Point-of-Care Testing

A Prospective, Randomized Clinical Trial of Efficacy in Coagulopathic Cardiac Surgery Patients

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ABSTRACT

Introduction: The current investigation aimed to study the efficacy of hemostatic therapy guided either by conventional coagulation analyses or point-of-care (POC) testing in coagulopathic cardiac surgery patients.

Methods: Patients undergoing complex cardiac surgery were assessed for eligibility. Those patients in whom diffuse bleeding was diagnosed after heparin reversal or increased blood loss during the first 24 postoperative hours were enrolled and randomized to the conventional or POC group. Thromboelastometry and whole blood impedance aggregometry have been performed in the POC group. The primary outcome variable was the number of transfused units of packed erythrocytes during the first 24 h after inclusion. Secondary outcome variables included postoperative blood loss, use and costs of hemostatic therapy, and clinical outcome parameters. Sample size analysis revealed a sample size of at least 100 patients per group.

Results: There were 152 patients who were screened for eligibility and 100 patients were enrolled in the study. After randomization of 50 patients to each group, a planned interim analysis revealed a significant difference in erythrocyte transfusion rate in the conventional compared with the POC group [5 (4;9) *versus* 3 (2;6) units [median (25^{th} and 75^{th} percentile)], $P < 0.001$]. The study was terminated early. The secondary outcome parameters of fresh frozen plasma and platelet transfusion rates, postoperative mechanical ventilation time, length of intensive care unit stay, composite adverse events rate, costs of hemostatic therapy, and 6-month mortality were lower in the POC group.

Conclusions: Hemostatic therapy based on POC testing reduced patient exposure to allogenic blood products and provided significant benefits with respect to clinical outcomes.

What We Already Know about This Topic

- Cardiac surgical patients experience rapid changes in coagulation status
- Point-of-care coagulation testing may speed up diagnosis of coagulopathies and improve management

What This Article Tells Us That Is New

- Point-of-care coagulation testing reduced allogenic blood transfusion and was associated with improved outcomes

IN patients undergoing cardiac surgery, perioperative coagulopathy and the use of allogenic blood products are independently associated with increases in mortality and major perioperative cardiac and noncardiac adverse events.[1–3] Early and specific diagnosis and effective and targeted therapy of the underlying hemostatic pathology are of high clin-

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ical relevance.[4] In this context, algorithm-based hemostatic therapy has been shown to be superior to empiric hemostatic therapy that is based on clinical judgment.[5]

There is some evidence from studies using viscoelastic analyses of clot formation and dissolution that the implementation of point-of-care (POC) measurements in hemostatic therapy algorithms may reduce the transfusion rate of allogenic blood products and positively influence clinical outcomes.[6–10] Additional implementation of aggregometric measures for platelet function analyses could synergistically expand the diagnostic spectrum by assessing the effects of antiplatelet drugs or cardiopulmonary bypass itself on platelet function, and therefore may allow for more targeted and effective coagulation management.

We conducted this trial to compare the efficacy of hemostatic therapy algorithms based either on conventional laboratory testing or on POC-guided coagulation management using viscoelastic and aggregometric measurements.

The primary outcome of this study was the amount of perioperatively transfused units of packed erythrocytes. Usage and costs of any other hemostatic therapy and clinical outcome parameters were secondary outcomes.

Materials and Methods

Trial Design

This prospective, randomized parallel-group single-center study was conducted at the University Hospital Frankfurt am Main, Germany. The current study complies with the declaration of Helsinki, was approved by the local Scientific and Ethics Review Board (Ethics-Committee of the Goethe-University Frankfurt, 60590 Frankfurt am Main, Germany), and was registered with ClinicalTrials.gov (Identifier: NCT00997841). All patients gave written informed consent.

Participants

Patients were suitable for this trial after two inclusion steps.

Step 1: Patients (≥18 yr) scheduled for elective, complex cardiothoracic surgery (combined coronary artery bypass graft and valve surgery, double or triple valve procedures, aortic surgery or redo surgery) with cardiopulmonary bypass (CPB) were preoperatively screened for eligibility, and written consent was obtained. Pregnancy was defined as an exclusion criterion.

Step 2: Patients were enrolled in the study after heparin reversal following CPB if at least one of the two inclusion criteria were fulfilled: (1) diffuse bleeding from capillary beds at wound surfaces requiring hemostatic therapy as assessed by the anesthesiologist and surgeon by inspecting the operative field and/or (2) intraoperative or postoperative (during the first 24 postoperative hours) blood loss exceeding 250 ml/h or 50 ml/10 min.

After enrollment in the study, patients were randomly assigned to the conventional group or POC group. The randomization list was computer-generated using a balanced (allocation ratio 1:1) blockwise (20*10) randomization by the software BiAS for Windows 9.07 © (Epsilon Inc., Darmstadt, Germany).

General Patient Management

For each patient, preoperative antiplatelet therapy, including aspirin, was ceased at least 6 days before surgery, and weight-adapted low-molecular-weight heparin was administered subcutaneously in prophylactic dosages until the day before surgery. Anesthetic, surgical, and CPB management were standardized in all patients. No changes in surgical, anesthetic, or perfusion techniques were made for the purposes of the study.

Anesthetic Management

On the evening before surgery, patients were given 20 mg clorazepat dipotassium (Tranxilium®, Sanofi-Aventis GmbH, Hoechst, Germany). After routine monitoring was applied, general anesthesia was induced with 0.3–1 μg/kg sufentanil (Sufenta®, Janssen-Cilag GmbH, Neuss, Germany), 1–2.5 mg/kg propofol (Disoprivan®, AstraZeneca GmbH, Wedel, Germany), and 0.6 mg/kg rocuronium (Esmeron®, Essex GmbH, Munich, Germany). For the maintenance of general anesthesia, all patients received 1–2 vol% sevoflurane (Sevoran®, Abbott, Wiesbaden, Germany) and intermittent boluses of sufentanil. Both isotonic crystalloid (Sterofundin®, B. Braun GmbH, Melsungen, Germany) and colloid fluids (6% HES 130/0.4, Voluven®, Fresenius Cabi, Bad Homburg, Germany) were perioperatively infused based on institutional standards. Postoperative weaning from mechanical ventilation and timing of extubation were according to our institutional protocol.

Management of Extracorporeal Circulation

The extracorporeal circuit included a membrane oxygenator (Quadrox® oxygenator, Maquet Cardiopulmonary AG, Hirlingen, Germany) and a roller pump system (HL20, Maquet Cardiopulmonary AG) equipped with a heat exchanger (Plegiox®, Maquet Cardiopulmonary AG). The circuit was primed with 500 ml crystalloid solution (Sterofundin®, B. Braun Melsungen AG), 500 ml colloid solution (6% HES 130/0·4, Voluven®, Fresenius Medical Care AG), and 250 ml 20% Mannitol (Mannitol Baxter®, Baxter, Unterschleissheim, Germany). Heparin (Heparin-Natrium Braun®, B. Braun Melsungen AG) was repeatedly administered after an initial bolus of 400 IU/kg to maintain an activated clotting time (ACT) of more than 400 s. During CPB, a nonpulsatile flow was maintained at 2.6–3 l/min/m^2, and the mean arterial blood pressure was targeted to 50–70 mmHg with the addition of norepinephrine (Arterenol®, Sanofi-Aventis GmbH, Hoechst, Germany) if needed. Myocardial protection was achieved with cold blood cardioplegia (20°C). Antifibrinolytic therapy consisted of the application of 2 g tranexamic acid (Cyclocapron®, MEDA Pharma GmbH &

Co. KG, Bad Homburg, Germany) after the induction of anesthesia, and another 2 g was added into the priming volume of the heart–lung machine and again during CPB. Extracorporeal circulation was performed in mild hypothermia. When surgery was completed, patients were rewarmed to 36°C and weaned from CPB. To reverse the anticoagulant effects of heparin, protamine sulfate (Protaminsulfat, Novo Nordisk Pharma GmbH, Vienna, Austria) was administered, guided by the ACT. If the target ACT was not obtained despite repeated heparin administrations, 500- 1,000 IU of antithrombin were infused.

Hematologic Analyses

Conventional Coagulation Tests. Laboratory coagulation testing included platelet count, hemoglobin concentration, fibrinogen concentration, international normalized ratio, and activated partial thromboplastin time and was performed at the local chemistry laboratory using the fully automated analyzers STA-R Evolution® (Roche AG, Grenzach, Germany) and Sysmex XE 2001 (Sysmex GmbH, Norderstedt, Germany). Intraoperatively, repetitive blood gas analyses (ABL 700, Radiometer GmbH, Willich, Germany) and ACT analyses (Actalyke MINI II®, Helena Laboratories, Beaumont, TX) were performed. Intraoperative international normalized ratio measurements were performed using CoaguChek XS® (Roche Diagnostics GmbH, Mannheim, Germany). Conventional coagulation tests (platelet count, fibrinogen concentration, international normalized ratio, and activated partial thromboplastin time) have been performed in both groups at fixed time points (preoperatively, at admission to the intensive care unit [ICU], and 24 h after admission to ICU) to enable a comparison of both groups at these time points. The attending physicians in the POC group were blinded to the results of conventional coagulation tests. In the conventional group additional conventional coagulation tests have been performed after randomization to the conventional group, after therapeutic interventions, and in case of ongoing bleeding after therapeutic interventions.

