

## The ongoing variability in blood transfusion practices in cardiac surgery

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**BACKGROUND:** Although blood utilization has been under considerable scrutiny for the past two decades, particularly for surgery, studies comparing perioperative blood transfusion practices between countries are rare, and the evolution of international standards remains unknown. Therefore, the objective of this evaluation was to compare the perioperative transfusion of blood components in cardiac surgery in multiple centers in different countries.

**STUDY DESIGN AND METHODS:** Transfusion practice was investigated prospectively in 70 centers among 16 countries. A total of 5065 randomly selected cardiac surgery patients of the Multicenter Study of Perioperative Ischemia Epidemiology II (EPI II) Study were evaluated. Utilization of red blood cells (RBCs), fresh-frozen plasma (FFP), and platelets (PLTs) was assessed daily, before, during, and after surgery until hospital discharge.

**RESULTS:** Intraoperative RBC transfusion varied from 9 to 100 percent among the 16 countries, and 25 to 87 percent postoperatively (percentage of transfused patients). Similarly, frequency of transfusion of FFP varied from 0 to 98 percent intraoperatively and 3 to 95 percent postoperatively, and PLT transfusion from 0 to 51 and 0 to 39 percent, respectively. Moreover, there were not only marked differences in transfusion rates between centers in different countries but also in inter-institutional comparison of multiple centers within countries.

**CONCLUSION:** In cardiac surgical patients, marked variability in transfusion practice exists between centers in various countries and suggests differences in perioperative practice patterns as well as possible inappropriate use. International standardization of perioperative practice patterns as well as transfusion regimes appears necessary.

Nearly 1 million coronary artery bypass graft (CABG) surgeries are performed annually throughout the world, consuming approximately 20 percent of all blood products transfused,<sup>1-4</sup> and costing more than \$700 for all blood components transfused per patient.<sup>5,6</sup> Although coronary

**ABBREVIATIONS:** CABG = coronary artery bypass graft; ICU = intensive care unit; MCSPI EPI II = Multicenter Study of Perioperative Ischemia Epidemiology II.

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\*See Appendix 1 for a complete list of the investigators and centers.

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revascularization is regarded as a standardized surgical procedure, several perioperative factors can vary between centers and may potentially affect blood utilization as well as morbid outcome.<sup>7-10</sup> Also, excessive administration of human blood components has been described, which may reflect a lack of application of the evidence-based indications for the transfusion of blood components<sup>11-13</sup> and/or noncompliance with existing transfusion guidelines.<sup>14-19</sup> Variability in transfusion practice has led to recommendations regarding standardization within countries.<sup>2,3,14,15,20-22</sup> Yet unknown, however, is the current impact of these recommendations, especially throughout the regions of the world where the increase in CABG procedures is greatest.

The EPI II database provides uniquely comprehensive information about the management of more than 5000 heart surgery patients, including all relevant data on medical history, demographics, and intra- and postoperative variables, as well as transfusion practices worldwide. Based on the hypothesis that there is continuing variability in blood transfusion practices and thus some patients receive transfusions inappropriately, the objective of this study was to conduct an international comparison of transfusion practice in the perioperative cardiac surgical setting. For this purpose, the transfusion of different blood products was evaluated and compared in an international observational study.

## MATERIALS AND METHODS

### Study design: the MCSPI EPI II study

The Multicenter Study of Perioperative Ischemia Epidemiology II (MCSPI EPI II Study) was prospective and longitudinal and included 5436 patients, admitted with coronary artery disease that was refractory to medication, who were scheduled to undergo CABG surgery at one of 72 medical institutions in 17 countries in North America, South America, Europe, the Middle East, and Asia. Enrollment began in November 1996 and ended in June 2000; the database was locked on October 15, 2001. Participation in the EPI II Study was voluntary. After approval had been obtained from the institutional review board at each institution and written informed consent had been obtained from the patients, at least 100 patients were to be prospectively enrolled at each institution according to a standardized sampling scheme. To be eligible for enrollment, the patient had to be at least 18 years old, scheduled to undergo CABG with the use of coronary bypass, be able to complete the preoperative interview, and could not be enrolled in another study or clinical trial. Three centers were unable to provide data for our study; thus, data from the 16 remaining countries were available for analysis.

Clinical decisions were not controlled by study protocol, and all patients qualifying for enrollment were

entered. Of the 5436 patients enrolled in the EPI II Study, 371 were subsequently excluded due to patient withdrawal (32); death before surgery (2); cancellation or rescheduling of surgery (97); change in procedure (132); inadvertent enrollment in another study (11); incomplete data (86); or incomplete blood sampling, shipping, or storage (11), leaving 5065 patients reported herein.

For each enrolled patient, approximately 7500 fields of data were collected throughout the patient's index hospitalization (admission until discharge). Data included demographic, historical, clinical, laboratory, electrocardiographic, specialized testing, resource utilization, and adverse outcome. Treating physicians were blinded to all research data. All data fields for each patient were queried centrally for completeness and accuracy, with all changes documented before database closure.

### Measurement of outcomes

All blood products administered intra- and postoperatively, including all forms of perioperative autologous and homologous blood usage (red blood cells [RBCs], whole blood, fresh-frozen plasma [FFP], and platelets [PLTs]) were recorded with dosage and date of administration. All patients with transfusions of either autologous or homologous RBCs or whole blood were defined as having had transfusion of RBCs.

### Statistical analysis

Descriptive statistics were performed on all study variables for patients receiving any blood product. All data are described as either mean  $\pm$  1 standard deviation (SD) for continuous variables or number and percentage (in parentheses) for categorical variables, as indicated. Comparison between groups was performed with the two-tailed chi-square test for categorical variables; for continuous variables, a Kruskal-Wallis test was applied. *p* Values of less than 0.05 were considered as statistically significant. All statistical analyses were performed with computer software (SAS Version 8.2, SAS Institute, Cary, NC).

## RESULTS

### Demographic and surgical data

Demographic and surgical data are provided in Table 1. Of the 5065 patients participating in the MCSPI EPI II Study, 4302 (84.9%) had isolated CABG surgery, 507 (10.0%) CABG plus valve, and 256 (5.1%) CABG plus other procedures (e.g., myectomy, carotid, other vascular, or thoracic surgeries). Overall, 4113 (81.2%) patients underwent elective procedures; 891 (17.6%) were urgent and 61 (1.2%) were emergent.

TABLE 1. Demographic and surgical data\*

Variable	US	G	UK	CA	IND	F	H	T	CO	R	A	N	I	IS	M	P	Total
Patients per country†	1591 (31.4)	976 (19.3)	711 (14.0)	532 (10.5)	199 (3.9)	149 (2.9)	110 (2.2)	110 (2.2)	106 (2.1)	101 (2.0)	100 (2.0)	99 (2.0)	97 (1.9)	94 (1.9)	59 (1.2)	31 (0.6)	5065 (100)
Sites per country	32	9	7	8	2	2	1	1	1	1	1	1	1	1	1	1	4.4
Age (year)	65.4 ± 10.0	64.8 ± 9.0	63.9 ± 9.2	65.4 ± 9.9	57.4 ± 9.3	64.2 ± 10.4	59.0 ± 10.2	61.2 ± 8.5	60.4 ± 8.5	59.8 ± 9.5	64.6 ± 8.2	63.8 ± 9.2	63.5 ± 9.8	63.3 ± 9.7	61.3 ± 10.2	62.0 ± 9.6	64.1 ± 9.8
Male gender	1264 (79.4)	761 (78.0)	576 (81.0)	415 (78.0)	186 (93.5)	123 (82.6)	80 (72.7)	83 (75.5)	85 (80.2)	83 (82.2)	72 (72.0)	69 (69.7)	80 (82.5)	79 (84.0)	47 (79.7)	24 (77.4)	4027 (79.5)
BMI (kg/m <sup>2</sup> )	28.6 ± 5.5	27.2 ± 3.6	27.8 ± 4.2	28.5 ± 4.3	24.7 ± 3.3	26.8 ± 4.1	27.4 ± 3.9	24.2 ± 2.9	25.9 ± 3.4	27.2 ± 3.2	26.7 ± 3.6	27.0 ± 3.3	26.4 ± 3.7	27.0 ± 3.3	26.8 ± 2.7	26.7 ± 4.2	27.6 ± 4.5
Euro score	5.4 ± 3.5	4.5 ± 3.0	3.8 ± 2.6	4.6 ± 3.0	3.3 ± 2.9	4.3 ± 2.9	3.4 ± 2.9	3.3 ± 2.6	3.8 ± 2.5	3.5 ± 3.1	3.7 ± 2.8	4.0 ± 2.7	3.9 ± 3.1	4.4 ± 2.4	3.9 ± 2.6	2.8 ± 2.8	4.5 ± 3.2
Pre-OP Hct (%)	39.0 ± 5.2	41.0 ± 4.5	40.7 ± 4.2	39.8 ± 4.6	38.7 ± 3.6	40.7 ± 4.5	41.2 ± 4.2	40.2 ± 5.2	44.8 ± 4.6	40.0 ± 5.0	41.9 ± 4.1	42.2 ± 4.2	43.1 ± 3.8	39.9 ± 4.1	42.4 ± 6.2	40.7 ± 3.4	40.2 ± 4.8
No. of grafts	3.0 ± 1.0	2.9 ± 0.9	3.0 ± 0.9	3.0 ± 0.9	3.2 ± 0.8	2.4 ± 0.8	3.0 ± 1.0	3.6 ± 0.9	2.4 ± 0.6	3.3 ± 1.0	2.9 ± 0.8	2.0 ± 0.5	2.4 ± 0.8	2.9 ± 0.9	3.0 ± 0.8	2.5 ± 0.9	2.9 ± 0.9
DSUR (h)	4.5 ± 1.5	3.8 ± 1.4	3.0 ± 0.9	3.1 ± 1.0	3.8 ± 1.0	4.1 ± 1.2	2.7 ± 0.7	4.3 ± 0.9	3.9 ± 0.9	5.1 ± 1.3	3.9 ± 1.1	3.0 ± 1.0	3.8 ± 0.9	3.8 ± 1.0	4.4 ± 0.7	3.7 ± 0.9	3.8 ± 1.4
DICU (d)	3.3 ± 6.7	3.5 ± 7.1	1.7 ± 5.9	1.9 ± 1.8	3.5 ± 3.4	3.7 ± 4.4	1.8 ± 2.5	2.0 ± 2.4	2.8 ± 2.7	4.0 ± 4.8	3.7 ± 5.4	2.1 ± 5.1	2.1 ± 3.9	2.0 ± 1.3	4.6 ± 6.5	1.6 ± 0.9	2.9 ± 5.8

\* All data are described as either mean ± 1 SD or number and percent per country (in parentheses).  
 † Percentage based on a total of 5065 patients; other percentages refer to number of patients per country.

