEG-based diagnostics as a single intervention may have resulted in a limited, albeit significant benefit in terms of patient's blood management.

Platelet function tests and surgical planning based on platelet function recovery: 2009–2011. Owing to the combined effects of the increasing diffusion of dual antiplatelet therapy, ongoing increase in platelet concentrate transfusion, and inadequacy of the TEG alone in detecting platelet dysfunction, at the end of 2009 we included a PFT device in our point-of-care coagulation laboratory (Multiplate). The first year (2010), we started measuring platelet function with ADP-test and TRAP-test in all patients under dual antiplatelet therapy scheduled for cardiac surgery. In the absence of established cut-off values, the test results were used to postpone surgery only in case of extremely low values of platelet function. This resulted only in a limited, albeit significant, postoperative bleeding reduction. On the basis of the data collected in 2010 and in the following years, we could identify an adequate platelet function range to admit patients to surgery, based on the ADP-test [9] or a combination of ADP-test and TRAP-test [10]. The application of these cut-off values (2011–2015) allowed a significant improvement in all our bleeding-related outcome indicators; of notice, for the first time we could achieve a significant decrease in surgical re-exploration rate and platelet concentrate transfusions.

Timing of surgery based on PFT rather than on a fixed discontinuation time was certainly the most relevant single intervention to control postoperative bleeding in our institution, and its role is now recognized even in surgical guidelines [17].

The FFP-free strategy: 2012–2015. Fibrinogen contribution to clot strength using FIBTEM was included in our point-of-care coagulation laboratory at the end of 2011, as an adjunct to standard TEG assessment in the bleeding patient. With this implementation, we started a policy based on a progressive replacement of FFP transfusions with the specific components PCC (based on the R-time at TEG) and fibrinogen concentrate (based on FIBTEM) following a recently published algorithm [18]. This intervention further reduced postoperative bleeding, and namely abated the use of FFP to ∼6% of the cases. These results are confirmative of what found in a randomized controlled trial [18], where FFP could be effectively replaced by purified components.

The combined effects of all the interventions

Given the multifactorial mechanism leading to postoperative bleeding in cardiac surgery, a comprehensive diagnostic and therapeutic algorithm is much more reasonable than isolated interventions for an effective control of surgical re-exploration

Table 3: Effectiveness of the interventions according to a before versus after analysis

Intervention	Postoperative bleeding (ml/12 h)	Surgical re-exploration rate	FFP	Platelets
TEG				
Before (2004–2005)	400 (225–675)	118 (3.4)	673 (21)	154 (4.9)
After (2006–2008)	375 (250–575)	181 (3.9)	656 (21)	249 (7.9)
P-value	0.006	0.206	0.595	0.001
Platelet function test				
Before (2009)	375 (250–550)	26 (2.2)	180 (15)	132 (11)
After (2010)	325 (150–550)	30 (2.6)	157 (14)	133 (12)
P-value	0.001	0.454	0.418	0.589
Timing of surgery based on PFTs				
Before (2006–2010)	350 (225–550)	166 (3.0)	993 (18)	514 (9.4)
After (2011–2015)	350 (200–500)	114 (2.1)	373 (6.8)	439 (8.1)
P-value	0.001	0.002	0.001	0.016
FFP-free strategy				
Before (2011)	350 (225–550)	25 (2.2)	108 (9.4)	101 (8.8)
After (2012–2015)	325 (200–500)	63 (2.0)	199 (6.3)	267 (8.5)
P-value	0.005	0.720	0.001	0.748
All interventions				
No (2000–2005)	375 (250–600)	352 (4.0)	1,293 (14.8)	275 (3.2)
Yes (2012–2015)	350 (200–500)	89 (2.1)	265 (6.2)	338 (7.9)
P-value	0.001	0.001	0.001	0.001

Data are expressed as median (interquartile range) or number (%).
FFP: fresh frozen plasma; PFT: platelet function test; TEG: thromboelastography.

