Orthopedic Surgery Transfusion Hemoglobin European Overview (OSTHEO) study: blood management in elective knee and hip arthroplasty in Europe*

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BACKGROUND: The purpose of this study was to assess current practices in blood management in elective orthopedic surgery in Europe.

STUDY DESIGN AND METHODS: For this 225-center prospective survey, data were collected on 3996 patients. Actual perioperative blood loss was compared to preoperative estimates. Differences in Hb levels and other outcome variables for patients receiving allogeneic versus autologous transfusions were evaluated. The probability of allogeneic transfusion based on selected predictor variables was estimated.

RESULTS: A total of 2640 (67%) hip and 1305 (33%) knee arthroplasty patients were evaluated. Estimated blood loss (median, 750 mL) was significantly lower than computed blood loss (median, 1944 mL). A total of 2762 (69%) patients received transfusions, including 1393 (35%) autologous-only and 1024 (25%) allogeneic-only. The probability of allogeneic transfusion decreased with increasing baseline Hb, but differentially so for men and women. Transfusion triggers were Hb levels of 8.93 ± 1.83 g per dL for allogeneic transfusions, and 21 percent of these occurred when the Hb level was greater than 10 g per dL. Autologous blood transfusion was associated with a significantly lower rate (1%) of wound infections than allogeneic blood transfusion (4.2%).

CONCLUSION: Accurate assessment of preoperative Hb levels, better estimation of perioperative blood loss, efficient use of autologous blood, adherence to transfusion guidelines, and pharmacologic alternatives contribute to effective and comprehensive blood and anemia management.

Blood transfusions are often necessary during and after total hip and total knee arthroplasty because of perioperative blood loss. Autologous blood transfusion techniques are the principal means of reducing allogeneic blood exposure. These techniques were developed to reduce the risk of transfusion reactions through storage-induced mechanisms, errors in blood administration, and immunosuppression and to prevent viral contamination. However, the risk of viral contamination has become small and some studies have demonstrated high cost-to-efficiency ratios related to autologous blood donation (ABD).[1,2] The use of WBC-depleted allogeneic blood to reduce the risk of immunosuppression is controversial, but the rate of infections is higher with allogeneic blood transfusion.[3,4] In addition, allogeneic blood is becoming increasingly scarce to the extent that, in Europe, orthopedic surgery delays have occurred.

The Orthopedic Surgery Transfusion Hemoglobin European Overview (OSTHEO) was a prospective study designed to examine blood management practices be-

ABBREVIATIONS: ABD = autologous blood donation; ANH = acute normovolemic hemodilution; CRF(s) = case report form(s); DVT = deep vein thrombosis; NSAID(s) = nonsteroidal anti-inflammatory drug(s).

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fore, during, and after elective total knee and total hip arthroplasties in Europe and to determine factors predictive of the risk associated with allogeneic transfusion. Specifically, the study examined various blood collection and transfusion factors including blood wastage; pre- and postoperative Hb evolution; transfusion-associated complications; and predictors of allogeneic transfusion.[5,6] Transfusion blood strategies can be better developed if the calculated total blood loss is known.[7,8] Therefore, this study compared estimated and computed total blood loss in approximately 4000 patients.

MATERIALS AND METHODS

Study design

The OSTHEO study was a prospective epidemiologic observational survey conducted in major orthopedic centers in six European countries (France, Germany, Greece, Italy, the Netherlands, and Spain) during a 9-month period (April-December 1999). Both private and public centers, identified from available lists of orthopedic surgery centers, were invited to participate (centers were chosen to achieve equal representation of private and public institutions and representation according to the number of elective orthopedic surgery performed). Selected centers were instructed to include all patients undergoing elective total hip or total knee replacement. To obtain representative data and avoid selection bias, enrollment of consecutive patients was requested with a limit of 20 patients per center.

This survey did not require any deviation from routine medical practice. In compliance with country-specific regulations, human subjects reviews were either waived or expedited.

Data collection

Data were collected with a one-page, printed case report form (CRF) (see Appendix 1). CRFs and detailed instructions for CRF completion were distributed to orthopedic surgeons at each participating center where either the surgeon or a designated clinician was responsible for CRF completion. Completed CRFs were returned to the data processing center. Because this was a survey, no source verification or query resolution was performed except by each investigator.

The following demographic data were collected: date of birth, sex, country, height, and weight. The existence of the following comorbid conditions was recorded: arterial hypertension, diabetes, coronary arterial disease, chronic obstructive pulmonary disease, rheumatoid arthritis, and hematologic disorders. Data pertaining to surgical procedure included location (total hip or total knee); procedure site (unilateral or bilateral); procedure type (primary or revision) and date; method of anesthesia (general, locoregional, or both); use, administration route, and duration of antibiotic therapy; clinically apparent deep vein thrombosis (DVT); and nonsteroidal anti-inflammatory drug (NSAID) prophylaxis. Physicians' estimates of the expected perioperative blood loss were recorded before the procedure.

