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Efficacy of a Simple Intraoperative Transfusion Algorithm for Nonerythrocyte Component Utilization after Cardiopulmonary Bypass

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Background: **Abnormal bleeding after cardiopulmonary bypass (CPB) is a common complication of cardiac surgery, with important health and economic consequences. Coagulation test–based algorithms may reduce transfusion of non-erythrocyte allogeneic blood in patients with abnormal bleeding.**

Methods: **The authors performed a randomized prospective trial comparing allogeneic transfusion practices in 92 adult patients with abnormal bleeding after CPB. Patients with abnormal bleeding were randomized to one of two groups: a control group following individual anesthesiologist's transfusion practices and a protocol group using a transfusion algorithm guided by coagulation tests.**

Results: **Among 836 eligible patients having all types of elective cardiac surgery requiring CPB, 92 patients developed abnormal bleeding after CPB (incidence, 11%). The transfusion algorithm group received less allogeneic fresh frozen plasma in the operating room after CPB (median, 0 units; range, 0–7 units) than the control group (median, 3 units; range, 0–10 units) (P = 0.0002). The median number of platelet units transfused in the operating room after CPB was 4 (range, 0–12) in the algorithm group compared with 6 (range, 0–18) in the control group (P = 0.0001). Intensive care unit (ICU) mediastinal blood loss was significantly less in the algorithm group. Multivariate analysis demonstrated that transfusion algorithm use resulted in reduced ICU blood loss. The control group also had a significantly greater incidence of surgical reoperation of the mediastinum for bleeding (11.8% *vs.* 0%; P = 0.032).**

Conclusions: **Use of a coagulation test–based transfusion algorithm in cardiac surgery patients with abnormal bleeding after CPB reduced non-erythrocyte allogeneic transfusions in the operating room and ICU blood loss.**

ABNORMAL bleeding after cardiopulmonary bypass (CPB) is a common complication of cardiac surgery that can result from inadequate surgical hemostasis and a variety of abnormalities in the coagulation system.[1–8] Insufficient surgical hemostasis also is an important cause of bleeding after CPB. The multifactorial nature of coagulation disorders after CPB complicates the decision of what therapeutic treatment is needed. The absence or delay of available laboratory data further complicates the decision of what therapeutic treatment is needed. Therefore, the treatment of excessive bleeding after CPB is often nonspecific and constitutes the transfusion of multiple types of blood products simultaneously (*e.g.*, additional protamine, platelet concentrates, fresh frozen plasma, and possibly cryoprecipitate). The multifactorial nature of coagulation disorders after CPB complicates clinical management, and treatment is often empirical.

Inappropriate use of blood products in cardiac surgical patients has important adverse health and economic consequences, and national practice guidelines have been published.[9–11] Excessive bleeding after CPB remains an important cause of patient morbidity and increased mortality and hospital costs in patients who require surgical reexploration of the thorax for excessive bleeding.[12,13] Excessive hemorrhage results in the transfusion of allogeneic blood products, which may expose the patient to additional risks (acquired immunodeficiency syndrome, hepatitis, and transfusion reactions)[11,14,15] and increased expense.[16] There is large variability between institutions in transfusion behavior for cardiac surgery patients.[17] Educational outreach has improved transfusion practice in surgery, and the decision to transfuse blood should be made with relevant laboratory data.[10,18] A prospective randomized study has documented a reduction in the use of allogeneic blood transfusions in cardiac surgery patients using routine coagulation tests to guide therapy and treatment of microvascular (nonsurgical) bleeding.[19] Another prospective randomized study found a reduction in chest tube blood loss and transfusion requirements in the intensive care unit (ICU) for patients whose blood transfusions were guided by a thromboelastography-based algorithm in the operating room.[20] A retrospective study found that after institution of these coagulation studies in the perioperative period, there was a significant reduction in number of blood transfusions and the incidence of mediastinal reexploration for hemorrhage in cardiac surgery patients.[21] Despite these studies and the American Society of Anesthesiologists' guidelines for transfusion therapy, large variability in transfusion practices exists between institutions for patients undergoing coronary artery bypass surgery.[22]

We designed a large, prospective, randomized study to determine whether allogeneic blood transfusion could

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be reduced in cardiac surgical patients using a coagulation test–based transfusion algorithm compared with the common practice of transfusion based solely on clinical judgment with or without laboratory tests.