Viscoelastic POC Testing. Thromboelastometry was performed at the bedside using the ROTEM® device (ROTEM®, Tem International GmbH, Munich, Germany). Methodologic details are described elsewhere.[11,12] The POC algorithms were based on four tests: the EXTEM®- and INTEM®-tests, which reflect the extrinsic or intrinsic initiation of coagulation, the FIBTEM®-test (platelet-inhibited extrinsic activation), which reflects the contribution of fibrin polymerization to clot firmness, and the HEPTEM®-test (heparinase-modified intrinsic activation), which identifies potential heparin effects compared with the INTEM®-test. Clotting time [CT (s)] in the EXTEM®, INTEM®, and HEPTEM® tests as well as the maximum clot firmness (mm) and the amplitude of clot firmness 10 min after CT [A10 (mm)] for each test, including FIBTEM®, were recorded.

Aggregometric POC Testing. Aggregometry for platelet function testing was performed at the bedside using multiple electrode aggregometry (Multiplate®, Verum Diagnostica GmbH, Munich, Germany).[13,14] Platelet aggregation was initiated using 32 μM thrombin receptor-activating peptide 6 (TRAPtest), 0.5 mM arachidonic acid (ASPItest), or 6.4 μM adenosine diphosphate (ADPtest) using commercially available reagents (Verum Diagnostica GmbH, Munich, Germany). Platelet aggregation in each test was quantified by the area under the aggregation curve (AUC) given in arbitrary aggregation units (AU). The reference ranges for healthy subjects given by the manufacturer were 87–147 AU for the TRAPtest, 51–109 AU for the ASPItest, and 61–96 AU for the ADPtest. Standard quality control procedures for each device were routinely performed following the manufacturer's recommendations.

POC tests have been performed solely in the POC group after randomization to this study group, after therapeutic interventions, and in case of ongoing bleeding after therapeutic interventions. POC tests have been performed at the bedside by the attending physician whereas conventional laboratory analyses were done in the central laboratory by a technician. Performance of POC testing required approximately 5 min of labor time and did not necessitate additional personnel. Nevertheless, intensive training in performing and interpreting viscoelastic and aggregometric tests is necessary.

Packed Erythrocytes Transfusion Protocol

Packed erythrocytes were transfused to maintain a hemoglobin concentration above 6 g/dl during CPB and 8 g/dl after CPB. Further indications for the transfusion of packed erythrocytes were according to national[15] and international guidelines:[16–18] (1) mixed venous oxygen saturation (SvO2) in patients with pulmonary artery catheter or central venous oxygen saturation ($ScvO_2$) in patients without pulmonary artery catheter less than 60% not due to low cardiac output and (2) individual bleeding dynamics strongly indicating the need for erythrocyte transfusion.

Hemostatic Therapeutic Options

Fibrinogen Concentrate. In the conventional group, fibrinogen concentrate (Hemocomplettan®P, CSL Behring GmbH, Marburg, Germany) was administered in a dose of 25–50 mg per kg body weight in bleeding patients with a prevalue of less than 200 mg fibrinogen per dl or an actual value of less than 150 mg fibrinogen per dl. In the POC group, fibrinogen concentrate was administered in a dose of 25–50 mg per kg body weight in bleeding patients with an A10 value in EXTEM® of equal or less than 40 mm and an A10 value in FIBTEM® of equal or less than 10 mm. Fibrinogen concentrate is approved in Germany since 1985 for hereditary hypofibrinogenemia, dysfibrogenemia, and afibrinogenemia and acquired hypofibrinogenemia while cryoprecipitate is not in use.

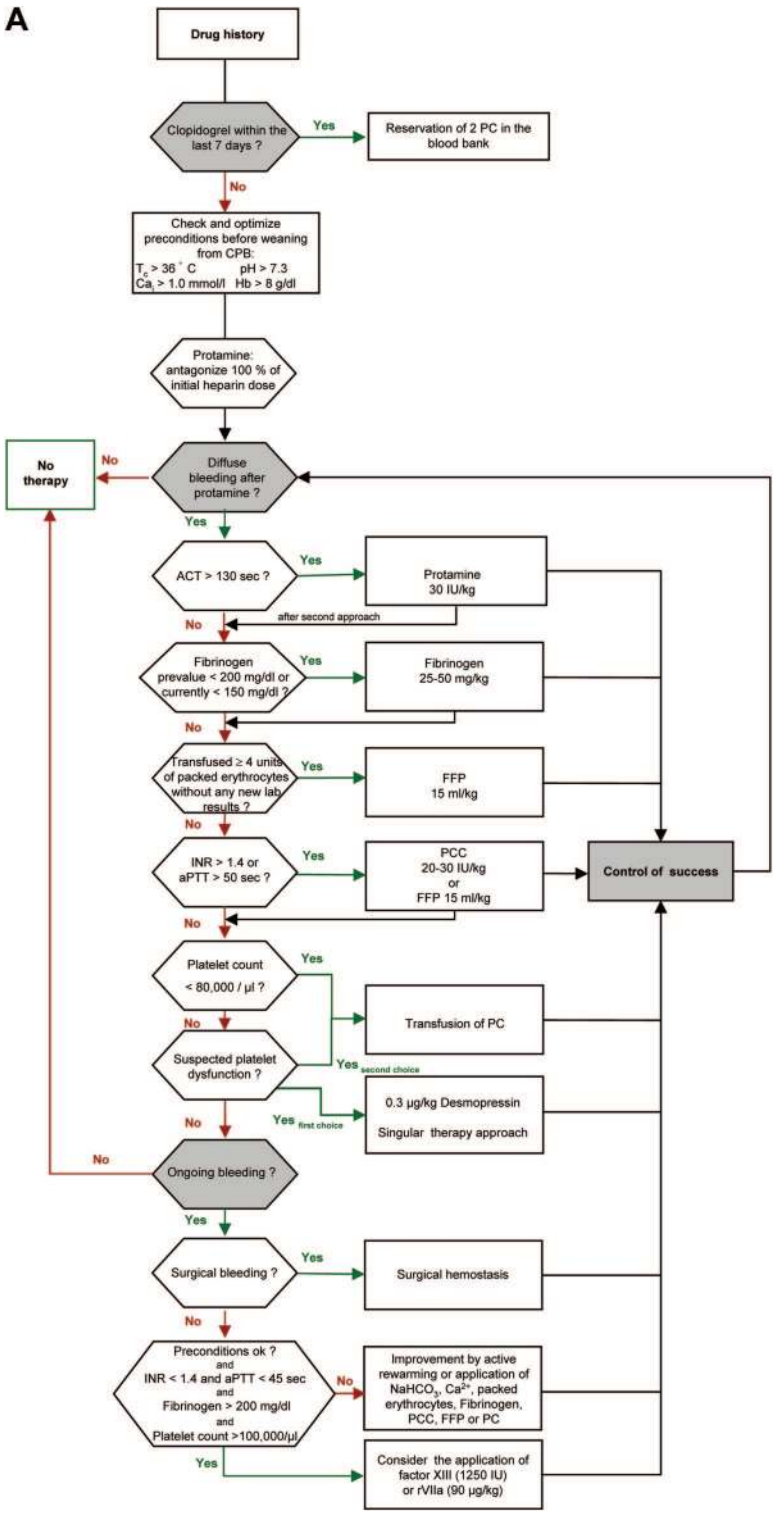

Fig. 1. Hemostatic therapy algorithms. (*A*) Intraoperative conventional algorithm. (*B*) Postoperative conventional algorithm. (*C*) Intraoperative POC algorithm. (*D*) Postoperative POC algorithm. ACT = activated clotting time; ADP = ADPtest®; aPPT = activated partial prothrombin time; ASPI = ASPItest®; AU = aggregation unit; A10 = amplitude of clot firmness 10 min after clotting time; Ca_i = ionized calcium; CPB = cardiopulmonary bypass; CT = clotting time; EX = EXTEM®; FFP = fresh frozen plasma; FIB = FIBTEM®; F XIII = factor XIII concentrate; HEP = HEPTEM®; ICU = intensive care unit; IN = INTEM®; INR = international normalized ratio; MCF = maximum clot firmness; PC = pooled platelet concentrate; PCC = prothrombin complex concentrate; rFVIIa = activated recombinant factor VII; Tc = core temperature; TRAP = TRAPtest®. Manufacturer of ROTEM® and Multiplate® were Tem International GmbH, Munich, Germany, and Verum Diagnostica GmbH, Munich, Germany, respectively.