Baseline Hb level (defined as the Hb level collected during the assessment office visit when the surgery was planned—21 $\pm$ 7 days before surgery) was recorded for all patients. For patients participating in an ABD program, baseline Hb information was obtained before any preoperative blood donation. Hb levels were also recorded at the following times: immediately before operation; during Postoperative Days 1 and 3, 4, or 5; and just before patient discharge from the surgery unit.

Information concerning transfusion alternatives (ABD, Cell Saver [Haemonetics, Braintree, MA], acute normovolemic hemodilution [ANH], and postoperative salvage), the use and route of iron supplementation, and the use and total dose of recombinant human erythropoietin were recorded. For each of these blood management methods, total RBCs as well as whole-blood volume donated and returned were recorded. Allogeneic blood transfusion information included Hb level before transfusion, total volume transfused, and whether or not the blood was WBC-depleted. The estimated blood volume was calculated using sex and body surface area. The amount of total perioperative blood loss was calculated with the sum of RBC volume transfused (from the various sources of transfusion) added to the RBC volume lost during the period from the day before surgery to Day 3, 4, or 5 after surgery (see Appendix 2 for the formulas used to calculate perioperative blood loss).

Complications developing while patients were on the surgery unit were monitored: wound infection, urinary tract infection, respiratory tract infection, septicemia and "other" infections, volume overload, suspected clinical DVT, and transfusion reactions. The determination of infection was made using physician clinical judgment.

As to data cleaning procedures, lead investigators identified allowable physiologic and demographic ranges for variables. When values exceeding these ranges were identified, the CRF was inspected for scanning error and, if necessary, corrected. Otherwise, values were set to missing. Domain and consistency edits were implemented based on algorithms identified by an independent third party. Missing data rates ranged from 1.3 percent (surgery location) to 40.8 percent (Hb level at discharge from the surgery unit). Individual analysis sample size was contingent on the number of cases having valid data for the variables being analyzed (see Appendix 3 for a summary of the effect of missing data on analysis subsample sizes).

TABLE 1. Demographics and baseline characteristics*

	All patients	Men	Women
Total	100 (3824)†	35 (1393)	61 (2431)
Age (mean years ± SD)	69 ± 11.2	66 ± 12.1	70 ± 10.5
Procedure type‡			
Primary unilateral hip	51 (2027)	39 (794)	57 (1164)
Primary bilateral hip	1 (27)	33 (9)	63 (17)
Primary unilateral knee	26 (1036)	28 (290)	68 (702)
Primary bilateral knee	0 (13)	23 (3)	77 (10)
Hip revision	7 (292)	39 (114)	57 (167)
Knee revision	2 (69)	26 (18)	67 (46)
Comorbidities§			
Hypertension	41 (1631)	32 (529)	65 (1059)
Coronary artery disease	12 (469)	44 (206)	51 (240)
Diabetes	10 (382)	39 (148)	57 (218)
Chronic obstructive pulmonary disease	8 (317)	50 (157)	46 (145)
Rheumatic	4 (149)	33 (49)	64 (95)
Hematologic	3 (106)	48 (51)	47 (50)

* Missing data for some variables causes discrepancy in numbers. Data are presented as number (%).
† Sex data missing or invalid for 172 patients.
‡ Men vs. women, within procedure.
§ Men vs. women, within comorbidity.

Statistical analysis

Statistical analyses were performed with computer software (SPSS 9.0 for Windows, SPSS Inc., Chicago, IL). Data were analyzed as an aggregate with all countries included. Descriptive statistics were used to explore sample characteristics, perioperative Hb values, and blood collection methods. Differences in Hb levels and other outcome variables for patients receiving allogeneic versus autologous transfusions were evaluated with parametric and nonparametric statistical tests after consideration of distributional characteristics and statistical test assumptions. A probability value of less than 0.05 was considered significant. Logistic regression was used for modeling the probability of transfusion based on selected predictor variables, with the logistic probability prediction equation[9] $1/(1 + e^{-z})$, where e is the value for the base of natural logarithms (2.718), Z is the constant + $B_1X_1 + B_2\chi^2 + \ldots + B_pX_p$, B is the logistic regression coefficient for variable X, and X is the value for significant variable.