US = United States; G = Germany; UK = United Kingdom; CA = Canada; IND = India; F = France; H = Hungary; T = Thailand; CO = Colombia; R = Romania; A = Austria; N = Netherlands; I = Italy; IS = Israel; M = Mexico; P = Poland (order of countries by decreasing number of patients enrolled in the study). BMI = body mass index; DICU = duration in ICU; q = days; DSUR = duration of surgery; h = hours; Pre-OP Hct = minimum preoperative Hct value.

Overall variability of transfusion practice

The comparison of perioperative transfusion practice showed an inconsistent pattern between the 16 countries for all blood products (Tables 2-5). A significant variability was observed both in the frequency of use and in the mean amount of RBCs, FFP, and PLTs transfused per patient, intraoperatively as well as postoperatively. The percentage per country of patients who received RBC transfusion ranged from 9 to 100 percent intraoperatively and from 25 to 87 percent postoperatively. Similarly, the frequency of FFP transfusion varied from 0 to 98 percent intraoperatively and from 3 to 95 percent postoperatively. PLT transfusion ranged from 0 to 51 percent intraoperatively and from 0 to 39 percent postoperatively. Conversely, 33 percent of patients did not receive RBC transfusion either intra- or postoperatively, 78 percent received no FFP, and 83 percent received no PLTs (Table 2).

Transfusion practice for RBCs

Overall, 66.7 percent (3380) of the study patients received homologous and/or autologous RBC transfusion either intra- and/or postoperatively, with a mean of 4.0 units per transfused patient (for frequency and amount of RBC transfusion per country see Tables 2-5). Intraoperatively, 41.3 percent of all patients received RBCs; 100 percent of the patients in the one study center in Thailand received RBCs, but only 8.7 percent in the two study centers in France, which had the lowest transfusion rate per country (Fig. 1A). In all transfused patients, a mean of 2.4 units of RBCs were administered intraoperatively, with a substantial range between 1.3 units for the one center in Poland and a mean of 3.1 units for the nine study sites in Germany (Fig. 1A). Postoperatively, 54.0 percent of all patients received RBCs, with the highest transfusion rate in the one study center in Thailand (87.3%) and the lowest in the one study center in Italy (24.7%; Fig. 2A). A mean of 3.0 units of RBCs were transfused postoperatively, with the largest mean number in the two study sites in France (4.2 units) and the smallest in the one center in Thailand (1.9 units; Fig. 2A). A total of 9.5 percent of the transfused patients were given autologous RBC perioperatively.

Transfusion practice for FFP

Overall, 22.4 percent (1137) of all patients received homologous and/or autologous FFP either intra- and/or postoperatively, with a mean of 4.9 units per transfused patient (Tables 2-5). Intraoperatively, 10.9 percent of all patients received FFP transfusion; in the one study center in Mexico almost all patients received FFP (98.3%), but no FFP was transfused intraoperatively in the two centers in France (Fig. 1B). A mean of 3.1 units of FFP were

TABLE 2. Number and percentage of patients without transfusion\*

Variable	US	G	UK	CA	IND	F	H	T	CO	R	A	N	I	IS	M	P	Total
<i>Patients with no transfusion intra- or postoperatively</i>																	
RBCs	485 (30.5)	261 (26.7)	323 (45.4)	300 (56.4)	9 (4.5)	75 (50.3)	46 (41.8)	0 (0)	30 (28.3)	32 (31.7)	12 (12.0)	26 (26.3)	57 (58.8)	26 (27.7)	1 (1.7)	2 (6.5)	1685 (83.3)
FFP	1234 (77.6)	658 (67.4)	596 (83.8)	475 (89.3)	145 (72.9)	141 (94.6)	86 (78.2)	100 (90.9)	88 (83.0)	52 (51.5)	93 (93.0)	93 (93.9)	88 (90.7)	73 (77.7)	0 (0)	6 (19.4)	3928 (77.6)
PLTs	1167 (73.4)	857 (87.8)	645 (90.7)	492 (92.5)	148 (74.4)	143 (96.0)	108 (98.2)	91 (82.7)	106 (100)	46 (45.5)	91 (91.0)	93 (93.9)	92 (94.8)	84 (89.4)	26 (44.1)	29 (93.5)	4218 (83.3)
<i>Patients with no transfusion intraoperatively</i>																	
RBCs	879 (55.2)	472 (48.4)	560 (78.8)	434 (81.6)	48 (24.1)	136 (91.3)	89 (80.9)	0 (0)	77 (72.6)	46 (45.5)	40 (40.0)	61 (61.6)	71 (73.2)	54 (57.4)	2 (3.4)	5 (16.1)	2974 (58.7)
FFP	1399 (87.9)	835 (85.6)	692 (97.3)	520 (97.7)	166 (83.4)	149 (100)	109 (99.1)	102 (92.7)	99 (93.4)	59 (58.4)	96 (96.0)	96 (97.0)	94 (96.9)	89 (94.7)	1 (1.7)	8 (25.8)	4514 (89.1)
PLTs	1333 (83.8)	918 (94.1)	699 (98.3)	525 (98.7)	171 (85.9)	147 (98.7)	110 (100)	95 (86.4)	106 (100)	50 (49.5)	95 (95.0)	97 (98.0)	97 (100)	92 (97.9)	32 (54.2)	31 (100)	4598 (90.8)
<i>Patients with no transfusion postoperatively†</i>																	
RBCs	755 (47.5)	435 (44.6)	359 (50.5)	334 (62.8)	36 (18.1)	79 (53.0)	51 (46.4)	14 (12.7)	34 (32.1)	52 (51.5)	25 (25.0)	33 (33.3)	73 (75.3)	32 (34.0)	9 (15.3)	7 (22.6)	2328 (46.0)
FFP	1354 (85.1)	727 (74.5)	605 (85.1)	480 (90.2)	149 (74.9)	141 (94.6)	86 (78.2)	107 (97.3)	95 (89.6)	83 (82.2)	93 (93.0)	95 (96.0)	89 (91.8)	76 (80.9)	3 (5.1)	22 (71.0)	4205 (83.0)
PLTs	1349 (84.8)	897 (91.9)	656 (92.3)	496 (93.2)	154 (77.4)	145 (97.3)	108 (98.2)	106 (96.4)	106 (100)	95 (94.1)	94 (94.0)	95 (96.0)	92 (94.8)	85 (90.4)	36 (61.0)	29 (93.5)	4543 (89.7)

\* All data are described as number (%).

† Postoperative is from ICU admission to ICU discharge.

US = United States; G = Germany; UK = United Kingdom; CA = Canada; IND = India; F = France; H = Hungary; T = Thailand; CO = Colombia; R = Romania; A = Austria; N = Netherlands; I = Italy; IS = Israel; M = Mexico; P = Poland (order of countries by decreasing number of patients enrolled in the study). RBCs = RBCs and/or whole blood. There were significant differences between the countries in RBC, FFP, and PLT use, both intra- and postoperatively (p < 0.0001).

administered intraoperatively; the largest amount was given in the one study site in Italy (4.7 units) and the lowest in the two study centers in France (0 units) (Fig. 1B). Postoperatively, 17.0 percent of all patients received FFP, with the highest transfusion rate in the one center in Mexico (94.9%) and the lowest rate in the one study site in Thailand (2.7%; Fig. 2B). A mean of 4.5 units of FFP were transfused postoperatively, the largest mean number in the nine study centers in Germany (6.9 units) and the smallest in the one study site in Poland (1.7 units; Fig. 2B). A total of 2.4 percent of the transfused patients were given autologous FFP perioperatively.

**Transfusion practice for PLTs**

Overall, 16.7 percent (847) of patients received homologous and/or autologous PLT transfusion either intra- and/or postoperatively, with a mean of 6.9 units per transfused patient (Tables 2-5). Intraoperatively, 9.2 percent of all patients received PLT transfusion; the largest rate of PLT transfusion was in the one study center in Romania (50.5%), while no patients in the centers in Colombia, Hungary, Italy, and Poland received PLTs (Fig. 1C). A mean of 6.3 units of PLTs were transfused intraoperatively; the largest amount was given in the one study center in Israel (8.0 units; Fig. 1C). Postoperatively, 10.3 percent of the patients received PLTs, with the highest frequency in the one site in Mexico (39.0%), and the lowest in the one center in Colombia, where no PLTs were transfused postoperatively (Fig. 2C). A mean of 5.8 units of PLT were transfused postoperatively; the largest number was in the one study site in Hungary (9.0 units) and the smallest (0 units) in the one study site in Colombia (Fig. 2C). Overall, 0.2 percent of the patients received autologous PLTs.

**Interinstitutional variability of transfusion practice**

Besides the international variability in transfusion practice, there was also a marked variation in perioperative transfusion practice within and between each of the four nations with the highest number of patients enrolled (see box plots in Figs. 3 and 4). These widespread differences were observed for all blood products transfused in the United States, Germany, the United Kingdom, and Canada (data shown for intraoperative and postoperative period). Corresponding variability in perioperative transfusion rates was observed among the different centers in the United States, Germany, the United Kingdom, and Canada (Figs. 5 and 6). For all blood products, regional differences in transfusion practice were apparent. In some centers none of the patients received any blood product intraoperatively, whereas in the postoperative period nearly all patients were transfused.