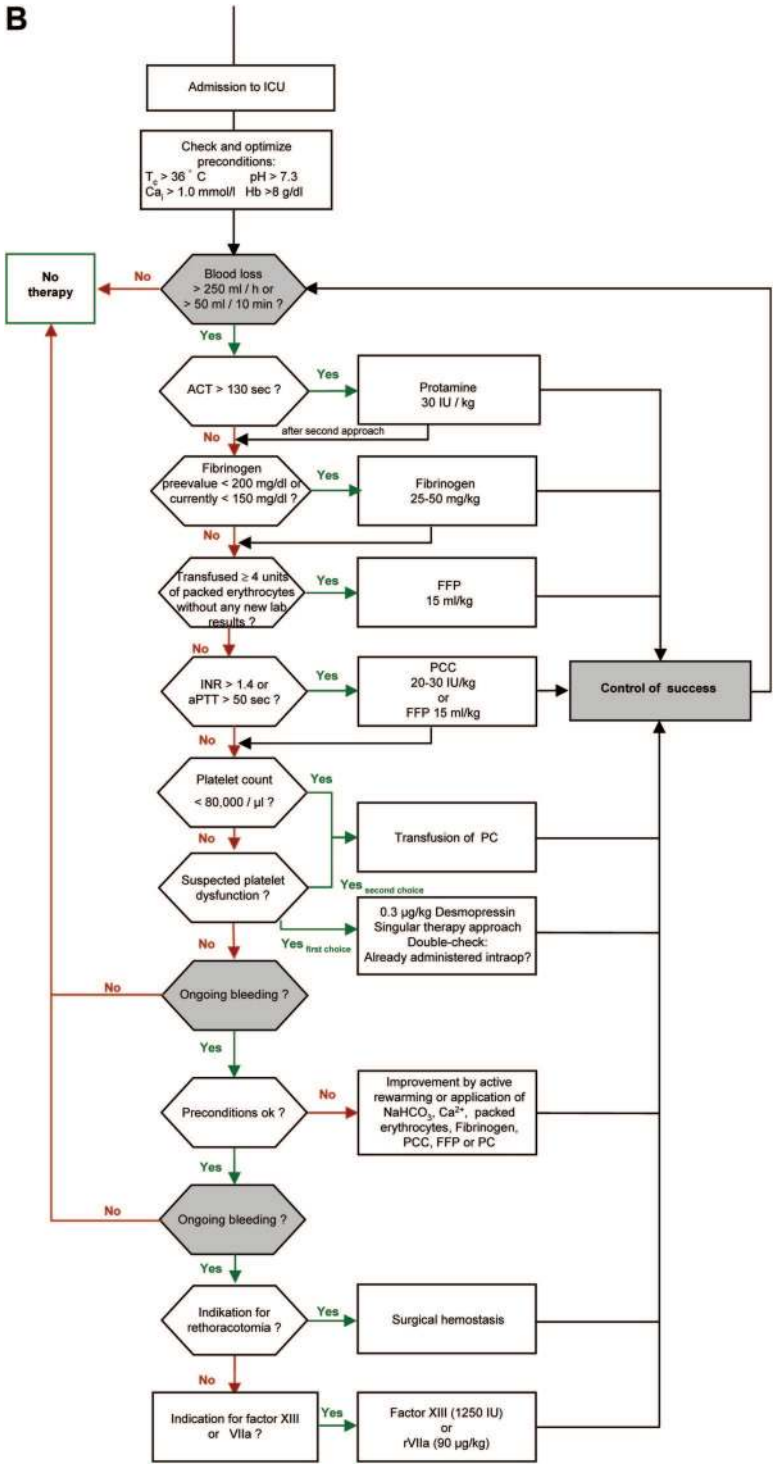

Fig. 1. (*Continued*)

Fresh Frozen Plasma. Fresh frozen plasma (FFP) was transfused in a dose of 15 ml per kg body weight in the conventional group if after transfusion of 4 units of packed erythrocytes new laboratory results were not available and/or bleeding did not stop after fibrinogen administration. In the POC group FFP was transfused in case of CT in EXTEM® exceeded 80 s or CT in HEPTEM® exceeded 240 s, especially if CT prolongation did not respond to administration of prothrombin complex concentrate (PCC).

Prothrombin Complex Concentrate. In the conventional group, PCC (PPSB-Konzentrat S-TIM 4/600 Immuno, Baxter Deutschland GmbH, Unterschleißheim, Germany) was administered in a dose of 20–30 IU per kg body weight if international normalized ratio exceeded 1.4 or activated

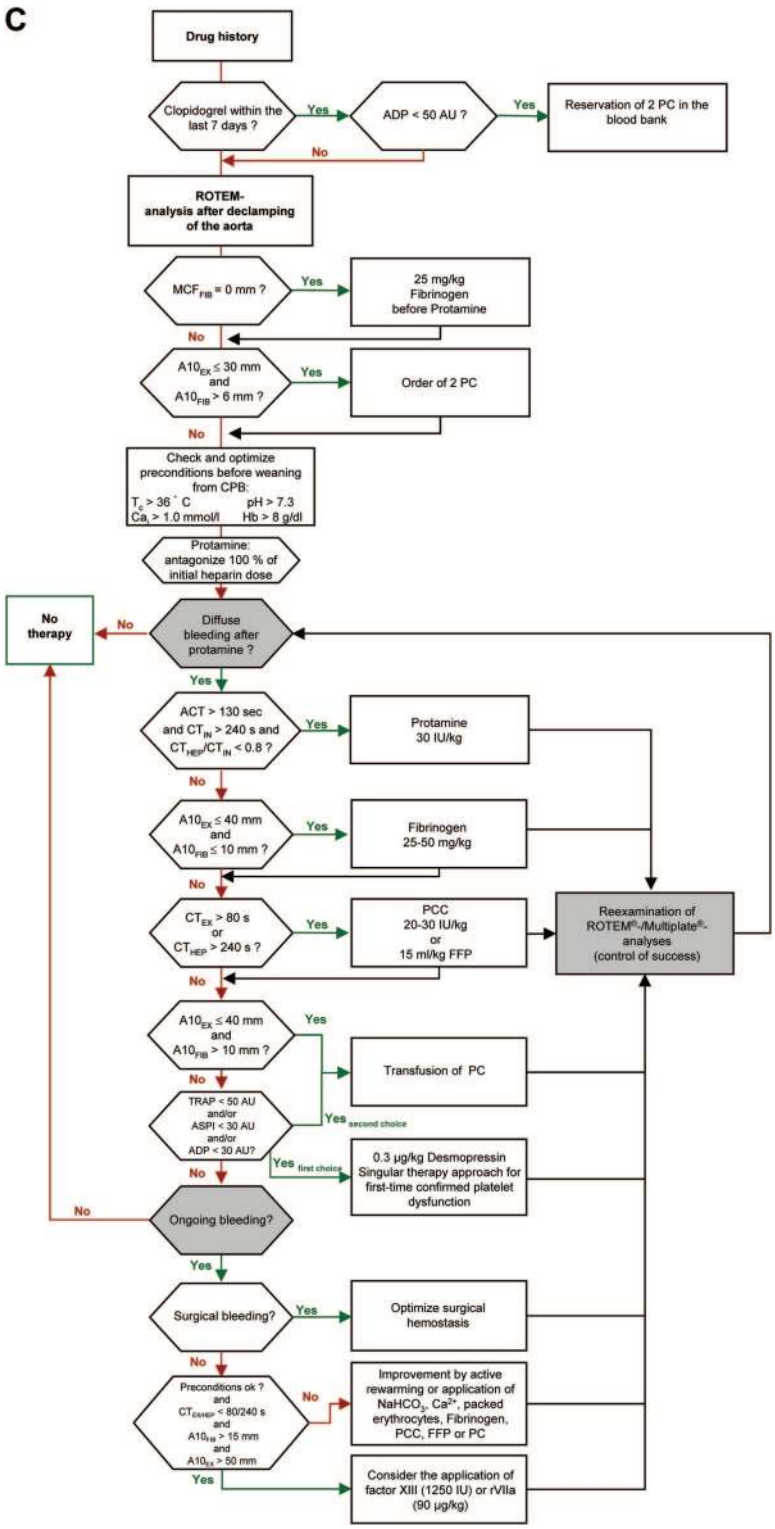

Fig. 1. (*Continued*)

partial thromboplastin time was prolonged longer than 50 s. In the POC group PCC was administered in case of CT prolongation in EXTEM® of more than 80 s. In contrast to the three-factor PCCs approved in the United States, four-factor PCCs used in Europe (such as PPSB Baxter and Beriplex®) contain balanced amounts of the coagulation factors II, VII, IX, and X, as well as protein C and S. PCC is approved in Germany since 1996 for the prophylaxis and ther-