RESULTS

Demographics and baseline characteristics

A total of 4013 CRFs from 225 centers were electronically scanned and entered into the database. Sixteen patients under the age of 18 were deleted, because only adults were to be included. The CRF of 1 patient did not have a valid identifier and was deleted. The final database contained data for 3996 patients, of which 3945 had valid values for location of surgery. A total of 2640 (67%) hip and 1305 (33%) knee arthroplasty patients were evaluated. Of the six participating countries, France enrolled the most patients (n = 2125; 53% of the total sample), followed by Spain (n = 594; 15%), Italy (n = 445; 11%), the Netherlands (n = 404; 10%), Germany (n = 229; 6%), and Greece (n = 199; 5%). This geographic variability was attributed to two factors: 1) centers were recruited on a voluntary basis, but had to adhere to a strict time schedule; and 2) the large number of patients from France was linked to the professional and public awareness of transfusion risks and questions about the integrity of the blood supply.

Table 1 summarizes demographic and baseline characteristics. Mean age for the sample was 69 ± 11.2 years (range, 19-97 years). Mean age for hip patients was 67 ± 21.1 years (range, 19-97 years) and for knee patients was 71 ± 7.5 years (range, 26-92 years). The majority of the patients were women (61%). The most frequently performed procedures were primary unilateral hip (51%) and primary unilateral knee (26%). There was a greater percentage of women for each type of procedure.

Comorbidities

The most frequent comorbidities were hypertension (41%), coronary artery disease (12%), and diabetes (10%). The prevalence of comorbid conditions was greater for women except for chronic obstructive pulmonary disease and hematologic disorders. There were significant differences between transfusion method groups for coronary artery disease ($\chi^2(3) = 12.82$, $p < 0.001$) and rheumatoid arthritis ($\chi^2(3) = 13.29$, $p < 0.001$). The autologous transfusion group had the lowest rate of coronary artery disease (9.5%), while the highest rate occurred in patients receiving both allogeneic and autologous transfusions (15%). The lowest preoperative rate of rheumatoid arthritis was found in the autologous-only transfusion group (3%).

Blood loss

There was a significant difference between estimated and calculated blood loss: the median preoperative estimate of blood loss was significantly lower than the median calculated blood loss for both total hip (median, 750 vs. 1944 mL; $p < 0.001$) and total knee (median, 800 vs. 1934 mL; $p < 0.001$) procedures. However, the median calculated blood loss rates for primary total hip (median, 1944 mL) and total knee (median, 1934 mL) procedures did not differ significantly, nor did the median calculated blood

loss rates for total hip (median, 2875 mL) and total knee (median, 2528 mL) revision (see explanation in discussion).

Table 2 shows summary statistics for calculated blood loss volume, estimated blood loss volume, and the ratio of the former to the latter, stratified by location and type of surgery, anesthetic method, use of NSAIDs, and autologous blood collection methods. These groups were not mutually exclusive; therefore, statistical testing was not always performed. Fifty-seven percent of patients in this study received NSAIDs. There was no significant difference in median estimated and median calculated blood loss whether or not NSAIDs drugs were used, nor if locoregional anesthesia or general anesthesia was used.

Blood management methods

Transfusions. Mean age for transfusion method groups differed significantly ($p < 0.001$) and ranged from 66 ± 11.6 years for the autologous-only group to 71 ± 10.7 years for the allogeneic-only group. Length of stay for the autologous-only group (12.3 ± 10.5 days) did not differ significantly from the allogeneic-only group (13.0 ± 8.1 days). Mean length of stay for patients who received autologous-only blood collected via the ABD method (11.9 ± 7.7 days) and for patients who did not received transfusions (10.7 ± 12.3 days) was significantly less ($p < 0.001$) than mean length of stay for patients who received any allogeneic transfusion (allogeneic-only or allogeneic and autologous transfusions) (13.5 ± 10.2 days).

Table 3 summarizes transfusion methods for the entire sample stratified by sex, ABD, and type of surgery. A total of 2762 (69%) patients received either allogeneic or autologous blood components during the perioperative period; therefore, 31 percent did not receive any blood. In this study, 1393 (35% of all patients and 50% of patients who received transfusions) received autologous-only transfusions, 1024 (25% of all patients and 37% of patients who received transfusions) received allogeneic-only transfusions. Women had a significantly higher overall transfusion rate than men ($\chi^2(3) = 74.53$, $p < 0.001$). Men had higher rates of autologous-only transfusions (63 vs. 45%).

Of the 1680 patients for whom no autologous blood collection method was used, 805 (48%) received transfusion with allogeneic blood. For the 1639 patients for whom some form of autologous blood collection method was used, 1493 (91%) received transfusion and 318 (16.4%) had at least one allogeneic transfusion.