Methods

Patients

After obtaining approval from the Mayo Medical Center Institutional Review Board (Rochester, MN) and written informed consent, adult men and nonpregnant adult women scheduled for elective cardiac surgery requiring CPB were randomized using a computer-generated randomization list with a block size of four to one of two groups. The two groups were a control group (transfusion support guided by empiric clinical judgment) and a protocol group (transfusion guided by an algorithm based on coagulation test results. Intraoperatively after CPB, the anesthesiologist and surgeon assessed extent of bleeding; abnormal microvascular bleeding (diffuse oozing with no visible clot) was determined by inspection of the operative field. Once it was determined that the patient had abnormal bleeding, transfusion therapy was determined by group designation. The patients were randomized on enrollment in the study. The surgeons and anesthesiologists were not made aware of which group the patients were placed in until after they decided that the patient had abnormal bleeding after CPB and they felt the patient needed to have transfusion of non-erythrocyte components. Therefore, the people making the transfusion decisions were blinded to group designation of the patients until after the determination of abnormal bleeding after CPB.

Intraoperative Management

All patients received a moderate-dose opioid-based anesthetic technique, supplemented with benzodiazepines, muscle relaxants, and inhalational anesthetic agents. CPB was conducted with a Univox membrane oxygenator (Bentley Inc., Irvine, CA) and a Sarns 9000 CPB machine using a roller head (Sarns Inc., Ann Arbor, MI) at a flow of $2.4\ l \cdot min^{-1} \cdot m^{-2}$. The CPB circuit was primed with 1.5 l of balanced salt solution, 10 mEq sodium bicarbonate ($NaHCO_3$), and 12.5 g mannitol. Porcine heparin was administered to patients as follows: an initial dose was given consisting of a bolus of 300 units/kg and an oxygenator priming dose of 10,000 units. Additional heparin (5,000 units) was administered when the celite activated clotting time (ACT) was less than 450 s or 750 s for patients on aprotinin therapy. After discontinuation of CPB, the initial protamine sulfate dose was 0.013 mg per unit of heparin administered. Heparin neutralization was regarded as adequate if the postprotamine ACT value was within 10% of the preheparin ACT value. Additional protamine (20–50 mg) was added at the discretion of the attending anesthesiologist if the ACT had not returned to that range, with the goal of returning the ACT to within 10% of the preheparin value. The designation of whether the patient had abnormal bleeding or not occurred 10 min after return of the ACT to within 10% of the preheparin value. Intraoperative blood salvage and reinfusion of shed mediastinal blood was used in all cases. Prophylactic antifibrinolytic therapy, aprotinin, tranexamic acid, and epsilon aminocaproic acid were used at the discretion of the attending anesthesiologist. Patients were not excluded if they received preoperative aspirin or antiplatelet therapy.

Transfusion Protocols

The control group received transfusion of blood products based on the clinician's judgment with or without guidance from laboratory tests. Twelve anesthesiologists and six surgical teams participated in the study. In the control group, the decisions for transfusion of blood components (varying combinations of platelets, fresh frozen plasma, or cryoprecipitate) were made by the attending anesthesiologist but could be empirical and precede the availability of any coagulation tests.

Participants in the treatment algorithm group had their transfusion therapy guided by an algorithm based on coagulation tests (fig. 1). The laboratory values used to guide therapy in the transfusion algorithm were determined from previous studies of patients undergoing cardiac surgery requiring CPB by performing receiver operator characteristic curve analysis at the following time point: in the operating room 10 min after protamine administration and return of the ACT to within 10% of baseline values.[23,24] The receiver operator characteristic curve analysis allowed us to determine which tests and test values produced greatest sensitivity, specificity, and accuracy for differentiating patients with abnormal bleeding from those without. Test values with the greatest accuracy were placed in our transfusion algorithm. Once it was determined that the patient was bleeding abnormally and the ACT had returned to within 10% of baseline, the laboratory tests for the algorithm were drawn. The algorithm directed transfusion of blood products, if any. Allogeneic platelets or desmopressin acetate were administered if the platelet count was less than 102,000/μl or the maximum amplitude of the thromboelastograph was less than 48 mm.