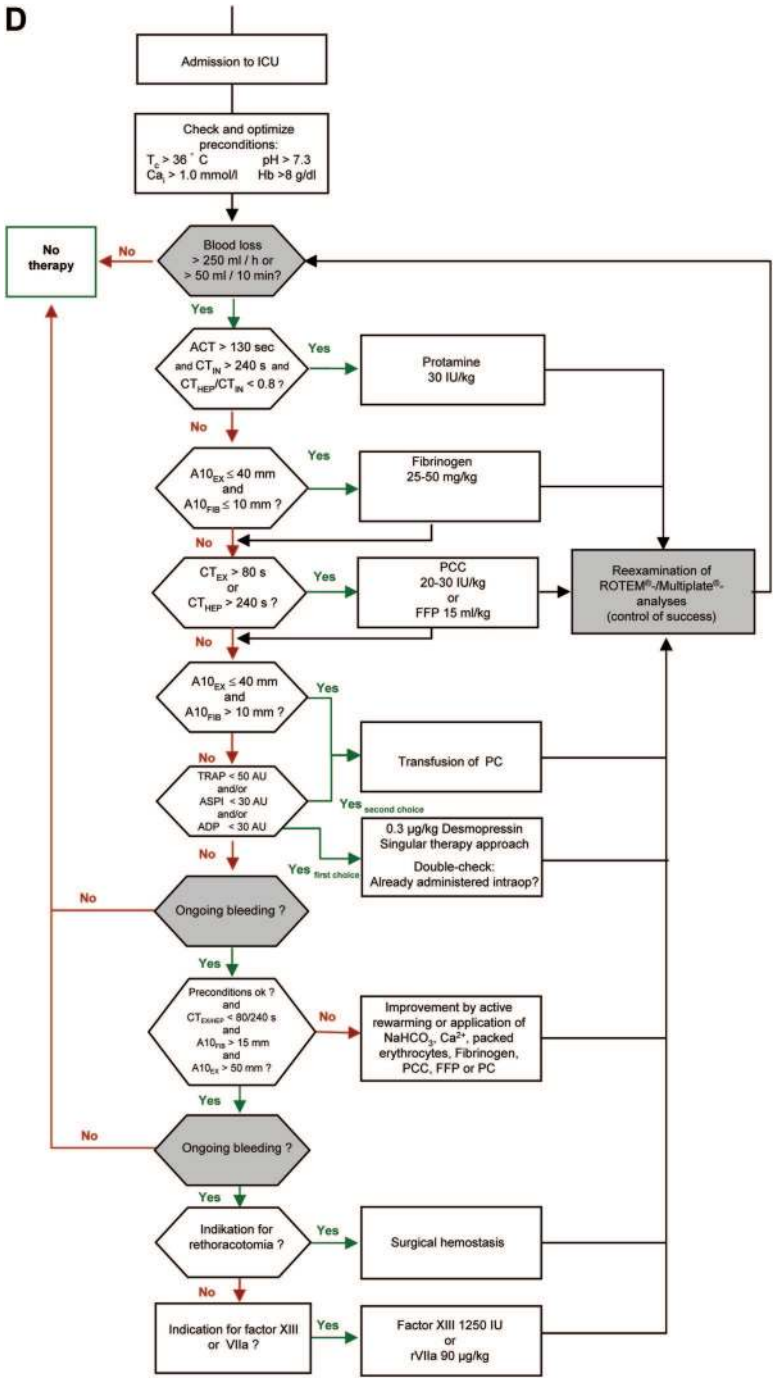

Fig. 1. (*Continued*)

apy of bleeding in patients with hereditary and acquired deficiency of vitamin K-dependent coagulation factors.

Antithrombin Concentrate. Antithrombin concentrate was only used when target ACT values were not achieved by heparin alone.

Desmopressin. In the conventional group, desmopressin (Minirin® parenteral, Ferring GmbH, Kiel, Germany) was administered as a singular therapy approach in a dose of 0.3 μg per kg body weight in case of suspected platelet dysfunction. In the POC group, desmopressin was administered as a single therapy approach in a dose of 0.3 per kg body weight for first-time confirmed platelet dysfunction in impedance aggregometry (AUC ASPItest less than 30 AU and/or AUC ADPtest less than 30 AU and/or AUC TRAPtest less than 50 AU).

Platelet Concentrates. In the conventional group, platelets were transfused as pooled (four donors; 2.4–3.6 $\times$ 10^{11} platelets per unit) concentrates if platelet count fell less than 80,000/μl in bleeding patients and in case of suspected platelet dysfunction, especially if bleeding did not stop after des-

mopressin administration. In the POC group platelet concentrates were transfused in bleeding patients with an A10 value in EXTEM® of equal or less than 40 mm and an A10 value in FIBTEM® of more than 10 mm. Furthermore, platelet concentrates were transfused in bleeding patients with confirmed platelet dysfunction in impedance aggregometry (AUC ASPItest less than 30 AU and/or AUC ADPtest less than 30 AU and/or AUC TRAPtest less than 50 AU), especially if bleeding did not stopped after desmopressin administration.

Further Therapeutic Options. In case of ongoing diffuse bleeding despite optimization of preconditions of hemostasis, surgical hemostasis, and conventional hemostatic therapy, administration coagulation factor XIII concentrate (1,250 IU FXIII per patient) (Fibrogammin®P, CSL Behring GmbH, Marburg), or activated recombinant factor VII (90 μg rFVIIa per kg body weight) (NovoSeven®, Novo Nordisk A/S, Bagsværd, Denmark) could be considered.

Hemostatic Therapy Algorithms

Hemostatic therapy algorithms for conventional laboratory analyses and for POC testing are shown in figure 1. Both types of algorithms give consideration to evidence-based hemostatic therapy management.[19,20] The POC-based algorithm has been used in several university hospitals in Germany since 2007 and its efficacy has recently been described in a retrospective study that included 3,865 cardiac surgery patients.[19,20] The cutoff values used in the conventional algorithms were based on the recommendation of the German cross-sectional guidelines for therapy with blood components and plasma derivatives.[15] The results of conventional coagulation tests were not used for guiding hemostatic therapy in the POC group. Both algorithms followed the same scheme and allowed for therapy control after each phase of the algorithms (*i.e.*, before surgery, drug history and the prevalence of potential platelet dysfunction were assessed). After declamping of the aorta, hemostatic therapy consisted of successive exclusion of excessive heparin therapy, hypofibrinogenemia, coagulation factor deficiency, platelet dysfunction, and surgical bleeding as potential causes for hemorrhage. The therapeutic options (protamine, tranexamic acid, desmopressin, fibrinogen concentrate, PCC, FFP, and platelet concentrates) were the same in both groups. In cases of ongoing bleeding despite algorithm-conforming therapy, both algorithms suggested the administration of coagulation factor XIII or rFVIIa concentrates.

Postoperative Hemodynamic Management and the Protocol for Surgical Reexploration and Cell-Saver Usage

According to local standard operating procedures, the targeted range of systolic blood pressure was 90–110 mmHg in patients suffering from increased bleeding after ICU admission. Surgical reexploration was performed if (1) chest tube blood loss exceeded 500 ml/h, (2) cumulative blood loss exceeded 1,200 ml, or (3) hemodynamically relevant hemopericardium occurred. If postoperative blood loss exceeded 800–1,000 ml, a cell-saver system (C.A.T.S. plus, Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany) was used, and salvaged washed erythrocytes were retransfused. Coagulopathy, as the reason for reexploration, was defined as diffuse bleeding in the operative field instead of surgical bleeding as assessed by the surgeon and anesthesiologist.

Data Collection

Demographics, clinical characteristics, and preoperative and postoperative routine laboratory data were recorded. Any exposure to antithrombotic therapy was also documented.

Outcome Analyses

Primary Outcome Variable. This is the number of transfused units of packed erythrocytes during the period between inclusion into the study and 24 h after ICU admission.

Secondary Outcome Variables. These variables are listed as follows.

- The number of transfused units of FFP, platelet concentrates (PC) and any other administered hemostatic therapy during the period between inclusion into the study and 24 h after ICU admission.
- Volume of intraoperatively and up to 24 h postoperatively retransfused salvaged washed erythrocytes.
- Postoperative chest tube blood loss 6, 12, and 24 h after ICU admission.
- Lowest hemoglobin concentration between inclusion into the study and 24 h after ICU admission.
- Number of rethoracotomies during the first 24 postoperative hours.
- Pa_{O_2}/Fi_{O_2} indices at 2, 4, 12, and 24 h after ICU admission.
- Postoperative time of mechanical ventilation.
- Length of ICU stay and hospital stay.
- Incidence of acute renal failure, sepsis, thromboembolism, and allergic complications.
- Mortality during a 6-month follow-up.
- Costs of hemostatic therapy as prescribed by local pharmacy and blood bank.