Blood wastage. Utilization (and waste) of autologous blood is summarized in Table 4. Overall, 33 percent of patients donated blood preoperatively with rates ranging from 23 percent for unilateral knee revision patients to 36 percent for primary unilateral hip patients. The overall blood discard rate was 13 percent with rates ranging from 8 percent for unilateral revision of knee arthroplasty to 14 percent for primary unilateral knee arthroplasty.

Blood collection. Valid data pertaining to blood collection methods (which includes "no blood collected") were available for 3319 patients (see Appendix 3). Fifty percent (n = 1639) of these patients had autologous blood collected for transfusion purposes (see Table 5). Of these 1639 patients, a single method of blood collection was used for 66 percent (n = 1089, 33% of all patients with valid blood collection data) of patients. Two or more methods in combination were used for 34 percent (n = 550, 17% of all patients with valid blood collection data) of patients; the ABD-only method was used for 38 percent (n = 634, 19% of all patients with valid blood collection data) of patients. The ANH method was utilized in less than 1 percent (n = 44) of patients, even when used in combination with other methods.

For all procedures except knee revisions, the ABD method was used most frequently and ranged from 9 percent (n = 5 of 58) for knee revisions to 23 percent (n = 397 of 1717) for primary unilateral hip procedures. A single blood collection method was utilized in

TABLE 2. Calculated blood loss by surgery, type of anesthesia, NSAID use, and blood collection technique*

	Number	Mean (mL)	Median (mL)	SD (mL)
Location and type of surgery				
Hip				
Primary†‡	1122	2143	1944	1165.4
Revision§	163	3060	2875	1702.6
Knee				
Primary‡	552	2072	1934	1145.3
Revision§	39	2634	2528	1100.4
Type of anesthesia				
General	879	2330	2106	1345.0
Locoregional	920	2103	1932	1156.8
Both	204	2100	1974	1021.2
NSAID use				
Yes¶	1017	2231	1979	1252.1
No¶	820	2145	1960	1223.8
Blood accrual technique				
ABD	704	2520	2350	1237.9
ANH	82	2101	1840	1328.0
Cell Saver	329	2759	2609	1354.9
Postoperative salvage	264	2501	2284	1288.6
No transfusion‖	602	1265	1243	621.5

* Missing data for some variables causes discrepancy in numbers.
† All p values are the results of U-tests on medians.
‡ $p = 0.323$.
§ $p = 0.235$.
‖ $p < 0.05$.
¶ $p = 0.127$.

TABLE 3. Summary of transfusion methods*

	Percentage of patients who received transfusion(s)	Of patients who received transfusion(s)			Percentage that were ABD patients
		Percentage that received allogeneic only	Percentage that received autologous only	Percentage that received allogeneic and autologous	
All patients	69 (2762)	37 (1024)	50 (1393)	13 (345)	32 (1290)
Men	65 (909)	27 (246)†	63 (564)†	11 (99)†	38 (533)
Women	72 (1749)	42 (732)†	45 (781)†	13 (236)†	29 (706)
ABD patients	91 (1170)	2 (27)	82 (964)	15 (179)	100 (1290)
Procedure					
Primary unilateral hip	68 (1387)	36 (496)‡	52 (728)‡	12 (163)‡	36 (735)
Primary bilateral hip	67 (18)	39 (7)‡	50 (9)‡	11 (2)‡	33 (9)
Primary unilateral knee	67 (696)	35 (242)§	54 (377)§	11 (77)§	27 (273)
Primary bilateral knee	85 (11)	27 (3)§	72 (8)§	0 (0)§	54 (7)
Hip revision	86 (252)	46 (115)‖	33 (83)‖	21 (54)‖	31 (90)
Knee revision	74 (51)	45 (23)‖	33 (17)‖	21 (11)‖	23 (16)

* Missing data may cause apparent discrepancies in counts. Data are presented as percentage (n).
† $\chi^2 = 91.125$; df = 3; $p < 0.001$.
‡ $\chi^2 = 0.112$; df = 3; p = NS.
§ $\chi^2 = 4.38$; df = 3; p = NS.
‖ $\chi^2 = 3.65$; df = 3; p = NS.

TABLE 4. Utilization of autologous blood*

Procedure	Number (%) of patients who donated blood before surgery	Number (%) of units† of autologous blood wasted
Hip replacement		
Primary unilateral (n = 2027)	735 (36)	304 of 2253 (13)
Revision unilateral (n = 286)	84 (29)	25 of 256 (9)
Knee replacement		
Primary unilateral (n = 1036)	273 (26)	112 of 793 (14)
Revision unilateral (n = 66)	15 (23)	3 of 36 (8)
Overall	1107 (33)	444 of 3338 (13)

* Missing data for some variables causes discrepancy in numbers.
† Primary data included transfused volume in mL. Volume was converted to units of blood: 1 unit = 250 mL.