**TABLE 3. Perioperative transfusion practice (frequency and amount) by country and transfusion product (first eight countries)\***

Blood component	US	G	UK	CA	IND	F	H	T
<i>Intraoperative transfusion</i>								
RBCs	712 (44.8)	504 (51.6)	151 (21.2)	98 (18.5)	151 (75.9)	13 (8.7)	21 (19.1)	110 (100)
Homo	659 (41.5)	494 (50.6)	143 (20.1)	87 (16.4)	83 (41.7)	12 (8.1)	20 (18.2)	110 (100)
Auto	65 (4.1)	11 (1.1)	8 (1.1)	11 (2.1)	71 (35.7)	1 (0.7)	1 (0.9)	6 (5.5)
RBC units	2.8 ± 2.0	3.1 ± 2.4	1.7 ± 0.9	1.9 ± 1.2	1.4 ± 0.7	2.3 ± 0.8	2.0 ± 0.6	2.7 ± 0.9
Homo	2.8 ± 2.0	3.1 ± 2.4	1.7 ± 0.9	1.9 ± 1.2	1.7 ± 0.7	2.3 ± 0.8	2.1 ± 0.6	2.7 ± 1.0
Auto	2.1 ± 1.2	1.9 ± 1.1	1.6 ± 1.1	1.5 ± 0.7	1.0 ± 0.1	2.0	1.0	1.2 ± 0.4
FFP	192 (12.1)	141 (14.4)	19 (2.7)	12 (2.3)	33 (16.6)	0	1 (0.9)	8 (7.3)
Homo	190 (12.0)	140 (14.3)	19 (2.7)	11 (2.1)	33 (16.6)	0	0	8 (7.3)
Auto	2 (0.1)	1 (0.1)	0	1 (0.2)	0	0	1 (0.9)	0
FFP units	3.6 ± 3.4	3.6 ± 2.2	1.8 ± 0.4	2.8 ± 1.1	2.0 ± 0.6	0	1.0	3.0 ± 1.1
Homo	3.6 ± 3.3	3.6 ± 2.2	1.8 ± 0.4	2.6 ± 1.1	2.0 ± 0.6	0	0	3.0 ± 1.1
Auto	8.5 ± 9.2	3.0	0	0	0	0	1.0	0
PLTs	258 (16.2)	58 (5.9)	12 (1.7)	7 (1.3)	28 (14.1)	2 (1.3)	0	15 (13.6)
Homo	252 (15.8)	58 (5.9)	12 (1.7)	7 (1.3)	28 (14.1)	2 (1.3)	0	15 (13.6)
Auto	6 (0.4)	0	0	0	0	0	0	0
PLT units	7.9 ± 7.3	4.7 ± 2.4	1.6 ± 2.1	5.0 ± 2.4	2.2 ± 1.0	2.0 ± 1.4	0	5.4 ± 3.4
Homo	7.8 ± 7.3	4.7 ± 2.4	1.6 ± 2.1	5.0 ± 2.4	2.2 ± 1.0	2.0 ± 1.4	0	5.4 ± 3.4
Auto	8.2 ± 2.9	0	0	0	0	0	0	0
<i>Postoperative transfusion†</i>								
RBCs	836 (52.6)	541 (55.5)	352 (49.5)	198 (37.2)	163 (81.9)	70 (47.0)	59 (53.6)	96 (87.3)
Homo	809 (50.9)	533 (54.7)	313 (44.0)	186 (35.0)	163 (81.9)	68 (45.6)	52 (47.3)	96 (87.3)
Auto	36 (2.3)	8 (0.8)	39 (5.5)	15 (2.8)	1 (0.5)	2 (1.3)	8 (7.3)	0
RBC units	3.0 ± 3.1	4.1 ± 6.4	2.3 ± 2.1	2.4 ± 2.0	2.4 ± 1.3	4.2 ± 5.4	2.7 ± 2.0	1.9 ± 1.4
Homo	3.0 ± 3.1	4.2 ± 6.5	2.4 ± 2.2	2.4 ± 2.0	2.4 ± 1.3	4.2 ± 5.5	2.7 ± 2.1	1.9 ± 1.4
Auto	1.8 ± 1.6	1.3 ± 0.5	1.9 ± 1.2	2.0 ± 1.5	1.0	2.0 ± 0	2.6 ± 0.5	0
FFP	237 (14.9)	249 (25.5)	106 (14.9)	52 (9.8)	50 (25.1)	8 (5.4)	24 (21.8)	3 (2.7)
Homo	234 (14.7)	246 (25.2)	98 (13.8)	48 (9.0)	50 (25.1)	8 (5.4)	19 (17.3)	3 (2.7)
Auto	3 (0.2)	3 (0.3)	8 (1.1)	4 (0.8)	0	0	5 (4.5)	0
FFP units	3.8 ± 3.5	6.9 ± 11.6	2.9 ± 2.0	3.6 ± 3.1	3.0 ± 1.8	5.6 ± 8.1	3.7 ± 1.6	2.0 ± 1.0
Homo	3.8 ± 3.5	7.0 ± 11.7	2.9 ± 2.1	3.8 ± 3.2	3.0 ± 1.8	5.6 ± 8.1	3.9 ± 1.8	2.0 ± 1.0
Auto	2.7 ± 0.6	5.0 ± 4.4	2.3 ± 0.7	1.8 ± 0.5	0	0	3.0 ± 0	0
PLTs	242 (15.2)	79 (8.1)	55 (7.7)	36 (6.8)	45 (22.6)	4 (2.7)	2 (1.8)	4 (3.6)
Homo	237 (14.9)	79 (8.1)	54 (7.6)	33 (6.2)	45 (22.6)	4 (2.7)	2 (1.8)	4 (3.6)
Auto	5 (0.3)	0	1 (0.1)	3 (0.6)	0	0	0	0
PLT units	6.4 ± 5.9	8.0 ± 10.2	2.4 ± 2.2	7.3 ± 3.7	2.4 ± 1.5	7.5 ± 5.4	9.0 ± 1.4	4.3 ± 2.2
Homo	6.4 ± 5.9	8.0 ± 10.2	2.4 ± 2.2	7.3 ± 3.8	2.4 ± 1.5	7.5 ± 5.4	9.0 ± 1.4	4.3 ± 2.2
Auto	3.6 ± 2.6	0	1.0	6.3 ± 2.3	0	0	0	0

\* All data are described as either mean ± 1 SD or number (%). Number of units is given per transfused patients only.

† Postoperative is from ICU admission to ICU discharge. US = United States; G = Germany; UK = United Kingdom; CA = Canada; IND = India; F = France; H = Hungary; T = Thailand; CO = Colombia; R = Romania; A = Austria; N = Netherlands; I = Italy; IS = Israel; M = Mexico; P = Poland (order of countries by decreasing number of patients enrolled in the study). Auto = autologous;

Homo = homologous; RBCs = RBCs and/or whole blood. p Value: significant difference between countries. Note that total of homologous and autologous blood products is not always identical with total number of blood product because of overlaps. There are significant differences between the countries in RBC, FFP, and PLT use intra- and postoperatively (p < 0.0001).

### Transfusion practice by types of surgery and priority of surgery

Intraoperatively, patients with valve and combined procedures received all blood products significantly more often and in greater amounts than patients with isolated CABG surgery (Table 6). Although there was a tendency for all blood products to be administered more frequently intraoperatively in urgent and emergent surgeries, these differences did not reach significant levels, except for RBCs (p = 0.04; Table 7).

## DISCUSSION

Our study comprehensively demonstrates among multiple centers in different countries that there exists con-

siderable and disturbing variability in perioperative transfusion practices for RBCs, FFP, and PLTs in patients undergoing the procedure of cardiac surgery. This enormous range may be attributed partially to a subjectively based instead of an evidence-based practice and may indicate unnecessary transfusion. Variation in perioperative transfusion practice patterns, however, may also be influenced by differences in patient population among the study centers, including comorbidities as well as other patient-related factors such as age, body size,<sup>7</sup> or preoperative anemia.<sup>10,23,24</sup> Moreover, preoperative medication with anti-PLT agents and anticoagulants as well as preoperative transfusion of blood products may impact intra- and postoperative transfusion needs.<sup>25,26</sup> Additionally, there are several surgical, procedure-related factors, that

**TABLE 4. Perioperative transfusion practice (frequency and amount) by country and transfusion product (last eight countries)\***