Sample Size Analysis

This analysis was based on expected group differences in the amount of transfused packed erythrocytes in the period between enrollment into the study and during the first 24 postoperative hours.

In a recent retrospective study, it was shown that performing algorithm-based hemostatic therapy was associated with a 28% decrease in the mean number of intraoperatively transfused packed erythrocytes.[20] Because the algorithm used in that paper was almost identical to the algorithms

used in the current study, we anticipated a reduction in perioperative erythrocyte transfusion of at least 20%. Considering the average transfusion rate of 5.8 ± 2.2 units of packed erythrocytes in a comparable patient cohort and time period at our hospital, the anticipated discrepancy between the two groups would consequently be at least 1 unit of packed erythrocytes. Sample size analysis (a 1 unit expected difference of means for transfused packed erythrocytes with an expected SD of 2.5 units, a desired power of 0.8, and an α of 0.05) revealed a required sample size of at least n = 100 per group to detect statistically significant group differences.

Interim Analysis, Ethical Review Board, and Stopping Guidelines

An interim analysis of the primary outcome variable was planned after inclusion of 50% (n = 100) of the study population. The study was planned to be terminated early if group differences in the number of transfused packed erythrocytes exceeded a level of significance defined as $P < 0.01$.

Statistics

The statistical analyses were performed using SigmaStat 3.5 and SigmaPlot 11 (Systat Software GmbH, Erkrath, Germany) software. Depending on the distribution of the data (determined *via* the Kolmogorov-Smirnov test), Student *t* tests and paired Student *t* tests or the Mann–Whitney rank sum test and Wilcoxon signed-rank test were used to describe differences between the groups and the measuring points, respectively. Primary outcome analyses were performed using the Mann–Whitney rank sum test. As a conservative choice, adjustments for multiple comparisons were only performed for Pao_2/FiO_2 indices and postoperative chest tube blood loss. The Fisher exact test was used to detect differences between the proportions of patients with respect to categorical data. Survival (6-month follow-up) between the groups was analyzed using the Kaplan–Meier method. Values were expressed as number (percent), mean ± SD, or median (25^{th} and 75^{th} percentiles), as appropriate. All tests were two-sided, and the level of significance was set to $P < 0.05$. We performed a univariate log regression with group allocation, redo surgery, and CPB as potential predictors for mortality. Subsequently, we performed a backward multivariate log regression for the significant predictors of the univariate analyses (exclusion criteria: $P > 0.10$). Univariate and multivariate analyses were performed using SPSS Statistics 20.0 (IBM Corp., Armonk, NY).

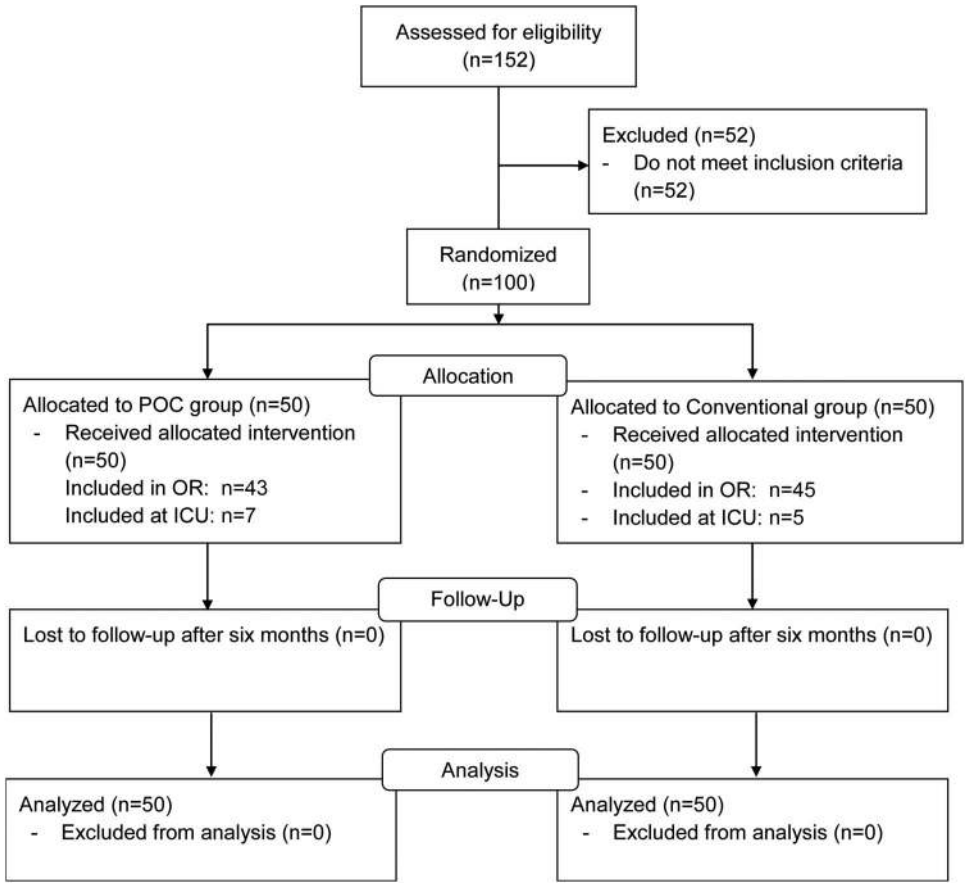

Fig. 2. Flow chart showing the number of patients at each phase of the trial. ICU = intensive care unit; OR = operating room; POC = point-of-care.

Results

A total of 152 patients were assessed for eligibility. Of those, 52 patients did not fulfill the inclusion criteria, and thus, a total of 100 patients were randomized: 50 to the conventional group and 50 to the POC group. Figure 2 shows the number of patients at each phase of the trial. Each of the randomized patients received the intended intervention. There were no losses or exclusions following randomization.

Eligible patients were recruited from May 2009 to April 2010. After inclusion of 100 patients, the study was terminated early in July 2010 because the planned interim analysis of the primary outcome variable revealed group differences with a $P < 0.001$. The 6-month follow-up of the last enrolled patient ended October 2010.

There were no group differences regarding baseline demographics or clinical or laboratory characteristics (table 1).

Apart from prophylactic weight-adapted low-molecular-weight heparin therapy, none of the patients received any anticoagulatory therapy for at least 6 days before surgery.

Table 2 shows the results of routine laboratory analyses obtained between the day before surgery and up to 24 h after ICU admission. With the exception of two parameters, there were no group differences: after admission to the ICU, fibrinogen and lactate were higher in the conventional group. At 24 h after admission to the ICU, these differences were no longer detectable. Table 3 gives the results of POC analyses after patients' enrollment into the study and after blood stanching as a result of the therapeutic intervention.

Table 4 depicts patients' intraoperative, postoperative, and cumulative exposure to allogenic blood products and coagulation factor concentrates. The cumulative dosages of packed erythrocytes during the study period were 5 (4, 9) units [median (25^{th} and 75^{th} percentile)] in the conventional group and 3 (2, 6) units in the POC group ($P < 0.001$).

Table 1. Baseline Demographic, Clinical, and Laboratory Characteristics

	Conventional Group n = 50	POC Group n = 50
Sex [male]	30 (60)	32 (64)
Age [years]	70 ± 8	72 ± 8
BMI [kg/m^2]	26 ± 5	26 ± 4
ASA score	3 (3; 4)	3 (3; 4)
euroSCORE	6.5 ± 2.1	6.9 ± 2.2
Creatinine [mg/dl]	1 (0.8; 1.2)	1 (0.8; 1.2)
Urea [mg/dl]	40 (35; 55)	47 (34; 60)
Redo surgery	13 (26)	14 (28)
Combined CABG and valve surgery	20 (40)	24 (48)
Double valve surgery	13 (26)	10 (20)
Triple valve surgery	1 (2)	2 (4)
Aortic surgery	8 (16)	6 (12)
CPB time [min]	166 ± 60	148 ± 46
Clamping time [min]	111 ± 45	104 ± 34

The data are presented as numbers (%), means ± SD or medians (25^{th}, 75^{th} percentile), as appropriate.

ASA = American Society of Anesthesiologists; BMI = body mass index; CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass; POC = point-of-care.

Compared with the conventional group, patients in the POC group received less FFP during the study period. Furthermore, the FFP dosage per transfused patient was lower in the POC group.

Intraoperatively, compared with the conventional group, patients in the POC group were transfused less often with PC, and in cases of transfusion, they received a smaller dosage of PC per transfused patient. There were no group differences with respect to PC transfusions in the postoperative period.

Intraoperatively and postoperatively, the number of patients receiving rFVIIa was higher in the conventional group. Patients in the conventional group also received higher dosages of rFVIIa in each of the study periods.

There were no group differences in the use of fibrinogen concentrates or PCC, either in the number of treated patients or in the average dosages.