34 percent (n = 589 of 1717) of primary unilateral total hip procedures, 33 percent (n = 287 of 866) of primary unilateral total knee procedures, and 33 percent (n = 3 of 9) of primary bilateral knee procedures.

Pharmacologic agents

The use of pharmacologic methods to manage blood was remarkably low. Of the 3996 patients in the sample, only 122 (3%) received recombinant human erythropoietin. A total of 2066 (52%) patients received iron therapy. Of the 122 patients who received recombinant human erythropoietin, 117 (96%) also received iron.

Hb levels

Figure 1 shows the distributions of Hb levels at baseline, the day before surgery, and at discharge. At baseline, 31 percent of patients had a Hb level less than 13.0 g per dL. The day before surgery 51 percent of patients had a Hb level of less than 13.0 g per dL. The difference between mean baseline Hb level (13.6 g/dL) and mean discharge Hb level (10.8 g/dL) for all patients was –2.8 g per dL. The mean baseline Hb level for women (13.2 g/dL) was 1.1 g per dL lower than for men (14.3 g/dL; $p < 0.001$). The mean discharge Hb level for women (10.7 g/dL) was 0.3 g per dL lower than for men (11.0 g/dL; $p < 0.001$). The change in Hb from baseline to discharge for men (–3.3 g/dL) was significantly greater than the change for women (–2.5 g/dL; $p < 0.001$). Note, however, that 40 percent of all patients had missing discharge Hb values, thus yielding a censored data set.

Hb level preceding transfusion

Among those patients who received transfusions on the day of surgery (n = 367, 9% of all patients in study) Hb levels between 8.0 and 8.9 g per dL were the most frequent (31%) trigger for first allogeneic transfusions, followed by 10 to 10.9 and 7 to 7.9 g per dL (both 11%). However, 21 percent of the Hb levels were greater than or equal to 10.0 g per dL and 10 percent exceeded 13.0 g per dL. Similarly, in the postoperative group that received transfusion of allogeneic-only blood (n = 222, 6% of all patients), Hb levels between 8.0 and 8.9 g per dL were the most frequent (37%) trigger as well, followed by 10.0 to 10.9 g per dL (27%) and 7.0 to 7.9 g per dL (21%).

Complications

As shown in Table 6, overall infection rates (urinary, pulmonary, wound, and other) ranged from 13 percent for WBC-depleted allogeneic transfusion to 4 percent for ABD-only patients. The overall wound infection rate was 2 percent (81 of 3996) and ranged from 4 percent for non-WBC-depleted allogeneic transfusions, allogeneic-

TABLE 5. Blood collection methods*

	No blood collected	Combination of methods	Single method only	Blood collection method (where a single method was used)			
				ABD only	ANH only	Cell saver only	Postoperative salvage only
All patients	51 (1680)	17 (550)	33 (1089)	19 (634)	1 (44)	6 (202)	6 (209)
Procedure							
Primary unilateral hip	49 (849)	16 (279)	34 (589)	23 (397)	1 (22)	6 (106)	4 (64)
Primary bilateral hip	57 (13)	17 (4)	26 (6)	17 (4)	0 (0)	9 (2)	0 (0)
Primary unilateral knee	51 (437)	16 (142)	33 (287)	14 (119)	1 (12)	6 (48)	13 (108)
Primary bilateral knee	56 (5)	11 (1)	33 (3)	22 (2)	0 (0)	0 (0)	11 (1)
Hip revision	51 (123)	25 (60)	25 (60)	12 (30)	2 (5)	8 (19)	3 (6)
Knee revision	55 (32)	19 (11)	26 (15)	9 (26)	0 (0)	5 (3)	12 (7)

* Missing data for some variables causes discrepancy in numbers. Data are presented as number (%).