Blood component	CO	R	A	N	I	IS	M	P
<i>Intraoperative transfusion</i>								
RBCs	29 (27.4)	55 (54.5)	60 (60.0)	38 (38.4)	26 (26.8)	40 (42.6)	57 (96.6)	26 (89.9)
Homo	24 (22.6)	55 (54.5)	56 (56.0)	34 (34.3)	25 (25.8)	38 (40.4)	56 (94.9)	10 (34.5)
Auto	5 (4.7)	0	5 (5.0)	4 (4.0)	1 (1.0)	2 (2.1)	1 (1.7)	22 (75.9)
RBC units	1.6 ± 0.6	2.5 ± 1.3	2.3 ± 1.5	1.8 ± 1.4	2.4 ± 1.0	1.8 ± 1.4	2.3 ± 1.1	1.3 ± 0.5
Homo	1.6 ± 0.6	2.5 ± 1.3	2.4 ± 1.6	1.9 ± 1.4	2.4 ± 1.0	1.8 ± 1.4	2.3 ± 1.1	1.1 ± 0.3
Auto	1.4 ± 0.5	0	1.6 ± 0.5	1.3 ± 0.5	4.0	1.5 ± 0.7	2.0	1.0 ± 0.2
FFP	7 (6.6)	42 (41.6)	4 (4.0)	3 (3.0)	3 (3.1)	5 (5.3)	58 (98.3)	23 (79.3)
Homo	7 (6.6)	42 (41.6)	2 (2.0)	3 (3.0)	3 (3.1)	5 (5.3)	58 (98.3)	4 (13.8)
Auto	0	0	2 (2.0)	0	0	0	0	19 (65.5)
FFP units	2.3 ± 1.0	2.6 ± 1.6	2.5 ± 2.4	2.3 ± 1.5	4.7 ± 1.2	2.0 ± 0.0	2.7 ± 1.1	1.0 ± 0.0
Homo	2.3 ± 1.0	2.6 ± 1.6	2.5 ± 2.1	2.3 ± 1.5	4.7 ± 1.2	2.0 ± 0.0	2.7 ± 1.1	1.0 ± 0.0
Auto	0	0	5.0	0	0	0	0	1.0 ± 0.0
PLTs	0	51 (50.5)	5 (5.0)	2 (2.0)	0	2 (2.1)	27 (45.8)	0
Homo	0	51 (50.5)	5 (5.0)	2 (2.0)	0	2 (2.1)	27 (45.8)	0
Auto	0	0	0	0	0	0	0	0
PLT units	0	4.5 ± 1.5	1.4 ± 0.5	1.0 ± 0.0	0	8.0 ± 2.8	6.3 ± 4.6	0
Homo	0	4.5 ± 1.5	1.4 ± 0.5	1.0 ± 0.0	0	8.0 ± 2.8	6.5 ± 4.5	0
Auto	0	0	0	0	0	0	0	0
<i>Postoperative transfusion†</i>								
RBCs	72 (67.9)	49 (48.5)	75 (75.0)	66 (66.7)	24 (24.7)	62 (66.0)	50 (84.7)	24 (77.4)
Homo	67 (63.2)	49 (48.5)	72 (72.0)	62 (62.6)	23 (23.7)	62 (66.0)	50 (84.7)	23 (74.2)
Auto	5 (4.7)	0	3 (3.0)	5 (5.1)	1 (1.0)	0	0	2 (6.5)
RBC units	2.2 ± 1.2	3.8 ± 4.2	3.1 ± 4.0	2.6 ± 3.5	2.9 ± 2.2	2.4 ± 1.6	3.1 ± 3.1	2.9 ± 2.3
Homo	2.2 ± 1.2	3.8 ± 4.2	3.2 ± 4.1	2.6 ± 3.6	3.0 ± 2.2	2.4 ± 1.6	3.1 ± 3.1	2.9 ± 2.3
Auto	1.8 ± 0.4	0	2.0 ± 0	2.2 ± 1.6	1.0	0	0	1.0 ± 0.0
FFP	11 (10.4)	18 (17.8)	7 (7.0)	4 (4.0)	8 (8.2)	18 (19.1)	56 (94.9)	9 (29.0)
Homo	10 (9.4)	18 (17.8)	4 (4.0)	4 (4.0)	8 (8.2)	18 (19.1)	56 (94.9)	9 (29.0)
Auto	1 (0.9)	0	3 (3.0)	0	0	0	0	0
FFP units	3.0 ± 1.8	5.4 ± 6.1	4.7 ± 2.8	1.8 ± 1.0	3.9 ± 3.1	2.5 ± 1.6	3.6 ± 2.3	1.7 ± 0.9
Homo	3.2 ± 1.8	5.4 ± 6.1	6.5 ± 2.4	1.8 ± 1.0	3.9 ± 3.1	2.5 ± 1.6	3.6 ± 2.3	1.7 ± 0.9
Auto	1.0	0	2.3 ± 0.6	0	0	0	0	0
PLTs	0	6 (5.9)	6 (6.0)	4 (4.0)	5 (5.2)	9 (9.6)	23 (39.0)	2 (6.5)
Homo	0	6 (5.9)	6 (6.0)	3 (3.0)	5 (5.2)	9 (9.6)	23 (39.0)	2 (6.5)
Auto	0	0	0	1 (1.0)	0	0	0	0
PLT units	0	3.3 ± 2.1	2.0 ± 1.3	2.0 ± 2.0	7.0 ± 1.2	5.3 ± 1.7	6.5 ± 4.5	1.0 ± 0.0
Homo	0	3.3 ± 2.1	2.0 ± 1.3	2.3 ± 2.3	7.0 ± 1.2	5.3 ± 1.7	6.5 ± 4.5	1.0 ± 0.0
Auto	0	0	0	1.0	0	0	0	0

\* All data are described as either mean ± 1 SD or number (%). Number of units is given per transfused patients only.

† Postoperative is from ICU admission to ICU discharge. US = United States; G = Germany; UK = United Kingdom; CA = Canada; IND = India; F = France; H = Hungary; T = Thailand; CO = Colombia; R = Romania; A = Austria; N = Netherlands; I = Italy; IS = Israel; M = Mexico; P = Poland (order of countries by decreasing number of patients enrolled in the study). Auto = autologous;

Homo = homologous; RBCs = RBCs and/or whole blood. p Value: significant difference between countries. Note that total of homologous and autologous blood products is not always identical with total number of blood product because of overlaps. There are significant differences between the countries in RBC, FFP, and PLT use intra- and postoperatively ( $p < 0.0001$ ).

is, cardiopulmonary bypass duration, urgency and type of surgery or redo surgery, and most importantly, intra- and postoperative blood loss, that trigger perioperative blood transfusion.<sup>27</sup> The extent of blood loss depends for the most part on surgical skill. The use of cell-saver devices and other blood conservation strategies, however, as well as the use of antifibrinolytics are also relevant factors.<sup>23,25,26,28</sup> Low priming volumes of the extracorporeal circulation and restrictive fluid management can prevent extensive hemodilution, which may be a cause for transfusion of blood products.<sup>27</sup> The transfusion thresholds, that is, the specific cutoff points of laboratory values that indicate the necessity for the transfusion of blood products to the treating physician, are crucial and may vary

between centers as well as between individual surgeons and anesthesiologists.<sup>8,9,21,29</sup>

Specifically, the transfusion of RBCs to prevent or correct organ ischemia has been the subject of numerous publications and discussions.<sup>13,30-32</sup> It had been believed that a uniform "transfusion trigger" such as an absolute hemoglobin (Hb) value of 10 g per dL or a hematocrit (Hct) level of 30 percent provided an appropriate basis for determining the need for perioperative RBC transfusion.<sup>18</sup> Other transfusion guidelines suggested that in healthy young patients, RBC transfusion is rarely indicated when the Hb concentration is greater than 10 g per dL and almost always indicated when it is less than 6 g per dL.<sup>33</sup> Transfusion for intermediate Hb concentrations

**TABLE 5. Total perioperative transfusion practice (frequency and amount) by transfusion product\***

Blood component	Intraoperative transfusion (total)	Postoperative transfusion† (total)
RBCs	2091 (41.3)	2737 (54.0)
Homo	1906 (37.7)	2628 (51.9)
Auto	214 (4.2)	125 (2.5)
RBC units	2.4 ± 1.9	3.0 ± 3.9
Homo	2.5 ± 2.0	3.0 ± 3.9
Auto	1.5 ± 0.9	1.9 ± 1.3
FFP	551 (10.9)	860 (17.0)
Homo	525 (10.4)	833 (16.5)
Auto	26 (0.5)	27 (0.5)
FFP units	3.1 ± 2.5	4.5 ± 6.9
Homo	3.2 ± 2.5	4.6 ± 7.0
Auto	2.0 ± 2.9	2.6 ± 1.6
PLTs	467 (9.2)	522 (10.3)
Homo	461 (9.1)	512 (10.1)
Auto	6.0 (0.1)	10 (0.2)
PLT units	6.3 ± 6.0	5.8 ± 6.2
Homo	6.3 ± 6.0	5.8 ± 6.3
Auto	8.2 ± 2.9	3.9 ± 2.8

\* All data are described as either mean ± 1 SD or number (%). Number of units is given per transfused patients only.  
 † Postoperative is from ICU admission to ICU discharge.  
 US = United States; G = Germany; UK = United Kingdom; CA = Canada; IND = India; F = France; H = Hungary; T = Thailand; CO = Colombia; R = Romania; A = Austria; N = Netherlands; I = Italy; IS = Israel; M = Mexico; P = Poland (order of countries by decreasing number of patients enrolled in the study). Auto = autologous; Homo = homologous; RBCs = RBCs and/or whole blood. p Value: significant difference between countries. Note that total of homologous and autologous blood products is not always identical with total number of blood product because of overlaps. There are significant differences between the countries in RBC, FFP, and PLT use intra- and postoperatively (p < 0.0001).

(6-10 g/dL) is only recommended when evidence of ischemia is present. Therefore, in coronary surgery, maintenance of Hb levels in the upper range may be warranted by the patient's individual status and the operative course. Several studies sought to identify predictors, especially in cardiac surgery, for perioperative RBC transfusion, such as anemia (preoperative Hb < 12 g/dL), emergency procedures, reoperation, complex surgery (valve replacement, on-pump procedures), age, female sex, low body mass index, prior anti-PLT therapy, excessive fluid administration, or chronic obstructive pulmonary disease.<sup>10,11,24,26,28,31,32,34-37</sup> In our study, however, the frequency of RBC transfusion varied more than 12-fold intraoperatively and 4-fold postoperatively among the 16 reporting countries. Although there may have been differences in the patients' risk profiles, the course of cardiac surgery, and bleeding rates, the extreme international inconsistency in transfusion practice strongly suggests that the wide range in RBC transfusion is due, at least partially, to institutional-based protocols and, thus, could reflect a lack of compliance with the established guidelines.<sup>7,8</sup>

Similarly, in our study, the perioperative transfusion practice for FFP was highly variable. Intraoperatively, the frequency of use of FFP varied from 0 to 98 percent and postoperatively from 3 to 95 percent among the 16 nations. Most guidelines, however, conclude that the administration of FFP is only indicated for urgent reversal of warfarin therapy, correction of coagulation factor deficiencies, or control of microvascular bleeding when the