Allogeneic fresh frozen plasma was transfused if the prothrombin time was greater than 16.6 s or the activated partial thromboplastin time (APTT) was greater than 57 s. Cryoprecipitate was transfused if the fibrinogen was less than 144 mg/dl. The fibrinogen concentration test was a slow laboratory test and was used to guide the transfusion of cryoprecipitate in the second round of allogeneic blood transfusion, if necessary. If the patient continued to have abnormal bleeding by observation of

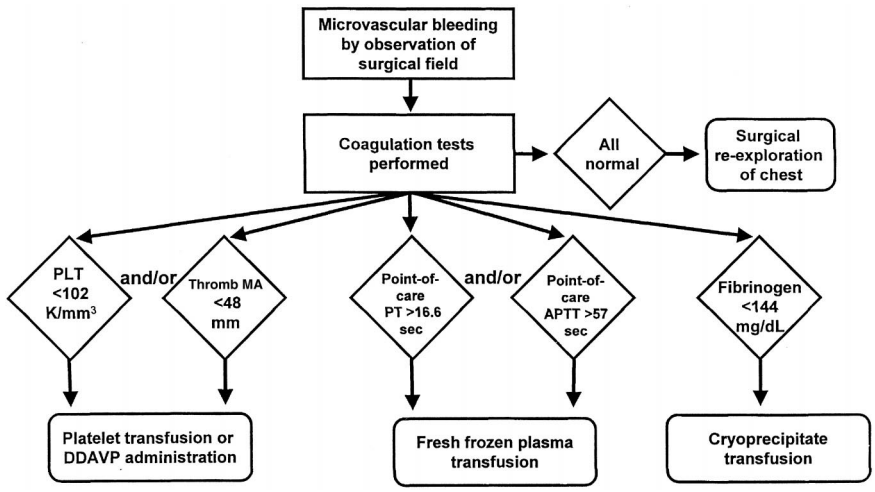

Fig. 1. The intraoperative transfusion algorithm was begun after the clinical diagnosis of abnormal bleeding. After initial treatment, the applicable coagulation tests were repeated to evaluate the effectiveness of the therapy. The fibrinogen concentration test was not a point-of-care test and was used to guide the transfusion of cryoprecipitate in the second round of allogeneic blood transfusion, if necessary. No transfusion algorithm was used in the intensive care unit. PLT = platelets concentrates; Thromb MA = thromboelastogram maximum amplitude; PT = prothrombin time; APTT = activated partial thromboplastin time; DDAVP® = desmopressin acetate.

the surgical field after the administration of allogeneic blood products, another round of laboratory tests for the algorithm were drawn. The algorithm directed transfusion of blood products, if any.

A subset of the control group, 25 patients, had the algorithm coagulation tests performed 10 min after protamine administration and normalization of the ACT. This was performed to compare coagulation test results between the two groups. The results of the coagulation tests in this subset were not provided to the clinician determining the type of and need for allogeneic blood transfusions.

Hematologic Assays

The point-of-care tests used in the transfusion algorithm were the whole blood prothrombin time and APTT measured with the Biotrack 512 Coagulation Monitor (currently known as the CoaguChek Plus, Roche Diagnostics, Indianapolis, IN), a portable battery-powered unit that uses disposable plastic reagent cartridges.[23] The results are obtained within 3–6 min and have an excellent correlation with the hospital laboratory prothrombin time and APTT.[25] The platelet counts were determined by the Coulter MD II (Coulter Corp., Hialeah, FL), and results were available within 5–10 min. The whole blood thrombelastogram (Haemoscope Corporation, Morton Grove, IL) maximum amplitude[21] results were available within 30 min. The fibrinogen concentration[26] results were available within 1 h.

Data Collected

All patients had laboratory-based tests (prothrombin time, APTT, platelet count) performed on arrival in the ICU. Mediastinal drainage in the ICU was recorded for the first 4, 12, and 24 h postoperatively. All allogeneic blood use was recorded intraoperatively, in the first 24 h postoperatively, and for the entire hospitalization period. Whether the patients with abnormal bleeding required reoperation for exploration of their mediastinum for bleeding was documented along with the findings of the reoperation. Use of antifibrinolytic therapy and preoperative aspirin or antiplatelet therapy was recorded.

Statistical Analysis

Power analysis was based on data from a previous retrospective study of patients who had undergone cardiac surgery at our clinic and a previous study by Despotis *et al.*[19] This power analysis determined that we could detect ($\alpha = 0.05$, 80% power) a change on the geometric scale from 6.4 to 1.6 units of allogeneic blood products transfused with 92 total patients having abnormal bleeding. We assumed 10% of our patients would develop microvascular bleeding, and thus planned to enroll up to 920 patients into the study.