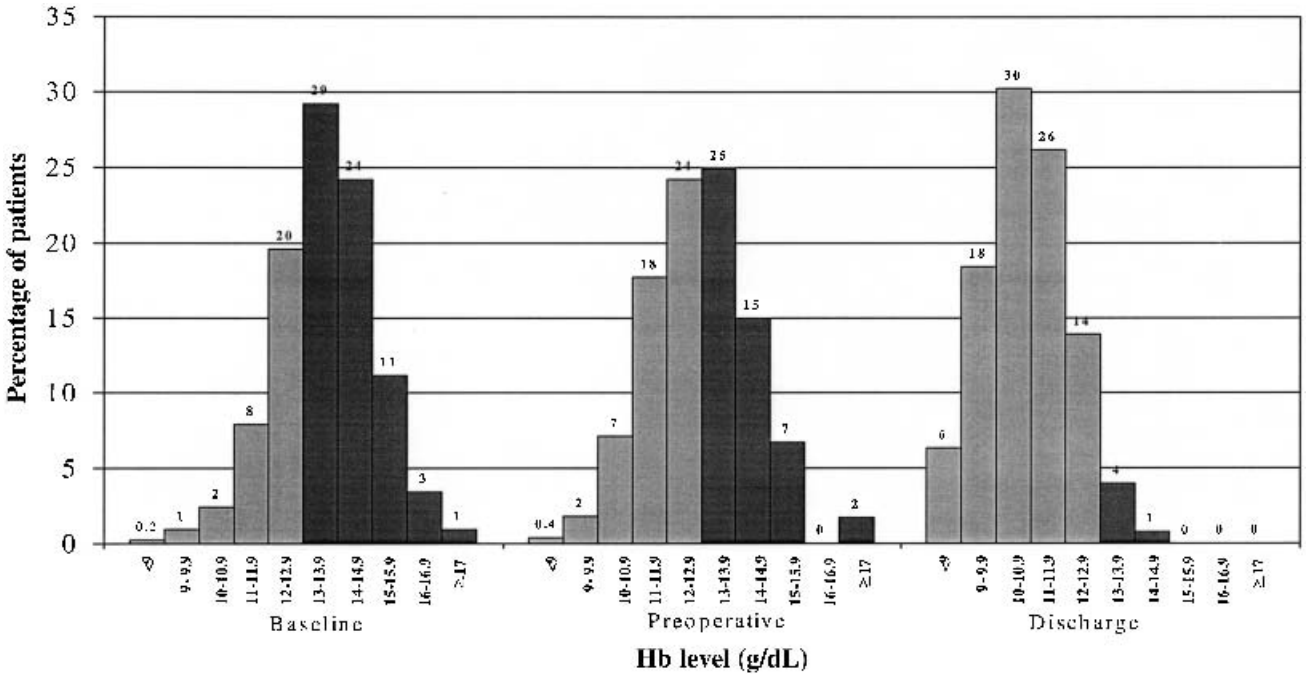

Fig. 1. Distribution of baseline, preoperative, and discharge Hb levels. (■) Hb level of at least 13 g per dL; (▩) Hb level of less than 13 g per dL.

only, and postoperative salvage procedures to 0 percent for ABD-only patients in primary total knee arthroplasty. Patients receiving both allogeneic and autologous transfusions had a wound infection rate of 2 percent, a rate similar to the no-transfusion subgroup. Wound infection rates between allogeneic-only and autologous-only groups differed significantly ($\chi^2(1) = 19.26$, $p < 0.001$). There was no significant difference in wound infection rates between WBC-depleted allogeneic transfusions (3%) and those with WBCs (4%). The wound infection rate (4%) for total knee replacement patients on postoperative salvage-only method was significantly higher than for ABD-only patients (0%) ($\chi^2(1) = 5.97$; $p < 0.05$), a finding also confirmed for total hip replacement patients (postoperative salvage-only, 4%; ABD only, 1%; $\chi^2(1) = 5.60$; $p < 0.05$).

The incidence of fluid overload ranged from 3 to 4 percent, while the incidence of clinical DVT ranged from 2 to 3 percent across transfusion methods (including no transfusion). No significant differences were observed.

Probability of transfusion

Figure 2 shows the logistic regression plots using baseline Hb to predict the probability of allogeneic transfusion for unilateral nonrevision patients who did not receive recombinant human erythropoietin. An inverse relationship between baseline Hb values and the probability of allogeneic-only transfusion was observed. At Hb levels of

TABLE 6. Infection rate by transfusion method*

Blood management technique	Overall infection rate†	Wound infection rate
Allogeneic-only transfusion	110/999 (11)	36/999 (4)‡§
Autologous-only transfusion	93/1311 (7)	11/1311 (1)‡
Allogeneic and autologous transfusions	30/329 (9)	8/329 (2)
No transfusions	94/1180 (8)	22/1180 (2)§
ABD transfusion only	25/615 (4)	4/615 (1)
Allogeneic transfusion		
WBC-depleted	82/637 (13)	18/637 (3)‖
Not WBC-depleted	42/464 (9)	18/464 (4)‖
Knee patients only		
ABD only	6/148 (4)	0/148 (0)¶
Postoperative salvage only	13/122 (11)	5/122 (4)¶
Hip patients only		
ABD only	19/462 (4)	4/462 (1)**
Postoperative salvage only	12/69 (17)	3/69 (4)**

* Missing data for some variables causes discrepancy in numbers.
† Data are presented as number (%).
‡ $\chi^2 = 19.26$; df = 1; $p < 0.001$.
§ $\chi^2 = 3.23$; df = 1; p = NS.
‖ $\chi^2 = 1.49$; df = 1; p = NS.
¶ $\chi^2 = 5.97$; df = 1; $p < 0.05$.
** $\chi^2 = 5.60$; df = 1; $p < 0.05$.