**TABLE 6. Intraoperative transfusion practice: types of surgery\***

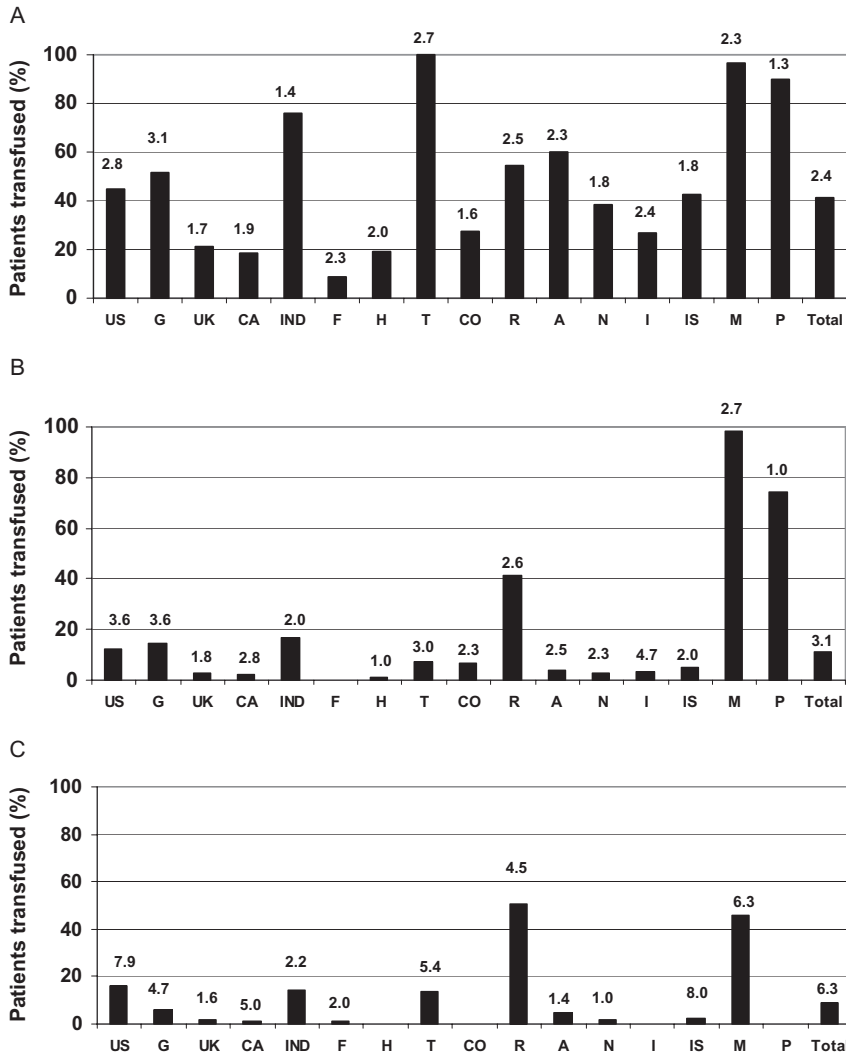
Variable	CABG only (n = 4302)	CABG with valve (n = 507)	CABG and combined procedures (n = 256)	Total (n = 5065)	p Values for units	p Values for frequencies
RBCs	2.3 ± 1.6 (38.3)	3.2 ± 2.3 (57.4)	3.3 ± 2.4 (60.5)	2.5 ± 1.9 (41.3)	<0.0001	<0.0001
FFP	2.8 ± 2.0 (8.7)	3.6 ± 2.9 (22.5)	3.8 ± 3.6 (24.6)	3.1 ± 2.5 (10.9)	0.0007	<0.0001
PLTs	5.5 ± 4.8 (7.1)	7.3 ± 6.2 (21.1)	8.4 ± 9.8 (20.7)	6.3 ± 6.0 (9.2)	0.0002	<0.0001

\* All data are described as either mean ± 1 SD or frequency of the given blood product (%). Number of units is given per transfused patients only. The first p values refer to the differences in number of units; the second to the differences in the frequencies. RBCs = RBCs and/or whole blood.

**TABLE 7. Intraoperative transfusion practice: priority of surgery\***

Variable	Elective (n = 4113)	Urgent (n = 891)	Emergent (n = 61)	Total (n = 5065)	p Values for units	p Values for frequencies
RBCs	2.3 ± 1.6 (41.6%)	3.2 ± 2.3 (38.8%)	3.3 ± 2.4 (54.1%)	2.5 ± 1.9 (41.3%)	0.7796	0.0424
FFP	3.1 ± 2.5 (11.0%)	3.4 ± 2.6 (9.9%)	2.6 ± 1.5 (14.8%)	3.1 ± 2.5 (10.9%)	0.1853	0.3828
PLTs	6.4 ± 6.2 (9.3%)	5.9 ± 5.3 (8.4%)	4.5 ± 3.5 (13.1%)	6.3 ± 6.0 (9.2%)	0.3007	0.4040

\* All data are described as either mean ± 1 SD or frequency of the given blood product (%). Number of units is given per transfused patients only. The first p values refer to the differences in number of units, and the second to the differences in the frequencies. RBCs = RBCs and/or whole blood.



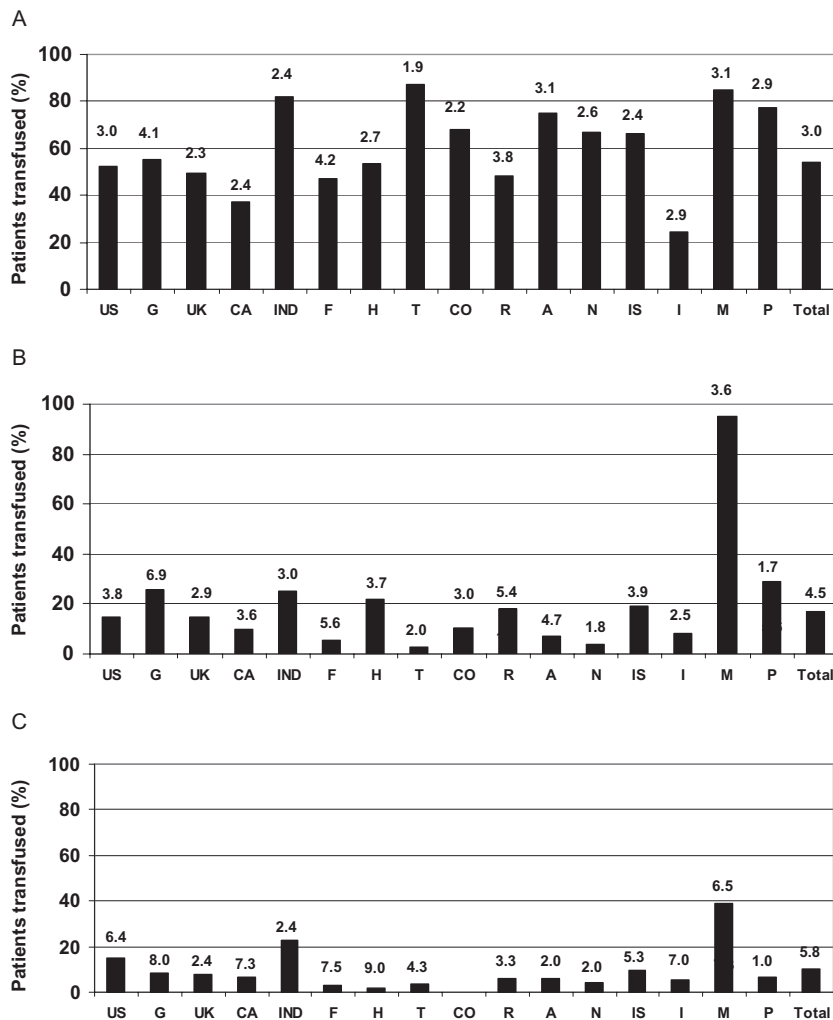
**Fig. 1. Frequency and amount of intraoperative homologous and autologous RBC (A), FFP (B), and PLT (C) transfusion. Percentage transfused and mean number of units per transfused patient (number above columns) for each country and overall total (all 5065 study patients). T = Thailand; M = Mexico; P = Poland; IND = India; A = Austria; R = Romania; G = Germany; US = United States; IS = Israel; N = Netherlands; CO = Colombia; I = Italy; UK = United Kingdom; H = Hungary; CA = Canada; F = France (order based on decreasing number of study centers per country). RBCs = RBCs and/or whole blood.**

prothrombin and/or partial thromboplastin times are more than 1.5 times normal.<sup>38</sup> Although some studies have identified factors that potentially trigger transfusion of FFP during CABG surgery<sup>31,32,39</sup> such as extracorporeal circulation with resultant consumption of coagulation factors, previous heart surgery, decreased ejection fraction, sex, and high dose of transfused RBCs, an overuse of FFP has been repeatedly reported.<sup>37,40,41</sup> Therefore, the wide range of frequency and volume of FFP transfusion observed in our study probably indicate a lack of application of the established guidelines. We assume that in study centers in some countries (e.g., Mexico, Poland, and Romania), FFP

might have been used for augmentation of plasma volume or albumin concentration, while the low frequency of FFP transfusion in study centers in other countries (e.g., Colombia) could reflect limited availability of the product.

Most guidelines agree that the use of PLT is only required if the PLT count is less than  $50 \times 10^9$  per L or in the case of clinically significant PLT dysfunction.<sup>38,42</sup> The frequency of PLT transfusion in our cohort varied intraoperatively from 0 to 51 percent by country, and postoperatively from 0 to 39 percent. Similar regional differences in PLT transfusion algorithms have been reported previously.<sup>43</sup> These observations might be due to various transfusion triggers such as a preoperative low PLT count<sup>23</sup> or prior use of PLT aggregation inhibitors. Although the use of extracorporeal circulation may additionally consume PLTs, it has been stated that numerous PLT transfusions are not necessarily therapeutic in the presence of excessive bleeding, but rather prophylactic to prevent bleeding events.<sup>29,39</sup> It has been reported that PLT transfusion is associated with infections, vasopressor and respiratory medication use, stroke, and death in patients undergoing CABG surgery.<sup>44</sup> Thus, the increased risk for serious adverse events after PLT transfusion underlines the importance of the correct use of this blood product, following published guidelines.