We compared blood loss, autologous blood returned, and the number of allogeneic blood products (erythrocytes, fresh frozen plasma, platelets, and cryoprecipitate) administered between groups. The Fisher exact test was used to assess differences between groups for categoric variables. Differences between groups for continuous variables were assessed using the Wilcoxon rank sum test. Multiple regression analyses were used to assess differences in fresh frozen plasma and platelet transfusion between groups after adjusting for preoperative variables that were significantly different between groups. In these regression analyses, the dependent variables were number of units of fresh frozen plasma and platelets transfused in the operating room. Finally, multiple regression analyses were performed to assess the effect of wound drainage on amount of fresh frozen plasma and platelets transfused. In these analyses, the dependent variables were the 4-, 12-, and 24-h chest tube drainage, whereas the independent variables were the amount of fresh frozen plasma and platelets transfused in the operating room. P values ≤ 0.05 were considered significant.

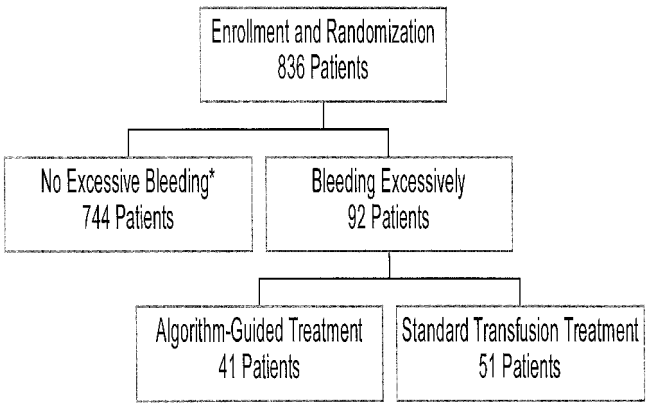

Fig. 2. A flow diagram and the numbers of patients at each phase of the trial. The disparity in patient numbers between the algorithm and control groups resulted from four patients being moved from the algorithm to the control group because the study personnel were not available. *The patients without abnormal bleeding by observation of the surgical field (no diffuse oozing) after CPB were not studied further.

Results

Among the 836 enrolled patients having elective cardiac surgery requiring CPB, 92 developed abnormal bleeding (11% incidence; fig. 2). Four of the patients initially randomized to the algorithm group were converted to the control group because of unavailability of study personnel. Thus, 41 patients were entered into the algorithm group, and 51 were entered into the control group.

The two groups were similar with regard to preoperative characteristics, except that 34.2% of patients in the algorithm group and 15.7% in the control group were receiving preoperative warfarin therapy ($P = 0.05$; table 1). There was no difference in intraoperative blood loss after CPB between the groups. No patients received epsilon amino-caproic acid or desmopressin acetate. There were no differences in coagulation test values, except for small differences in the preoperative platelet count (table 2). No patients had autologous blood available for surgery.

The percentage of patients who received different types of allogeneic blood transfusions in the operating room and the first 24 h in the ICU are shown in figure 3. The algorithm group received a median of 0 units (range, 0–7 units) of allogeneic fresh frozen plasma in the operating room after CPB compared with a median of 3 units (range, 0–10 units) in the control group ($P = 0.0002$). The median number of platelet units transfused in the operating room after CPB was 4 (range, 0–12) in the algorithm group compared with 6 (range, 0–18) in the control group ($P = 0.0001$). Our transfusion algorithm did not guide erythrocyte transfusions in the operating room, and there was no difference in the amount of erythrocyte units transfused in the operating room. The algorithm group received a median of 1 unit (range, 0–12 units) of allogeneic erythrocytes in the operating room after CPB compared with a median of 1 unit (range, 0–6 units) in the control group ($P = 0.85$).

During the first 24 h in the ICU, there were no differences in allogeneic platelet and fresh frozen plasma transfusions between the groups. The algorithm group received significantly less allogeneic erythrocytes, with a median of 0 units (range, 0–6 units) in the ICU compared with a median of 1 unit (range, 0–6 units) in the control group ($P = 0.0028$). There was no transfusion algorithm used in the ICU.