There were no group differences with respect to the amount of intraoperatively or postoperatively infused crystalloid or colloid fluids. Whereas the volume of intraoperatively retransfused salvaged washed erythrocytes was higher in the conventional group, there were no group differences with respect to the amount of postoperatively retransfused packed erythrocytes. Patients in the conventional group lost more blood after admission to the ICU at each of the postoperative measuring points (table 5, fig. 3). The lowest hemoglobin concentration between patient enrollment into the study and the first 24 postoperative hours was 8.2 (7.7; 9.1) g/dl in the conventional group and 8.8 (8.1; 9.6) g/dl in the POC group ($P = 0.017$). There were no group differences in the number of patients requiring surgical reexploration during the study period (eight in the conventional group *vs.* five in the POC group, $P = 0.554$). Coagulopathy was identified as the primary reason for surgical reexploration in 75% in the conventional group *versus* 20% in the POC group ($P = 0.112$).

Table 5 shows postoperative Pa_{O_2}/Fi_{O_2} indices, durations of mechanical ventilation, durations of ICU and intermediate care unit treatment, and durations of the overall hospitalization. Whereas there were no group differences 2 h after ICU admission, patients in the conventional group had lower Pa_{O_2}/Fi_{O_2} indices at 4, 12, and 24 h after admission to the ICU. Both time of mechanical ventilation and duration of ICU treatment were longer in the conventional group. There were no group differences regarding the duration of intermediate care unit treatment or overall hospitalization.

During the ICU period, the incidence of acute renal failure was 10 of 50 (20%) in the conventional group *versus* 3 of 50 (6%) in the POC group ($P = 0.071$), the incidence of sepsis was 7 of 50 (14%) in the conventional group *versus* 1 of 50 (2%) in the POC group ($P = 0.059$), and the incidence of thrombotic complications was 2 of 50 (4%) in the conven-

Table 2. Routine Clinical Chemistry Analyses and Physiologic Parameters at Different Time Points

	Conventional Group n = 50	POC Group n = 50	*P* Value
Platelet count [/nl]	—	—	—
Preoperatively	218 (162; 260)	205 (170; 240)	0.612
At ICU admission	124 (100; 159)	113 (94; 141)	0.101
24 h after ICU admission	137 (113; 180)	121 (100; 165)	0.129
Hb [g/dl]	—	—	—
Preoperatively	12.3 (11.4; 13.9)	13 (11.7; 14.0)	0.341
At ICU admission	9.8 (9.1; 10.4)	9.9 (9.2; 10.4)	0.279
24 h after ICU admission	10.1 (9.4; 11.6)	10.2 (9.4; 10.9)	0.519
INR	—	—	—
Preoperatively	1.1 (1; 1.2)	1.1 (1; 1.2)	0.836
At ICU admission	1.39 (1.28; 1.51)	1.48 (1.27; 1.62)	0.093
24 h after ICU admission	1.35 (1.26; 1.5)	1.34 (1.22; 1.47)	0.467
aPTT [s]	—	—	—
Preoperatively	37 (35; 39)	36 (33; 40)	0.218
At ICU admission	47 (42; 52)	46 (41; 53)	0.437
24 h after ICU admission	41 (37; 46)	40 (37; 44)	0.469
Fibrinogen [mg/dl]	—	—	—
Preoperatively	359 (299; 441)	351 (307; 395)	0.454
At ICU admission	229 (181; 268)	197 (176; 232)	0.045
24 h after ICU admission	325 (273; 382)	288 (236; 351)	0.129
ACT [s]	—	—	—
At ICU admission	117 (108; 128)	116 (105; 129)	0.725
Temperature [°C]	—	—	—
At ICU admission	36.6 (36.4; 36.8)	36.6 (36.3; 36.9)	0.890
24 h after ICU admission	37.2 (36.7; 37.4)	37.2 (36.8; 37.4)	0.890
pH	—	—	—
At ICU admission	7.35 (7.3; 7.4)	7.35 (7.3; 7.4)	0.986
24 h after ICU admission	7.4 (7.35; 7.4)	7.36 (7.31; 7.4)	0.101
BE [mM]	—	—	—
Before CPB	1.1 (−1.4; 2.6)	0.55 (−1; 1.9)	0.725
At ICU admission	−3.1 (−4.2; −0.7)	−2.5 (−4.5;−1.35)	0.967
24 h after ICU admission	−0.3 (−3.4; 1.8)	−2.1 (−4.1; 0.6)	0.262
Lactate [mg/dl]	—	—	—
Before CPB	7.5 (5; 9)	7.5 (5; 10)	0.692
At ICU admission	22 (11; 31)	15 (10; 22)	0.020
24 h after ICU admission	17.5 (11; 22.5)	17.5 (11.5; 21)	0.960

The data are presented as medians (25^{th}, 75^{th} percentile). *P* values are reported without adjustment for multiple comparisons.
ACT = activated clotting time; aPTT = activated partial thromboplastin time; BE = base excess; CPB = cardiopulmonary bypass; Hb = hemoglobin concentration; ICU = intensive care unit; INR = international normalized ratio; POC = point-of-care.

tional group *versus* 0 of 50 in the POC group ($P = 0.495$). We did not observe any allergic reactions during the study period. The overall incidence of composite adverse events (acute renal failure, sepsis, thrombotic complications, and allergic reactions) was significantly lower in the POC group (4 of 50, or 8%) compared with the conventional group (19 of 50, or 38%) ($P < 0.001$). Figure 4 shows a Kaplan–Meier curve of postoperative survival. There were 10 of 50 patients (20%) in the conventional group and 2 of 50 patients (4%) in the POC group who died during the 6-month follow-up period ($P = 0.013$).

In univariate log regression, performed to assess whether the known potential risk factors CPB time and redo surgery might have had an effect on mortality in our study in addition to group allocation, only group allocation ($P = 0.014$) and CPB time ($P = 0.001$) were significant predictors of mortality, whereas redo surgery was not ($P = 0.07$). In the subsequent multivariate analysis, both, group allocation ($P = 0.039$; odds ratio = 0.212) and CPB time ($P = 0.006$; odds ratio = 1.163 per 10 min) were independent significant predictors for 6-month mortality.

Table 6 shows the cumulative costs of transfused allogenic blood products and hemostatic therapy (including coagulation factor concentrates) and the costs of disposables for POC analyses. The costs analyses did not include the acquisition costs of the POC devices, the costs for disposables in the central laboratory and labor costs for the technicians in the central laboratory.

Discussion

Our study compared the efficacy of hemostatic therapy algorithms in patients undergoing complex cardiac surgery suffering from coagulopathy after weaning from CPB. One algorithm was based on conventional laboratory analyses,

Table 3. Results of Point-of-Care Testing Using Thromboelastometry (ROTEM®) and Whole Blood Impedance Aggregometry (Multiplate®)

	After Enrollment	After Therapeutic Intervention and Blood Stanching
CT EXTEM [s]	97 (78; 117) (n = 50)	74 (64; 84) (n = 42)
CT INTEM [s]	220 (202; 279) (n = 50)	201 (186; 215) (n = 42)
CT HEPTEM [s]	209 (195; 227) (n = 50)	203 (199; 210) (n = 42)
A10 EXTEM [mm]	42 (37; 47) (n = 50)	48 (45; 51) (n = 42)
A10 FIBTEM [mm]	6 (4; 8) (n = 50)	10 (9; 11) (n = 42)
AUC TRAPtest [AU]	62 (47; 76) (n = 49)	74 (62; 85) (n = 36)
AUC ASPItest [AU]	40 (16; 53) (n = 49)	52 (41; 65) (n = 36)
AUC ADPtest [AU]	38 (23; 56) (n = 49)	49 (39; 62) (n = 36)

The data are presented as medians (25^{th}, 75^{th} percentile). ROTEM® parameter: CT = clotting time; A10 = amplitude of clot firmness 10 min after CT; Multiplate® parameter: AU = aggregation unit; AUC = area under the curve. Manufacturers of ROTEM® and Multiplate® were Tem International GmbH, Munich, Germany, and Verum Diagnostica GmbH, Munich, Germany, respectively.

whereas the other used POC testing based on viscoelastic and aggregometric measures.[20] To the best of our knowledge, this is the first prospective, randomized study to have integrated both thromboelastometry and impedance aggregometry in POC algorithms for perioperative coagulation management. The primary study results showed that the use of hemostatic therapy algorithms based on POC testing was associated with (1) reduced perioperative exposure to allogenic blood products and (2) improved clinical outcome.