8 g per dL, probabilities for allogeneic-only transfusion were 75 percent for women and 69 percent for men. These decreased to 13 and 7 percent, respectively, at Hb levels of 16 g per dL. As Hb levels increased, the probability for allogeneic-only transfusion decreased significantly.

DISCUSSION

Potential risks and costs associated with blood transfusions, in particular allogeneic blood transfusions, have been documented both in general[6,10] and specifically for total hip and knee arthroplasty patient populations.[11] This European study, which complements a similar study by Bierbaum et al.[11] in the US, documents blood management methods used before, during, and after primary and revision total hip and total knee arthroplasties. It confirms previous findings, yet also highlights differences specific to European clinical practice. In addition, for the first time, blood usage for these types of surgery was evaluated by computing total perioperative blood loss.

The overall allogeneic transfusion rate of 25 percent of all patients (50% of patients who received transfusions) was substantially greater than the 18 percent rate reported by Bierbaum et al.[11] We found that for 51 percent of patients no autologous blood collection method was used and that about half of this subgroup had allogeneic transfusions subsequently. Of the 50 percent of patients for whom some form of autologous blood collection was used, 13 percent subsequently had allogeneic transfusions. The 17 percent allogeneic transfusion rate for ABD patients (breakthrough transfusions) was consistent with results of a recent meta-analysis.[12]

Twenty-one percent of all patients who received transfusions with allogeneic blood at Hb levels greater than 10 g per dL, even in the presence of transfusion guidelines. The rate of presurgery blood donation reported by Bierbaum et al.[11] was 60 percent as opposed to 33 percent in this study. Both of these factors help explain the breakthrough transfusion rate in the present study. Also, the minimal use of ANH (1%) in Europe confirms another meta-analysis that failed to demonstrate the efficacy of ANH in a similar orthopedic population.[11]

Several factors were found to influence allogeneic transfusion rates. Participation in an ABD program or utilization of other autologous blood collection methods reduced the probability of a subsequent allogeneic transfusion. However, if insufficient time is allowed for erythropoiesis after donation, preoperative Hb levels may be suboptimal, thus increasing the likelihood of allogeneic transfusion. Recombinant human erythropoietin has been shown to effectively accelerate erythropoiesis.[5,13-15]

Baseline, day-of-surgery, and postoperative Hb levels less than 10 g per dL were associated with higher allogeneic transfusion rates. In fact, the probability of transfusion steadily increases for decreasing baseline and preoperative Hb levels. Therefore, efforts to maintain preoperative Hb levels of 13 g per dL or greater seem warranted. If patients are anemic at baseline, recombinant human erythropoietin can be used to increase Hb levels before surgery, assuming, however, an adequate time interval between baseline and surgery so as to allow for erythropoiesis to occur.[4,13-17]

Decreases in Hb between baseline and day before surgery is attributed to presurgery donation of autologous blood. Accurately estimating expected perioperative blood loss is critical for establishing an effective blood management plan or strategy. Estimated blood loss is the bleeding that can be seen during surgical procedure or in suction drains. However, hematoma or bleeding around the prosthesis and the muscles is not visible; therefore, only computed blood loss is reflective of total blood loss. During and after hip arthroplasty, approximately one-third of blood loss is absorbed by sponges, one-third is evacuated by suction devices, and the remaining one-third forms hematoma. Blood loss during and after knee arthroplasty with tourniquet typically occurred postoperatively and only half of the cases were detectable. This contributes to the assumption that knee arthroplasty blood loss should be less than that for hip arthroplasty.