The amount of blood transfused to the algorithm group throughout the hospitalization was less than the control group. The algorithm group received a median of 2 units (range, 0–10 units) of allogeneic fresh frozen plasma throughout the hospitalization period compared with a median of 4 units (range, 0–75 units) in the control group ($P = 0.0005$). The median number of platelet units transfused throughout the hospitalization period was 6 (range, 0–18) in the algorithm group compared with 6 (range, 0–144) in the control group ($P < 0.0001$). The algorithm group received a median of 2 units (range, 0–9 units) of allogeneic erythrocytes throughout the hospitalization period compared with a median of 3 units (range, 0–70 units) in the control group ($P = 0.039$).

There was greater blood loss in the ICU for the control group compared with the algorithm group (table 3). The control group also had a greater incidence of surgical reoperation of the mediastinum for bleeding than the transfusion algorithm group (six control patients, zero algorithm patients; $P = 0.032$).

Since four patients in the algorithm group were moved to the control group because of the unavailability of study personnel, we repeated the analysis as an intention-to-treat analysis. Despite these patients not having their transfusion therapy guided by the algorithm, there still was a significant reduction in platelet and fresh frozen plasma transfusions in the operating room for the algorithm group relative to the control group. The algorithm group received a median of 2 units (range, 0–8 units) of allogeneic fresh frozen plasma in the operating room after CPB compared with a median of 3 units (range, 0–10 units) in the control group ($P = 0.0019$). The median number of platelet units transfused in the operating room after CPB was 6 (range, 0–12) in the algorithm group compared with 6 (range, 0–18) in the control group ($P < 0.0001$). The algorithm group received a median of 0 units (range, 0–6 units) of allogeneic erythrocytes in the first 24 h in the ICU compared with a median of 1 unit (range, 0–6 units) in the control group ($P = 0.0056$).

Because there were some differences between the groups in the preoperative warfarin use, preoperative platelet count, and the presence of other cardiac proce-

Table 1. Demographic and Surgical Variables

	Control		Algorithm		
Variable	Median	Range	Median	Range	*P* Value
Age (yr)	68	20, 85	69	28, 85	0.56
Height (cm)	171	146, 203	173	152, 191	0.64
Weight (kg)	77	37, 124	85	52, 135	0.44
Anesthesia duration (min)	394	201, 600	366	220, 638	0.09
Surgery duration (min)	330	148, 538	306	162, 563	0.11
CPB duration (min)	112	28, 257	110	36, 292	0.64
Cross-clamp time (min)	72	0, 150	73	24, 229	0.85
Circ arrest time (min)	0	0, 23	0	0, 15	0.35
OR time/protamine (min)	108	30, 270	108	45, 235	0.80
Heparin total (1,000 units)	41	22, 113	40	20, 90	0.88
Protamine total (mg)	350	150, 760	365	230, 620	0.99
Hematocrit on CPB (%)	26	14, 34	26	18, 36	0.52
Variable	N	%	N	%	*P* Value
Sex (male)	38	74.5	29	70.7	0.81
Preop aspirin (yes)	23	45.1	17	41.5	0.83
Preop coumadin (yes)	8	15.7	14	34.2	0.05
Preop intravenous heparin (yes)	9	17.7	10	24.4	0.45
Previous sternotomy (yes)	18	35.3	12	29.3	0.66
CABG (yes)	27	52.9	26	63.4	0.40
Total number of grafts					
0	24	47.1	15	36.6	0.67
1	5	9.8	4	9.8	
2	9	17.7	8	19.5	
3	9	17.7	12	29.3	
4	2	3.9	2	4.9	
5	2	3.9	0	0	
IMA					
Right		3.9		2.4	1.00
Left		39.2		39	
Left + right		2		0	
Valve (yes)	36	70.6	28	68.3	0.82
Valve type					
1 = Aortic	23	45.1	14	34.2	0.45
2 = Mitral	7	13.7	7	17.1	
3 = Tricuspid	2	3.9	0	0	
4 = Pulmonic	0	0	2	4.9	
5 = Combined	4	7.8	5	12.2	
Other surgery					
1 = Maze	1	2	0	0	
2 = Pfo closure	0	0	5	12.2	0.03
3 = Aortic arch	0	0	1	2.4	
4 = Other	16	31.4	10	24.4	
Antifibrinolytic drugs					0.53
1 = Aprotinin	15	29.4	8	19.5	
2 = Tranexamic acid	27	52.9	26	63.4	

No patients received desmopressin acetate or epsilon amino-caproic acid.