With regard to reduction in transfusion requirements, hemostatic therapy, and costs, our results are in line with our retrospective cohort study[20] but the dimension of the observed reduction in mortality exceeded our expectations. However, this study was not powered for differences in mortality and therefore these results have to be analyzed carefully. Of note, in another recently published retrospective analysis including 1,188 patients undergoing cardiac surgery with CPB, postoperative hemorrhage was independently associated with worse clinical outcomes, increased 30-day mortality (5.5% *vs.* 22.4% in the nonbleeding and bleeding patients, respectively), and hospital costs.[21,22]

Because the amount of transfused packed erythrocytes represents a reliable surrogate parameter for the efficacy of hemostatic therapy, it was defined as the primary outcome variable of the current study. Bleeding and the consecutive need for transfusion of packed erythrocytes in the intraoperative period and the first 24 h after surgery most likely reflect the surgery-associated coagulopathy and thus the potential effects of different hemostatic strategies. Furthermore, we did not analyze the transfusion requirements during the entire hospital stay so that survival bias was minimized.[23,24] The planned interim analysis after inclusion of 50% of the entire study population showed that patients in the POC group received significantly fewer packed erythrocytes during the study period. The mean amount of units transfused was 5 (4, 9) in the conventional group (which is comparable with data obtained by Hardy *et al.*[25]) *versus* 3 (2, 6) in the POC group ($P < 0.001$). Based on this analysis, the study had to be terminated early according to the protocol and after ethical review.

In complex cardiac surgery, more than 20% of blood transfusions (and more specifically 15% of packed erythrocytes, 32% of FFP, and up to 47% of PC transfusions) have been considered inappropriate.[26] This issue of inappropriateness of blood transfusion did not dramatically change during the past 20 yr.[27–29] However, a reduction in patient exposure to allogenic blood products may minimize the incidence of transfusion-related complications, may beneficially influence clinical outcome, and definitely reduces the primary and secondary costs of transfusions.[1,30,31]

Hemostatic management should follow therapy algorithms based on the latest and most relevant laboratory data.[4,32] However, considering the multifactorial pathophysiology of perioperative hemorrhage during cardiac surgery, standard laboratory coagulation tests are of limited diagnostic value.[32] Furthermore, in most cases, they have a long turnaround time of at least 30–45 min.[33–35] In contrast, thromboelastometric and aggregometric analyses, which synergistically assess different parts of hemostasis, are usually available after 15–20 min and precisely analyze different causes of perioperative hemorrhage. Two recently published prospective observational studies reported a median turnaround time for conventional coagulation tests, performed in the central laboratory, of 88 min (range: 29–235 min) and 53 min (interquartile range: 45–63 min), respectively.[34,35] In contrast, A10 values of ROTEM® tests were already available after a median turnaround time of 23 min (interquartile range: 21–24 min).[35] In this study published by Haas *et al.*,[35] ROTEM® analysis was performed in the central laboratory and submitted online to a screen in the operation room. Because we performed the POC testing at the bedside in the operating room or at the ICU, an additional reduction of the turnaround time by approximately 5 min, usually needed for transportation of the blood sample to the laboratory, can be considered. A10 values in ROTEM® tests have been shown to reliably predict maximum clot firmness.[36] Compared with kaolin-activated thrombelastographic tests (TEG®; Haemonetics Corp., Niles, IL), clotting times (R-time + K-time *vs.* CT + clot formation time) are achieved 7–9 min earlier in tissue factor-activated ROTEM® tests (EXTEM® and FIBTEM®).[37]

The test time for whole blood impedance aggregometry (Multiplate®) is standardized on 9 min, including 3 min for incubation of the blood sample.[38] Therefore, the

Table 4. Allogenic Blood Product Exposure and Administered Coagulation Factor Concentrates

	Intraoperative			Postoperative			Cumulative		
	Conventional Group	POC Group	*P* Value	Conventional Group	POC Group	*P* Value	Conventional Group	POC Group	*P* Value
Packed erythrocytes	—	—	—	—	—	—	—	—	—
Transfused patients	45 (90)	33 (66)	0.007	41 (82)	32 (64)	0.07	49 (98)	42 (84)	0.031
Units transfused [U]	3 (2; 5)	2 (0; 3)	<0.001	2 (1; 4)	2 (0; 2)	0.041	5 (4; 9)	3 (2; 6)	<0.001
FFP	—	—	—	—	—	—	—	—	—
Transfused patients	39 (78)	16 (32)	<0.001	19 (38)	7 (14)	0.011	40 (80)	20 (40)	<0.001
Units transfused [U]	4 (2; 5)	0 (0; 3)	<0.001	0 (0; 2)	0 (0; 0)	0.016	5 (3; 8)	0 (0; 3)	<0.001
PC	—	—	—	—	—	—	—	—	—
Transfused patients	24 (48)	10 (20)	0.006	26 (52)	23 (46)	0.689	33 (66)	28 (56)	0.412
Units transfused [U]	0 (0; 3)	0 (0; 0)	0.001	1 (0; 2)	0 (0; 2)	0.402	2 (0; 5)	2 (0; 2)	0.010
Desmopressin	—	—	—	—	—	—	—	—	—
Treated patients	27 (54)	26 (52)	1.0	9 (18)	10 (20)	1.0	35 (70)	36 (72)	1.0
Units administered [μg]	26 (0; 28)	23 (0; 32)	0.892	0 (0; 0)	0 (0; 0)	0.984	28 (0; 32)	28 (0; 32)	0.660
Fibrinogen	—	—	—	—	—	—	—	—	—
Treated patients	26 (52)	23 (46)	0.689	14 (28)	16 (32)	0.828	30 (60)	32 (64)	0.837
Units administered [g]	2 (0; 4)	0 (0; 4)	0.177	0 (0; 2)	0 (0; 2)	0.743	2 (0; 6)	2 (0; 4)	0.481
PCC	—	—	—	—	—	—	—	—	—
Treated patients	16 (32)	13 (26)	0.66	16 (32)	12 (24)	0.504	26 (52)	22 (44)	0.433
Units administered [IU]	0 (0; 1,200)	0 (0; 600)	0.382	0 (0; 1,200)	0 (0; 0)	0.253	1, 200 (0; 1,800)	0 (0; 1,800)	0.155
rVIIa	—	—	—	—	—	—	—	—	—
Treated patients	9 (18)	1 (2)	0.016	4 (8)	0 (0)	0.117	12 (24)	1 (2)	0.002
Units administered [IU]	0 (0; 0)	0 (0; 0)	0.009	0 (0; 0)	0 (0; 0)	0.043	0 (0; 0)	0 (0; 0)	0.001

The data are presented as numbers (%) or medians (25^{th}, 75^{th} percentiles).

FFP = fresh frozen plasma; IU = international units; PC = pooled platelet concentrate; PCC = prothrombin complex concentrate; POC = point-of-care; rVIIa = recombinant activated factor VIIa concentrate.

turnaround time for Multiplate® analyses performed at bedside in the operating room is usually approximately 10–15 min.

However, the short turnaround time of these POC tests is not the only advantage compared with conventional coagulation tests. Whereas conventional coagulation tests are quantitative tests designed to measure the exact concentration of a coagulation factor or blood cells, POC tests such as thromboelastometry and impedance aggregometry focus on functionality. Therefore, they are able to detect tissue factor expression on circulating cells, fibrin polymerization disorders, *e.g.*, due to colloid infusion, hyperfibrinolysis, as well as platelet dysfunction due to CPB or antiplatelet drugs.[38–44] Of note, Multiplate® results have been shown to bear a good correlation to bleeding and thromboembolic complications in patients undergoing coronary stenting and cardiac surgery.[44,45] This may allow for more specific goal-directed interventions to reduce both transfusion requirements and thromboembolic complications.[20,46]

Although patients in the conventional group had higher intraoperative and postoperative blood loss, we detected no group differences in the hemoglobin concentration. Thus, the higher blood loss in the conventional group was compensated by a higher transfusion rate of packed erythrocytes in the conventional group. The cause of both the lower blood loss and the consequently lower erythrocyte transfusion rate in the POC group was most likely due to more efficient hemostatic therapy management. Patients in the POC group had a lower exposure to FFP and PC during the study period, and they received equal (or, with respect to rFVIIa, lower) dosages of coagulation factor concentrates.