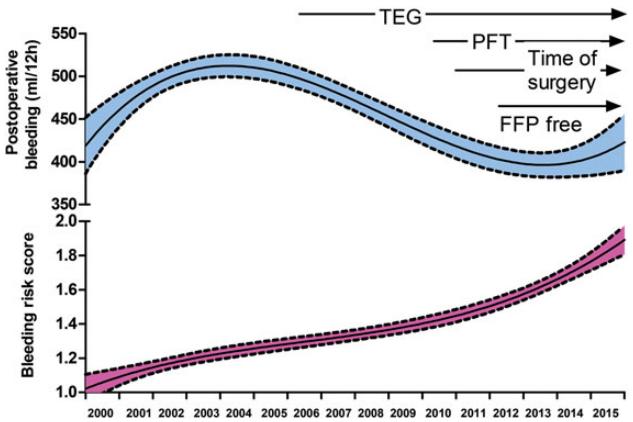

Figure 5: Association between time of surgery and bleeding risk score and postoperative blood loss. Polynomial regression analyses with 95% confidence bands (dashed lines). FFP: fresh frozen plasma; PFT: platelet function test; TEG: thromboelastography.

and transfusions rate. Comparing the era of 'no interventions' (2000–2005) with the present era, this concept appears quite evident. Despite a bleeding risk score that is ~60% higher, the combined application of all the described strategies resulted in a significant decrease in postoperative bleeding, with half the rate of surgical re-exploration rate (from 4 to 2%) and a FFP transfusion rate that is 60% less (from 15 to 6%). A word apart is deserved by the platelet concentrate transfusion rate, that is presently significantly higher (8 vs 3%) than in the no-interventions era. A first point is that the present value is, however, lower than the peak value observed in 2010 (12%); the second comment is that once a platelet dysfunction is diagnosed or strongly suspected, there are no alternatives to platelet concentrate transfusions (except the possible and still debated use of desmopressin). It is not surprising that a refinement of platelet function diagnostics, together with the skyrocketing use of old and new antiplatelet agents, inevitably lead to an increased need for platelet concentrate transfusions.

Limitations

There are, of course, a number of limitations in our study. The main one is the retrospective nature which only allowed us a before–after analysis. Additionally, we cannot account for surgeon's-derived different accuracy in controlling surgical haemostasis after CPB. This may be an important factor that we cannot address because our database does not include the names of the surgeons in charge for this (who are usually different from the leading surgeon of the operation). Another important limitation is that it is difficult to elucidate the role of preoperative drugs which may affect bleeding. Actually, no major changes were applied during the study period with respect to salicylates and warfarin, and low-molecular weight heparin was always discontinued 12 h before surgery. The main determinants of preoperative drugs-induced postoperative bleeding are P_2Y_{12} platelet inhibitors. Unfortunately, no data on platelet function are available until 2011, in the period when a 5-day time between drug discontinuation and surgery was considered adequate at our institution.

CONCLUSION

In conclusion, this 16-year analysis of a real-world scenario highlights that the combination of a number of different interventions to control postoperative bleeding is certainly effective, and results in a reduction of postoperative bleeding, surgical re-exploration and FFP transfusion rate. Given the rapidly changing scenario of bleeding risk, basically dominated by the increasing use of new anticoagulants and by the development of new antiplatelet agents, together with an increasing patient and procedure-related

severity, the approach to bleeding control should remain as much dynamic as possible, through the development of new monitoring tools and new interventions to continuously and effectively tackle the future needs.

AUTHORS' CONTRIBUTION

Marco Ranucci confirms that he had full access to all the data in the study and had final responsibility for the decision to submit for publication. Marco Ranucci designed the study, analysed the data and wrote the manuscript; Ekaterina Baryshnikova and Valeria Pistuddi collected the data; Lorenzo Menicanti contributed to study design and manuscript revision; Alessandro Frigiola contributed to study design, data interpretation and manuscript preparation.

Funding

The study was funded by local research funds of the IRCCS (Clinical Research Hospital) Policlinico San Donato, partially funded by the Italian Ministry of Health.

Conflict of interest: Marco Ranucci received honoraria and speaker's fees from Medtronic, CSL Behring, Grifols, Roche Diagnostics, TEM International.

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