CPB = cardiopulmonary bypass; cross-clamp = aortic cross-clamp; circ = circulatory; OR time/protamine = duration of time in the operating room after protamine administration; preop = preoperative; CABG = coronary artery bypass graft; IMA = internal mammary artery grafting; pfo = patent foramen ovale.

dures, a multiple regression analysis was performed to adjust for these factors on transfusion outcome. The dependent variables were the amount of fresh frozen plasma and platelet units transfused in the operating room. The independent variables were preoperative warfarin use (0 = no, 1 = yes), preoperative platelet count, maze procedure (0 = no, 1 = yes), patent foramen ovale closure (0 = no, 1 = yes), aortic arch procedure (0 = no, 1 = yes), other cardiac surgical procedure (0 = no, 1 = yes), and group (0 = control, 1 = algorithm). After adjusting for preoperative warfarin use, preoperative platelet count, and other cardiac procedures performed, the algorithm group had significantly fewer units of fresh frozen plasma ($P = 0.0001$) and platelets ($P = 0.0001$) transfused in the operating room.

The amount of chest tube drainage was also significantly reduced in the algorithm group at all time points in the first 24 h in the ICU compared with the control group. Because chest tube drainage in the ICU might be affected by the amount of blood given in the operating

Table 2. Laboratory Values

Variable	Control		Algorithm		
	Median	Range	Median	Range	*P* Value
Preoperative					
Hgb (g/dl)	12.7	9.3, 16.4	13	8.2, 16.7	0.83
Hct (%)	38	28, 48	38	24, 51	0.45
Plt (10^9/l)	173	108, 493	208	101, 391	0.06
PT (s)	12.2	9.2, 24.6	11.7	9.4, 20.2	0.82
APTT (s)	35	20, 140	32	19, 115	0.43
Intraoperative 10 min postprotamine					
Hgb (g/dl)	9.3	6.8, 13.0	9.5	7.5, 13.6	0.34
Hct (%)	28	23, 37	27	16, 40	0.40
Plt (10^9/l)	96	24, 206	92	33, 203	0.58
PT (s)	15.8	12.5, 20.2	15.9	12.2, 23.4	0.95
APTT (s)	46	23, 83	42	18, 73	0.43
Fibrinogen (mg/dl)	171	85, 369	175	71, 317	0.44
Thromboelastogram R (mm)	15.5	10.5, 30.5	17	10.0, 62.0	0.29
Thromboelastogram R + K (mm)	24.8	15.5, 126.0	24.5	15.5, 129.0	0.86
Thromboelastogram angle (degrees)	45.5	10.0, 67.0	45.5	9.5, 65.0	0.61
Thromboelastogram MA (mm)	51.3	20.5, 62.5	51.8	0.5, 67.0	0.49
Thromboelastogram Lys + 30 (%)	1.5	0.0, 65.5	1.5	0.0, 28.0	0.32
Postoperative ICU entry					
Hgb (g/dl)	10	7.6, 15.6	11.2	8.6, 14.8	0.0008
Hct (%)	29	22, 45	33	25, 43	0.0012
Plt (10^9/l)	144	23, 274	144	85, 235	0.82
PT (s)	12.3	10.8, 24.0	12.5	9.5, 18.1	0.23
APTT (s)	36	26, 132	35	25, 71	0.51
Fibrinogen (mg/dl)	190	126, 253	162	122, 230	0.8

Hgb = hemoglobin concentration; Hct = hematocrit; Plt = platelet count; PT = prothrombin time; APTT = activated partial thromboplastin time; R = reaction time; R + K = reaction + bikoatugerung time; MA = maximum amplitude; Lys + 30 = % decrease from maximum amplitude after 30 minutes; ICU = intensive care unit.

room, a multiple regression analysis was performed to determine if the group differences remained significant after adjusting for the amount of fresh frozen plasma and platelet units transfused in the operating room. In this regression, the dependent variables were 4-, 12-, and 24-h chest tube drainage. The independent variables were fresh frozen plasma and platelet units transfused in the operating room. After adjusting for the fresh frozen plasma and platelet units transfused, there were no longer significant differences between the groups in 4-h chest tube drainage ($P = 0.15$), the 12-h chest tube drainage ($P = 0.1$), or the 24-h chest tube drainage ($P = 0.14$).