There were no group differences with respect to demographic or surgical parameters, including anesthetic and surgical risk stratification scores (table 1), only CPB time approaches statistical significance with a slight but nonsignificant favor ($P = 0.104$) to shorter CPB times for the POC group (95% CI for the difference of mean CPB times is −39 to 4 min). How-

Table 5. Volume of Infused Crystalloids, Colloids, and Retransfused Salvaged Washed Erythrocytes, Postoperative Chest Tube Blood Loss and Pa_{O_2}/F_{IO_2} Indices, Durations of Mechanical Ventilation and Lengths of ICU, IMC, and Hospital Stay

	Conventional Group	POC Group	*P* Value
Crystalloids	—	—	—
Intraoperative [ml]	1,500 (1,500; 2,000) (n = 50)	1,500 (1,500; 2,000) (n = 50)	0.149 —
Postoperative [ml]	1,000 (1,000; 1,500) (n = 50)	1,000 (500; 1,500) (n = 50)	0.463 —
Colloids	—	—	—
Intraoperative [ml]	500 (500; 1,000) (n = 50)	1,000 (500; 1,000) (n = 50)	0.073 —
Postoperative [ml]	1,000 (500; 1,500) (n = 46)	1,000 (500; 1,500) (n = 46)	0.560 —
Retransfused salvaged washed erythrocytes	—	—	—
Intraoperative [ml]	794 (480; 1,050) (n = 50)	400 (250; 550) (n = 50)	<0.001 —
Postoperative [ml]	495 (365; 825) (n = 10)	290 (180; 900) (n = 8)	0.374 —
Cumulative postoperative chest tube blood loss	—	—	—
6 h [ml]	600 (350; 800) (n = 50)	338 (200; 500) (n = 50)	0.015 —
12 h [ml]	800 (550; 1,050) (n = 50)	425 (250; 750) (n = 50)	0.003 —
24 h [ml]	900 (600; 1,288) (n = 43)	600 (263; 875) (n = 35)	0.021 —
Postoperative Pa_{O_2}/F_{IO_2}–indices	—	—	—
At ICU admission	323 (201; 402) (n = 50)	355 (282; 460) (n = 50)	0.345 —
2 h after ICU admission	326 (219; 393) (n = 50)	338 (277; 423) (n = 50)	0.435
4 h after ICU admission	309 (256; 373) (n = 50)	358 (300; 407) (n = 50)	0.075
12 h after ICU admission	299 (222; 371) (n = 48)	398 (328; 467) (n = 45)	0.005
24 h after ICU admission	228 (137; 312) (n = 23)	327 (259; 468) (n = 17)	0.045
Time of mechanical ventilation	—	—	—
Including patients who died in the ICU [min]	827 (440; 2,835) (n = 50)	316 (230; 513) (n = 50)	<0.001
Excluding patients who died in the ICU [min]	700 (386; 1,095) (n = 42)	315 (229; 527) (n = 49)	<0.001
ICU period	—	—	—
Including patients who died in the ICU [h]	24 (20; 87) (n = 50)	21 (18; 31) (n = 50)	0.019
Excluding patients who died in the ICU [h]	24 (21; 87) (n = 42)	20 (18; 30) (n = 49)	0.012
IMC period [d]	3 (2; 5) (n = 20)	3 (1; 5) (n = 13)	0.524
Hospitalization period	—	—	—
Including patients who died or were discharged to other hospitals [d]	12 (9; 23) (n = 50)	12 (9; 22) (n = 50)	0.718
Excluding patients who died or were discharged to other hospitals [d]	12 (9; 22) (n = 39)	12 (9; 20) (n = 48)	0.925

The data are presented as medians (25^{th}, 75^{th} percentiles). *P* values are reported without adjustment for multiple comparisons. ICU = intensive care unit; IMC = intermediate care unit; POC = point-of-care.

ever, in univariate log regression and subsequent multivariate analysis, both group allocation and CPB time have been shown to be independent significant predictors of mortality.

Both types of hemostatic therapy algorithms conform to evidence-based hemostatic therapy management and were comparable in their structural progression of therapy escalation.[9,19,47] The clinical applicability of both algorithms can be assumed because all patients had hemostatic testing before therapy and none of them received therapy that deviated from the allocated algorithm. Therefore, the observed group

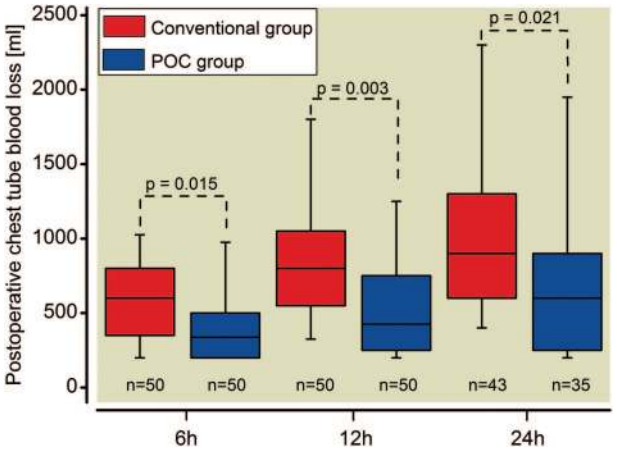

Fig. 3. Postoperative chest tube blood loss. POC = point-of-care.

differences are most likely due to methodical advantages associated with the POC diagnostic method itself. This conclusion was also supported by the lower usage of rFVIIa. This difference is remarkable because the use of rFVIIa was indicated at the end of both algorithms and, therefore, represented a form of "ultima ratio therapy."

Patients in the POC group had higher postoperative Pa_{O_2}/Fi_{O_2} indices, shorter postoperative ventilation times and lengths of ICU stay (table 5), lower incidence of composite adverse events, and lower mortality during a 6-month follow-up (fig. 4). It is important to note that the sample size analysis of the current study was not designed to legitimate final conclusions regarding clinical outcome. However, these data suggest that POC-guided hemostatic therapy is, at least in part, associated with improved clinical outcome.

Finally, the choice of hemostatic therapy is of economic relevance. Irrespective of any secondary costs of transfusion, analyses of the cumulative costs of hemostatic therapy showed that conventional coagulation management was nearly twice as expensive as POC-guided coagulation management. The mean costs of hemostatic therapy were on average 3,109 € per patient in the conventional group and 1,528 € per patient in the POC group (table 6).

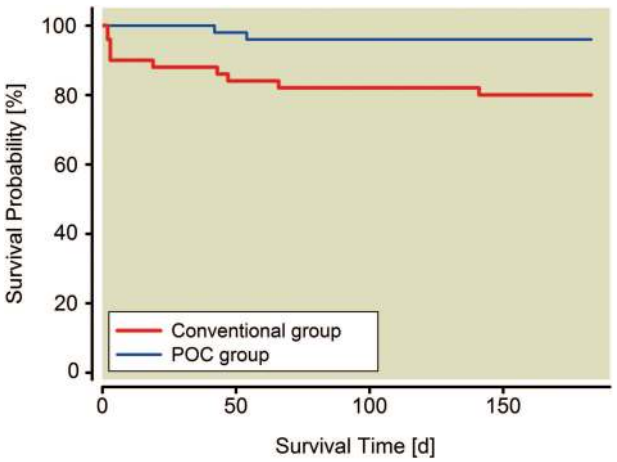

Fig. 4. Kaplan–Meier curve demonstrating survival by type of performed coagulation management during the 6-month follow-up period. POC = point-of-care.

Table 6. Cumulative Costs of Transfused Allogenic Blood Products, Hemostatic Therapy (Including Coagulation Factor Concentrates), and Costs of Performed POC Analyses

	Conventional Group	POC Group
Allogenic blood products	—	—
Packed erythrocytes [72 €/U]	18,648	13,176
FFP [0.162 €/g]	13,530	4,665
PC [231 €/U]	28,755	15,123
Other hemostatic therapy	—	—
Desmopressin [3.3 €/μg]	3,128	3,412
Fibrinogen [233 €/g]	35,882	27,727
PCC [114 €/600 IU]	10,944	6,726
rVIIa [2,784 €/240 kIU]	44,544	5,568
Total blood products and hemostatic therapy	155,431	76,397
Expendable materials POC Diagnostics	—	—
ROTEM®	—	4,093
Multiplate®	—	2,427
Cumulative [€]	155,431	82,918
Mean costs per patient [€]	3,109	1,658

The data are presented in Euro [€]. Manufacturers of ROTEM® and Multiplate® were Tem International GmbH, Munich, Germany, and Verum Diagnostica GmbH, Munich, Germany, respectively.

FFP = fresh frozen plasma; IU = international units; PC = pooled platelet concentrate; PCC = prothrombin complex concentrate; POC = point-of-care; rVIIa = recombinant activated factor VIIa concentrate.

Limitations to the Study

This trial was performed as a single-center study and therefore cannot account for potential interinstitutional differences in clinical and/or transfusion management of hemorrhagic patients. After patient randomization to the conventional or POC group, coagulation analyses and algorithm-based hemostatic therapy were performed in a nonblinded fashion—thus there is a chance of bias. Furthermore, the study population was too small to draw final conclusions concerning morbidity and mortality outcomes, although the reduction in the incidence of composite adverse events and 6-month mortality achieved statistical significance in the POC group. In addition, the difference in CPB time could not be excluded to have an effect on the observed reduction in 6-month mortality in the POC group.

Conclusions

In conclusion, hemostatic therapy algorithms in conjunction with POC testing reduced the number of transfused units of packed erythrocytes when compared with conventional lab-

oratory coagulation testing. Moreover, POC-guided therapy was associated with lower FFP and PC usage and costs as well as an improved clinical outcome in this prospective randomized single-center study. A multicenter study with a larger study population is needed to establish whether this effect can be reproduced in other facilities.

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