We also observed that all transfusion components were administered more frequently and in greater amounts to patients with valve and/or combined procedures than in isolated CABG surgery, findings consistent with Moskowitz and colleagues,<sup>12</sup> who reported that the type of surgery is a primary determinant for use of RBCs. Regarding urgency for surgery, only a few studies have suggested an association.<sup>12,28</sup> In the current investigation, no significant differences were observed in the perioperative administration of blood products in elective, urgent, or emergent surgery (except for RBCs), although there was a tendency for emergent patients to receive more blood products. The latter observation may be explained by factors such as reintervention due to hemorrhage, complex procedures, or the patient's risk profile. Importantly, an analysis of the EuroSCOREs of the countries with



**Fig. 2. Frequency and amount of postoperative homologous and autologous RBC (A), FFP (B), and PLT (C) transfusion. Percentage transfused and mean number of units per transfused patient (number above columns) for each country and overall total (all 5065 study patients). T = Thailand; M = Mexico; P = Poland; IND = India; A = Austria; R = Romania; G = Germany; US = United States; IS = Israel; N = Netherlands; CO = Colombia; I = Italy; UK = United Kingdom; H = Hungary; CA = Canada; F = France (order based on decreasing number of study centers per country). RBCs = RBCs and/or whole blood.**

the highest and lowest frequencies of use or amounts of each type of blood product transfused failed to demonstrate a correlation between EuroSCOREs and maximum versus minimum frequency of use or amount of blood product administered (data not shown).

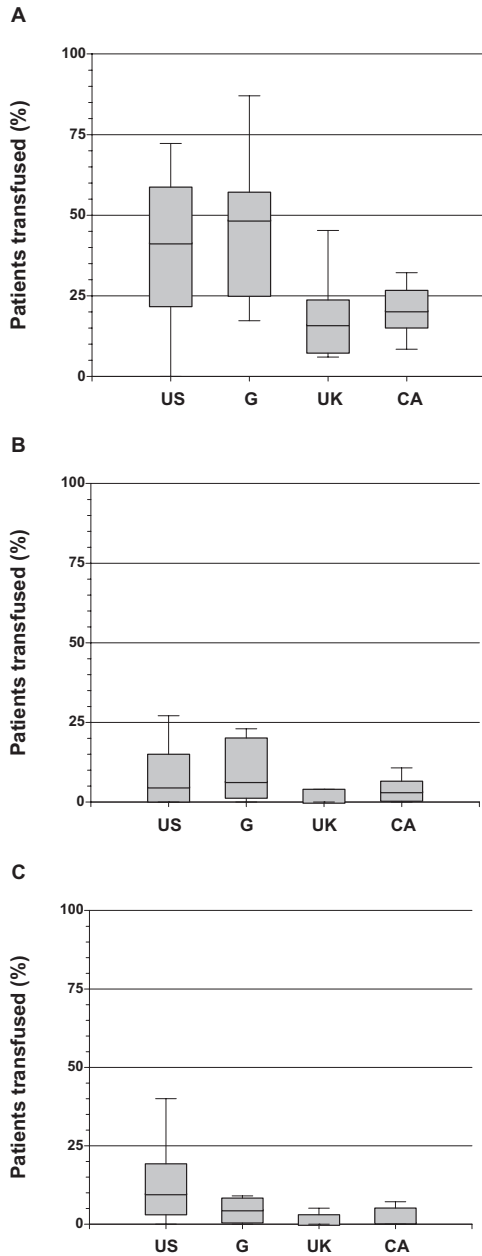
Overall, the results of our study indicate that marked variations in perioperative practice patterns exist, both regionally and internationally. Thus, it appears that transfusion guidelines are not uniformly applied and that informal institutional-specific standards, local conditions (e.g., availability of blood products, national medical standards), and individual physicians continue to drive transfusion practice.<sup>2,3,7,8,15,18,19,30,37</sup> Unfortunately, despite

critical commentary regarding blood transfusion<sup>32,45,46</sup> as well as continuing education efforts by medical societies, the marked variability in transfusion practice has not changed during the past decades. One decade ago, our study group emphasized the problem in US centers, observing a median transfusion rate in the United States of 50 percent for RBCs, 6 percent for FFP, and 9 percent for PLTs in low-risk CABG patients,<sup>3</sup> while in our current study (including low- and high-risk patients) 70 percent of the patients received RBCs, 22 percent FFP, and 16 percent PLTs (Table 2). Similar data were reported by the Sanguis study of patients undergoing CABG surgery, performed in 43 hospitals in 10 European countries; in these countries, the perioperative transfusion rate was 88 percent for RBCs, 39 percent for FFP, and 8 percent for PLTs.<sup>20</sup>

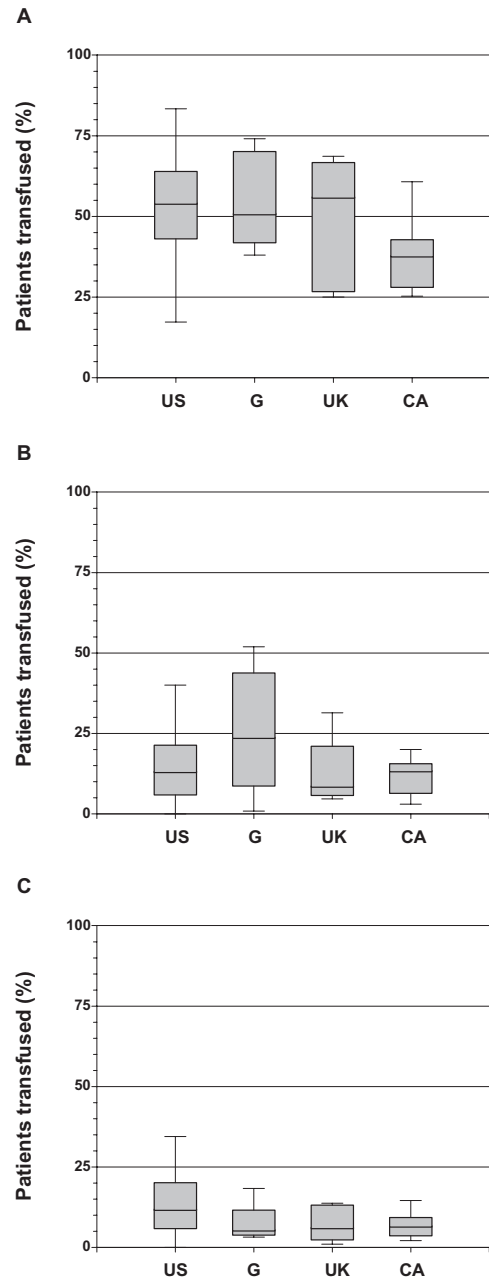
The excessive use of blood components not only results in unnecessarily increased costs<sup>5,6,47</sup> but also exposes patients to enhanced perioperative risks due to transmission of infectious diseases, volume overload, transfusion-related acute reactions, immunomodulation, pneumonia, and transfusion-related acute lung injury.<sup>6,33,48-55</sup> In recent studies, associations between the number of RBCs transfused and longer intensive care unit (ICU) and hospital stay, as well as increased mortality, have been described.<sup>55,56</sup> A study by Vincent and coworkers<sup>57</sup> further confirmed that ICU and overall mortality rates were higher in critically ill patients who had received RBC transfusion. Similarly, Spiess and colleagues<sup>58</sup> reported that high Hct

values ( $\geq 34\%$ ) on ICU entry are associated with an increased rate of myocardial infarction. Moreover, there is a dose-response relationship between the amount of FFP or PLT administered and exposure to transfusion-related morbid risks,<sup>31,32,37,53,59,60</sup> as well as increased subsequent mortality.<sup>41</sup>

A limitation of this study was that no specific laboratory tests were evaluated in regard to transfusion, for example, the prothrombin, partial thromboplastin time, or Hb level, which made it impossible to directly compare the transfusion of each individual with the guidelines. Thus, the indications for the transfusion of the respective blood product could not be evaluated in individual



**Fig. 3.** Interinstitution variability of intraoperative homologous and autologous RBC (A), FFP (B), and PLT (C) transfusion rates for the four most-patient-enrolling countries. US = United States; G = Germany; UK = United Kingdom; CA = Canada (order based on decreasing number of study centers per country). RBCs = RBCs and/or whole blood. The bottom and top of the box are the 25th and 75th percentiles. The length of the box is the interquartile range (IQR), representing the middle 50 percent of the data; the line through the middle of the box is the median (the 50th percentile). The upper bar is the largest observation that is less than or equal to the 75th percentile plus 1.5 times IQR; the lower bar is the smallest observation that is greater than or equal to the 25th percentile minus 1.5 times IQR.



**Fig. 4.** Interinstitution variety of postoperative homologous and autologous RBC (A), FFP (B), and PLT (C) transfusion rates for the four most-patient-enrolling countries. US = United States; G = Germany; UK = United Kingdom; CA = Canada (order based on decreasing number of study centers per country). RBCs = RBCs and/or whole blood. The bottom and top of the box are the 25th and 75th percentiles. The length of the box is the interquartile range (IQR), representing the middle 50 percent of the data; the line through the middle of the box is the median (the 50th percentile). The upper bar is the largest observation that is less than or equal to the 75th percentile plus 1.5 times IQR; the lower bar is the smallest observation that is greater than or equal to the 25th percentile minus 1.5 times IQR.