Discussion

In the year 2000, approximately 500,000 patients in the United States underwent cardiac surgery using CPB.[27] The majority of these patients (50–75%) likely received allogeneic blood transfusion.[17,22] Between 10 and 20% of the approximately 12 million units of eryth-

Table 3. Chest Tube Blood Loss and Incidence of Mediastinal Surgical Exploration

Variable	Control		Algorithm		
	Median	Range	Median	Range	*P* Value
Postoperative blood loss					
0–4 h CT drain (ml)	350	80, 1,290	250	50, 910	0.028
0–12 h CT drain (ml)	670	190, 2,940	420	130, 1,830	0.025
0–24 h CT drain (ml)	850	290, 10,190	590	240, 2,335	0.019
Variable	N	%	N	%	*P* Value
Reoperation (yes)	6	11.8	0	0	0.032
Surgical bleeding (yes)	2	4	0	0	0.50
Coagulopathy (yes)	1	2	0	0	1.00
Indeterminate (yes)	3	5.9	0	0	0.25

CT drain = chest tube drainage; reoperation = surgical exploration of the mediastinum for abnormal bleeding; surgical bleeding = a surgical source for bleeding found; coagulopathy = diffuse bleeding noted throughout the mediastinum; indeterminate = unable to determine whether the bleeding is from surgical or coagulopathy source.

rocytes transfused in the United States annually are given to cardiac surgical patients at a direct societal cost of 0.2–0.4 billion dollars.[28,29] Approximately 50% of the more than 7 million units of platelets transfused annually are to patients undergoing cardiac surgery, and use of platelet transfusion continues to grow.

Clinicians are limited in their ability to predict abnormal bleeding after CPB and identify patients who will require blood transfusion. In fact, the decision to transfuse cardiac surgery patients today in many institutions remains a highly subjective and relatively antiquated activity. There is large variability between institutions in transfusion behavior for cardiac surgery patients.[17] Approximately 20% of blood transfusion in cardiac surgery patients are inappropriate.[9,17] Specifically, 47% of platelets, 32% of fresh frozen plasma, and 15% of erythrocytes are considered inappropriate transfusions.[9] The decision to transfuse blood should be made with relevant laboratory data,[8,10,11] yet this may not be commonly performed. The most recent consensus conference by the American Society of Anesthesiologist stated, "the lack of data from prospective, randomized studies with adequate sample size, control groups, clinical outcome measurements, and other features of well designed clinical effectiveness research impedes development of evidence-based clinical practice guidelines for blood component therapy."[11] We previously determined in our patient population the coagulation test values that would most effectively guide transfusion of blood products in our cardiac surgical patients, and these values were incorporated into a transfusion algorithm used in this study.[23,24] Our prospective randomized study has demonstrated a significant reduction in allogeneic platelet and fresh frozen blood transfusions in the operating room in the algorithm group compared with the control group. Furthermore, there was a reduction in use of intraoperative combination therapy, transfusion of platelets with fresh frozen plasma or cryoprecipitate, from 90% in the control group down to 32% in the algorithm group (fig. 3). Use of the transfusion algorithm resulted in greater use of specific types of blood components solely or not at all. This represented a reduction in the use of unnecessary or inappropriate blood component transfusions. This reduction occurred in the area of greatest non-erythrocyte component use, the operating room (fig. 3).

An unanticipated but important finding of our study is that the lower number of coagulation product transfusions in the operating room in the algorithm group may have resulted in less bleeding in the ICU than the control group. This striking reduction in blood loss in the ICU after the use of the algorithm in the operating room compared with the control group was also found in another prospective randomized study. In this study, Despotis *et al.*[19] reported that a coagulation test–based intraoperative transfusion algorithm in cardiac surgery patients who had microvascular (nonsurgical) bleeding was effective in reducing allogeneic blood product transfusion. In both our study and that by Despotis *et al.*,[19] the more directed transfusion therapy may have corrected the hemostatic problem more effectively, which resulted in reduced bleeding in the ICU. In addition, the algorithm group had a significantly lower incidence of mediastinal reexploration for hemorrhage than the control group. Mediastinal reexploration for hemorrhage increases patients' morbidity and mortality, and increases hospital costs.[12,13]

In the current study, we did not extend the transfusion algorithm to the ICU, and there were no differences in transfusion coagulation components in the ICU. There was, however, a reduction in erythrocyte transfusions in the algorithm group.

Outside of the operating room and the ICU, thromboelastography is not often used. We used the maximum amplitude as a point-of-care test of platelet function. Others have used this test to guide transfusion therapy.[20,21] The maximum amplitude is influenced by platelet function,[30] platelet count,[31] and fibrinogen concentration.[32]

Study Limitations

Four patients were reassigned from the algorithm group to the control group because of the unavailability of study personnel, and this may have introduced bias in our study. However, reanalysis of our data based on intention to treat resulted in similar significant reductions in platelet and fresh frozen plasma transfusions in the algorithm group. Another limitation of our study is that we used the maximum amplitude as our platelet function test. Newer point-of-care platelet function tests have recently become available, which may be better tests of platelet function and the need for desmopressin acetate or platelet transfusion therapy. A further limitation of our study is that no test for residual heparin was used beyond return of the ACT to within 10% of the preheparin value. Residual heparin could prolong the APTT after CPB. An algorithm in this study did not guide the erythrocyte transfusions. Therefore, the differences found in erythrocyte transfusions in the ICU should be viewed with caution. Furthermore, the control patients entered the ICU with a lower hemoglobin concentration than the algorithm patients, which may explain the difference in ICU erythrocyte transfusions.

There also were small differences in the incidence of preoperative warfarin use, preoperative platelet count, and the presence of other cardiac procedures, but these seem unlikely to account for the observed differences in blood component transfusions. Dietrich *et al.*[33] found that preoperative phenprocoumon (a warfarin analog) therapy reduced bleeding after CPB. We performed a

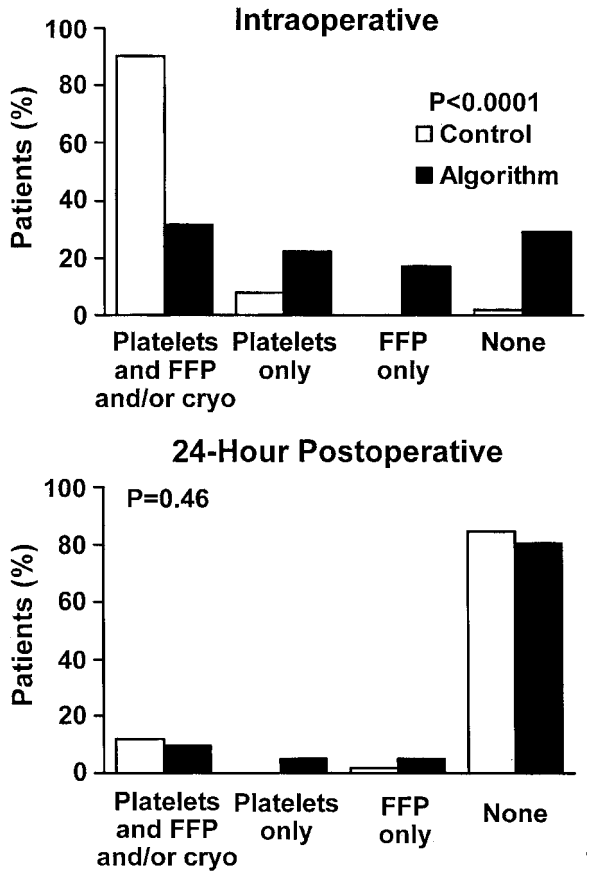

Fig. 3. The percentage of patients who received different types of allogeneic blood transfusions in the operating room and the first 24 h in the intensive care unit. Platelets and FFP and/or cryo = transfusion of platelets with fresh frozen plasma and/or cryoprecipitate; Platelets = only platelet transfusion; FFP = only fresh frozen plasma transfusion; None = no transfusion of platelets, fresh frozen plasma, or cryoprecipitate. Erythrocyte transfusion data not shown. No patients received only a cryoprecipitate transfusion in the operating room. In the first 24 h in the intensive care unit, one patient received only a cryoprecipitate transfusion in the control group.

multivariate analysis to attempt to control for these factors and found there were still significantly fewer units of fresh frozen plasma and platelets transfused in the algorithm group. Furthermore, differences between groups are also unlikely because randomization of all 836 patients occurred when they enrolled in the study before surgery.

In conclusion, the cause of abnormal bleeding after CPB is multifactorial, and assessment of the coagulation system is needed to efficiently treat this bleeding. Intraoperative use of a coagulation test–based transfusion algorithm in cardiac surgery patients reduced allogeneic transfusions in the operating room. Because of large variances in transfusion practice among medical institutions, the overall impact of our transfusion algorithm must be weighed against local factors influencing decisions. A multicenter study will be needed to address this. If this algorithm is successful in other institutions, large reductions in both the amounts of blood products transfused and the institutional costs for the care of cardiac surgery patients may be seen.

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