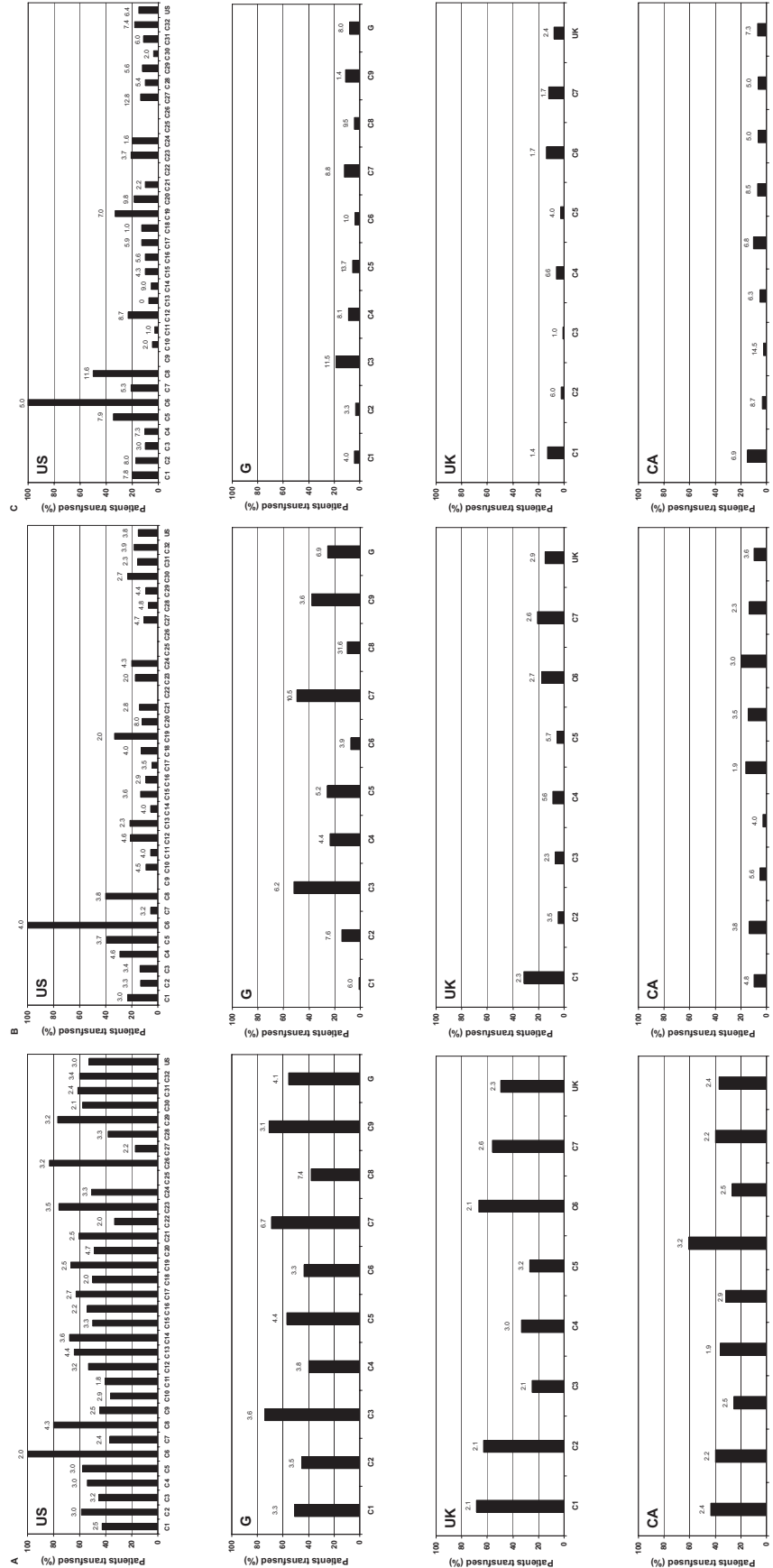


Fig. 6. Frequency and amount of postoperative homologous and autologous RBC (A), FFP (B), and PLT (C) transfusion for the centers in the United States (US), Germany (G), the United Kingdom (UK), and Canada (CA). Percentage transfused and mean number of units per transfused patient (number above columns) for each center (C) and all centers per country (last column). RBCs = RBCs and/or whole blood.

patients. Additionally, a number of factors that influence perioperative blood transfusion, that is, preoperative medication with anti-PLT agents and anticoagulants, previous transfusion, intraoperative blood loss, the use of antifibrinolytics and intraoperative fluid management, or specific blood conservation strategies were not specifically evaluated.<sup>61</sup> Since the aim of this observational study was a description of transfusion practice in cardiac surgery, a specific multivariate analysis was not performed to further determine the impact of a specific center and/or country on transfusion practice. Furthermore, the number of study centers was different among the participating countries with a resultant disparity in numbers of patients per country (Table 1). Almost 75 percent of the participating countries had only one or two study centers. Thus, it is not clear if these study sites were representative of the transfusion practice in the respective country. Additionally, there were differences in demographic data, some of which may have been relevant for transfusion practice. Parameters such as preoperative Hct levels, however, were within the normal range and demonstrated no clinically relevant differences.

In conclusion, this study demonstrated that a marked variability in the perioperative use of RBCs, FFP, and PLTs persists on a national as well as international basis, resulting from varying practice patterns that probably reflect misuse and/or overuse of these blood products in cardiac surgical patients. Owing to their cost, the limited availability, and the potentially harmful effects of the perioperative administration of blood products, their appropriate utilization, based on established transfusion guidelines, is essential. Continued reevaluation of local perioperative practice patterns, including transfusion algorithms, seems necessary. Importantly, increasing appropriate institutional regulation of blood usage and standardized multidisciplinary transfusion strategies would markedly reduce inappropriate exposure of cardiac surgical patients to blood products.

## APPENDIX 1

The Ischemia Research and Education Foundation (IREF) is an independent nonprofit foundation, formed in 1987, which develops clinical investigators via observational studies and clinical trials addressing ischemic injury of the heart, brain, kidney, and gastrointestinal tract. IREF provided all funding for execution of the study, collection of the data, and analysis and publication of the findings. The Multicenter Study of Perioperative Ischemia (MCSPI) Research Group, formed in 1988, is an association of 160 international medical centers located in 23 countries, organized through, and supported by grants from, IREF. *The following institutions and persons coordinated the MCSPI EPI II study*

Study Chairman—D. Mangano; Senior Editors—J. Levin, L. Saidman; Study Design and Analysis Center: Ischemia Research and Education Foundation—P. Barash, C. Dietzel, A. Herskowitz, Y. Miao; Editorial/Administrative Group—D. Beatty, I. Lei, B. Xavier.

*The following institutions and persons participated in the MCSPI EPI II Study.*

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#### REFERENCES

- Mangano D. Perioperative cardiac morbidity. *Anesthesiology* 1990;72:153-84.
- Stover EP, Siegel LC, Body SC, Levin J, Parks R, Maddi R, D'Ambra MN, Mangano DT, Spiess BD. Institutional variability in red blood cell conservation practices for coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 2000;14:171-6.
- Stover EP, Siegel LC, Parks R, Levin J, Body SC, Maddi R, D'Ambra MN, Mangano DT, Spiess BD. Variability in transfusion practice for coronary artery bypass surgery persists despite national consensus guidelines: a 24-institution study. *Anesthesiology* 1998;88:327-33.
- Nalysnyk L, Fahrbach K, Reynolds M, Zhao S, Ross S. Adverse events in coronary artery bypass graft (CABG) trials: a systematic review and analysis. *Heart* 2003;89:767-72.
- Glennard AH, Persson U, Söderman C. Costs associated with blood transfusions in Sweden—the societal cost of autologous, allogeneic and perioperative RBC transfusion. *Transfus Med* 2005;15:295-306.
- Amin M, Fergusson D, Aziz A, Wilson K, Coyle D, Hébert P. The cost of allogeneic red blood cells—a systematic review. *Transfus Med* 2003;13:275-85.
- Ferraris VA, Ferraris SP, Saha SP, Hessel EA II, Haan CK, Royston BD, Bridges CR, Higgins RS, Despotis G, Brown JR; Society of Thoracic Surgeons Blood Conservation Guideline Task Force; Spiess BD, Shore-Lesserson L, Stafford-Smith M, Mazer CD, Bennett-Gerrero E, Hill SE, Body S; Society of Cardiovascular Anesthesiologists Special Task Force on Blood Transfusion. Perioperative blood transfusion and blood conservation in cardiac surgery. *Ann Thorac Surg* 2007;83:S27-86.
- Van der Linden P, Dierick A. Blood conservation strategies in cardiac surgery. *Vox Sang* 2007;92:103-12.
- Murphy GJ, Angelini GD. Indications for blood transfusion in cardiac surgery. *Ann Thorac Surg* 2006;82:2323-34.
- Kulier A, Levin J, Moser R, Rumpold-Seitlinger G, Tudor IC, Snyder-Ramos SA, Moehnle P, Mangano DT; Investigators of the Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation. Impact of preoperative anemia on outcome in patients undergoing coronary artery bypass graft surgery. *Circulation* 2007;116:471-9.
- Khanna M, Herbert P, Fergusson D. Review of the clinical practice literature on patients' characteristics associated with perioperative allogeneic red blood cell transfusion. *Transfus Med Rev* 2003;17:110-9.
- Moskowitz DM, Klein JJ, Shander A, Cousineau KM, Goldweit RS, Bodian C, Perelman SI, Kang H, Fink DA, Rothman HC, Ergin MA. Predictors of transfusion requirements for cardiac surgical procedures at a blood conservation center. *Ann Thorac Surg* 2004;77:626-34.
- Scott BH, Seifert FC, Glass PS, Grimson R. Blood use in patients undergoing coronary artery bypass surgery: impact of cardiopulmonary bypass pump, hematocrit, gender, age, and body weight. *Anesth Analg* 2003;97:958-63.
- American Society of Anesthesiologists Practice Guidelines for Perioperative Transfusion. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. *Anesthesiology* 2006;105:198-208.
- Goodnough L, Despotis G, Hogue CJ, Ferguson TJ. On the need for improved transfusion indicators in cardiac surgery. *Ann Thorac Surg* 1995;60:473-80.
- Consensus Conference. Fresh-frozen plasma. Indications and risks. *JAMA* 1985;253:551-3.
- Consensus Conference. Platelet transfusion therapy. *JAMA* 1987;257:1777-80.
- Consensus Conference. Perioperative red blood cell transfusion. *JAMA* 1988;260:2700-3.
- Sazama K, DeChristopher PJ, Dodd R, Harrison CR, Shulman IA, Cooper ES, Labotka RJ, Oberman HA, Zahn CM, Greenburg AG, Stehling L, Lauenstein KJ, Price TH,

- Williams LK. Practice parameter for the recognition, management, and prevention of adverse consequences of blood transfusion. College of American Pathologists. Arch Pathol Lab Med 2000;124:61-70.
20. Sirchia G, Giovanetti AM, McClelland DB, Fracchia GN, editors. Safe and Good Use of Blood in Surgery (SANGUIS) use of blood products and artificial colloids in 43 European hospitals. Luxembourg: European Commission; 1994. p. 139-47.
  21. Karkouti K, Yau TM, Rensburg A, McCluskey SA, Callum J, Wijeyesundera DN, Beattie WS. The effects of a treatment protocol for cardiac surgical patients with excessive blood loss on clinical outcomes. Vox Sang 2006;91:148-56.
  22. DeAnda A Jr, Baker KM, Roseff SD, Green JA, McCarthy H, Aron T, Spiess BD. Developing a blood conservation program in cardiac surgery. Am J Med Qual 2006;21:230-7.
  23. Karkouti K, O'Farrell R, Yau TM, Beattie WS; Reducing Bleeding in Cardiac Surgery Research Group. Prediction of massive blood transfusion in cardiac surgery. Can J Anaesth 2006;53:781-94.
  24. Slight RD, Bappu NJ, Nzewi OC, Lee RJ, McClelland DB, Mankad PS. Factors predicting loss and gain of red cell volume in cardiac surgery patients. Transfus Med 2006;16:169-75.
  25. Brown JR, Birkmeyer NJ, O'Connor GT. Meta-analysis comparing the effectiveness and adverse outcome of anti-fibrinolytic agents in cardiac surgery. Circulation 2007;115:2801-13.
  26. Picker SM, Kaleta T, Hekmat K, Kampe S, Gathof BS. Anti-platelet therapy preceding coronary artery surgery: implications for bleeding, transfusion requirements and outcome. Eur J Anaesthesiol 2007;24:332-9.
  27. Slight RD, Bappu NJ, Nzewi OC, McClelland DB, Mankad PS. Perioperative red cell, plasma, and blood volume change in patients undergoing cardiac surgery. Transfusion 2006;46:392-7.
  28. Niranjana G, Asimakopoulos G, Karagounis A, Cockerill G, Thompson M, Chandrasekaran V. Effects of cell saver autologous blood transfusion on blood loss and homologous blood transfusion requirements in patients undergoing cardiac surgery on- versus off-cardiopulmonary bypass: a randomised trial. Eur J Cardiothorac Surg 2006;30:271-7.
  29. Arnold DM, Crowther MA, Cook RJ, Sigouin C, Heddle NM, Molnar L, Cook DJ. Utilization of platelet transfusions in intensive care unit: indications, transfusion triggers, and platelet count response. Transfusion 2006;46:1286-91.
  30. Dietrich W, Luth JU, Kormann J, Wick S, Kaiser W, Eberle B, Karliczek F, Junger A, Gille A, Schwerdt M, Eleftheriadis S, Jaschik M. Intraoperative blood requirements and allogeneic blood transfusion in cardioanesthesia. Data analysis of 7729 patients in 12 cardiac surgical clinics. Anaesthesist 1999;48:876-83.
  31. Covin R, O'Brien M, Grunwald G, Brimhall B, Sethi G, Walczak S, Reiquam W, Rajagopalan C, Shroyer AL. Factors affecting transfusion of fresh frozen plasma, platelets, and red blood cells during elective coronary artery bypass graft surgery. Arch Pathol Lab Med 2003;127:415-23.
  32. Surgenor DM, Churchill WH, Wallace EL, Rizzo RJ, Chapman RH, McGurk S, Bertholf MF, Goodnough LT, Kao KJ, Koerner TA, Olson JD, Woodson RD. Determinants of red cell, platelet, plasma and cryoprecipitate transfusions during coronary artery bypass graft surgery: the Collaborative Hospital Transfusion Study. Transfusion 1996;36:521-32.
  33. Crosby E. Perioperative haemotherapy. I. Indications for blood component transfusion. Can J Anaesth 1992;39:695-707.
  34. Ouattara A, Niculescu M, Boccara G, Landi M, Vaissier E, Leger P, Riou B, Gandjbakch I, Coriat P. Identification of risk factors for allogeneic transfusion in cardiac surgery from an observational study. Ann Fr Anesth Reanim 2003;22:278-83.
  35. Parr KG, Patel MA, Dekker R, Levin R, Glynn R, Avorn J, Morse DS. Multivariate prediction of stored blood product use in cardiac surgery. J Cardiothorac Vasc Anesth 2003;17:176-81.
  36. Shevde K, Pagala M, Kashikar A, Tyagaraj C, Shahbaz N, Iqbal M, Idupuganti R. Gender is an essential determinant of blood transfusion in patients undergoing coronary artery bypass graft procedure. J Clin Anesth 2000;12:109-16.
  37. Despotis G, Grishaber J, Goodnough L. The effect of an intraoperative treatment algorithm on physicians' transfusion practice in cardiac surgery. Transfusion 1994;34:290-6.
  38. Crosby E. Perioperative haemotherapy. II. Risk and complications of blood transfusion. Can J Anaesth 1992;39:822-37.
  39. Hartmann M, Sucker C, Boehm O, Koch A, Loer S, Zacharowski K. Effects of cardiac surgery on hemostasis. Transfus Med Rev 2006;20:230-41.
  40. Luk C, Eckert K, Barr R, Chin-Yee I. Prospective audit of the use of fresh-frozen plasma, based on Canadian Medical Association transfusion guidelines. Research letter. CMAJ 2002;166:1539-40.
  41. Vamvakas E, Taswell H. Long-term survival after blood transfusion. Transfusion 1994;34:471-7.
  42. American Society of Anesthesiologists. Questions and answers about transfusion practices. Park Ridge, IL: American Society of Anesthesiologists; 1998. p. 12-13, 21.
  43. Bracey AW, Grigore AM, Nussmeier NA. Impact of platelet testing on presurgical screening and implications for cardiac and noncardiac surgical procedures. Am J Cardiol 2006;98:25-32.
  44. Spiess BD, Royston D, Levy JH, Fitch J, Dietrich W, Body S, Murkin J, Nadel A. Platelet transfusion during coronary artery bypass graft surgery is associated with serious adverse outcome. Transfusion 2004;44:1143-8.
  45. Hebert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, Tweeddale M, Schweitzer I, Yetisir E. A multi-

- center, randomized, controlled clinical trial of transfusion requirements in critical care. *Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group*. *N Engl J Med* 1999;340:409-17.
46. Thurer R. Blood transfusion in cardiac surgery. *Can J Anaesth* 2001;48:6-12.
  47. Blumberg N, Heal J. Mortality risks, costs, and decision making in transfusion medicine. *Am J Clin Pathol* 2000; 114:934-7.
  48. Carson JL, Altman DG, Duff A, Noveck H, Weinstein MP, Sonnenberg FA, Hudson JJ, Provenzano G. Risk of bacterial infection associated with allogeneic blood transfusion among patients undergoing hip fracture repair. *Transfusion* 1999;39:694-700.
  49. Heiss MM, Fraunberger P, Delanoff C, Stets R, Allgayer H, Strohlein MA, Tarabichi A, Faist E, Jauch KW, Schildberg FW. Modulation of immune response by blood transfusion: evidence for a differential effect of allogeneic and autologous blood in colorectal cancer surgery. *Shock* 1997;8: 402-8.
  50. Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ. The risk of transfusion-transmitted viral infections. *N Engl J Med* 1996;334:1685-90.
  51. Spiess B. Blood transfusion: the silent epidemic. *Ann Thorac Surg* 2001;72:1832-7.
  52. Kopko P, Marshall C, MacKenzie M, Holland P, Popovsky M. Transfusion-related acute lung injury: report of a clinical look-back investigation. *JAMA* 2002;287:1968-71.
  53. Leal-Noval SR, Rincon-Ferrari MD, Garcia-Curiel A, Herruzo-Aviles A, Camacho-Larana P, Garnacho-Montero J, Amaya-Villar R. Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery. *Chest* 2001;119:1461-8.
  54. Vamvakas E, Carven J. Transfusion and postoperative pneumonia in coronary artery bypass graft surgery: effect of the length of storage of transfused red cells. *Transfusion* 1999;39:701-10.
  55. Vamvakas E, Carven J. RBC transfusion and postoperative length of stay in the hospital or the intensive care unit among patients undergoing coronary artery bypass graft surgery: the effects of confounding factors. *Transfusion* 2000;40:832-9.
  56. Corwin HL, Gettinger A, Pearl RG, Fink MP, Levy MM, Abraham E, MacIntyre NR, Shabot MM, Duh MS, Shapiro MJ. The CRIT Study: anemia and blood transfusion in the critically ill-current clinical practice in the United States. *Crit Care Med* 2004;32:39-52.
  57. Vincent JL, Baron JF, Reinhart K, Gattinoni L, Thijs L, Webb A, Meier-Hellmann A, Nollet G, Peres-Bota D; ABC (Anemia and Blood Transfusion in Critical Care) Investigators. Anemia and blood transfusion in critically ill patients. *JAMA* 2002;288:1499-507.
  58. Spiess BD, Ley C, Body SC, Siegel LC, Stover EP, Maddi R, D'Ambra M, Jain U, Liu F, Herskowitz A, Mangano DT, Levin J. Hematocrit value on intensive care unit entry influences the frequency of Q-wave myocardial infarction after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 1998;116:460-7.
  59. Fernandez-Montoya A. Variations in transfusion practice in Spain. *Sangre* 1999;44:30-7.
  60. Capraro L, Kuitunen A, Salmenpera M, Kekomaki R. On-site coagulation monitoring does not affect hemostatic outcome after cardiac surgery. *Acta Anaesthesiol Scand* 2001;45:200-6.
  61. Boodhwani M, Williams K, Babaev A, Gill G, Saleem N, Rubens FD. Ultrafiltration reduces blood transfusions following cardiac surgery: a meta-analysis. *Eur J Cardiothorac Surg* 2006;30:892-7. 