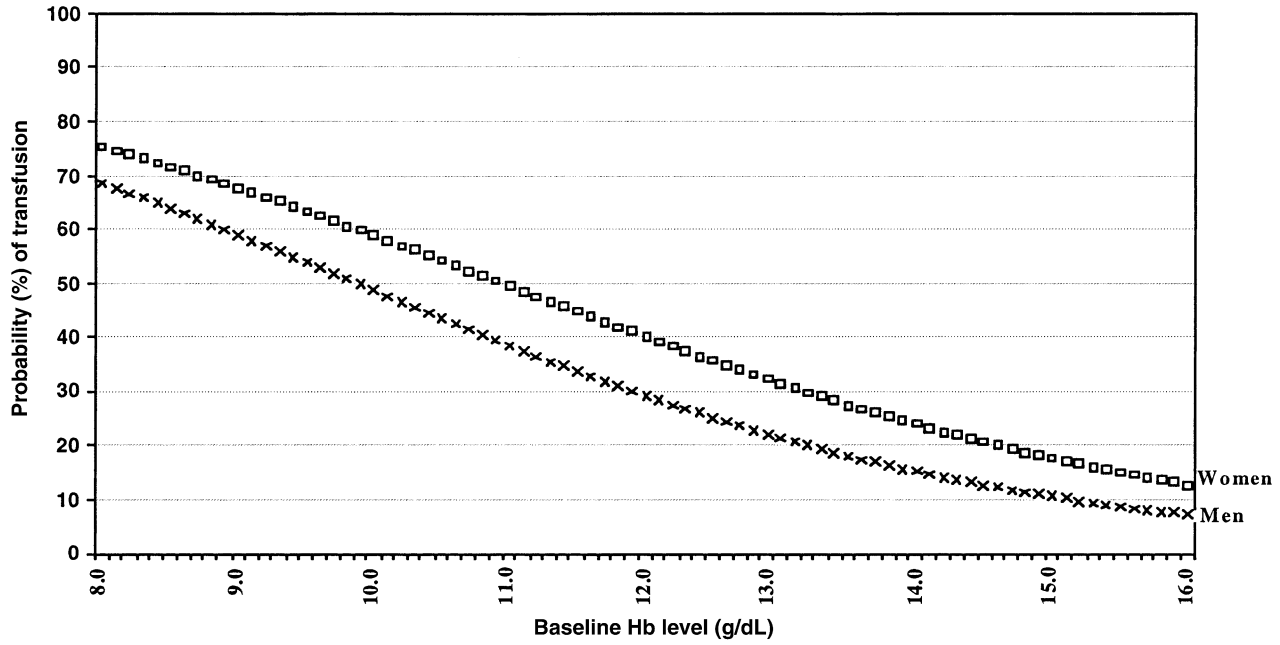

Fig. 2. Probability of allogeneic transfusion only in knee and hip replacements unilateral, nonrevision, no erythropoietin. (×) Men; (□) women.

However, when the amount of blood transfused in both treatment groups is taken into account the blood loss is nearly the same.

If the median of total blood loss can be determined for individual centers, an algorithm for a transfusion strategy could be devised to minimize the amount of "breakthrough" transfusions and wasted donated autologous blood. Accurate estimates would allow for adequate amounts of blood to be available for judicious transfusion and for appropriate preoperative Hb management. The results of the present study demonstrate that preoperative estimates of blood loss for both total knee and hip procedures were about 40 percent of the calculated blood loss, thus confirming results reported by Mercuriali and Inghilleri.[8] Calculated blood loss estimates for total knee surgery and total hip surgery were similar. This underscores the general problem of discrepancies between estimates and calculations of surgical blood loss in knee and hip arthroplasties. It also confirms that tourniquets probably do not reduce blood loss in knee surgery and therefore may be an inadequate method for preventing blood loss during knee arthroplasty.[18] Consequently, if the Hb levels drop below an acceptable level and if inadequate amounts of autologous blood are available, either allogeneic blood must be transfused or suboptimal Hb levels must be imposed on patients.

The amount of donated autologous blood discarded (13%) and the 17 percent breakthrough transfusion rate are indicators of the effectiveness of blood management. The 13 percent discard rate in this European study was less than the 46 and 45 percent discard rates reported for the US in 1989[19] and 1999.[4,6,11] Although this is indicative of a more efficient use of donated blood, this efficiency is offset by the higher allogeneic rate in the current study. Excessive autologous presurgery donation may be much less of a problem in Europe than it is in the US. However, the risk associated with increased allogeneic transfusion to cover surgical blood loss outweigh the cost, inconvenience, and low risk associated with appropriate autologous presurgery donation.

The allogeneic blood transfusion trigger is still high despite published guidelines. In fact, transfusions at Hb levels greater than 10 g per dL occurred most frequently on the day of surgery. This can be explained by the knowledge that two-thirds of bleeding in this patient population tends to occur the day after surgery.

Another risk of allogeneic blood transfusion is thought to be immunosuppression with increased risk of infection.[3,4,21] This assertion is still being debated.[20] Indeed, patients who received transfusion with allogeneic blood tend to be anemic or have severe bleeding. Various diseases cause anemia secondary to decreased erythropoiesis. Increased risk of infection may well be due to the condition-causing anemia as much as to the anemia itself. Also, lengthy and/or difficult surgery often results in increased blood loss and hypothermia, thus further increasing the risk of infection. Many hospitals deplete WBCs from RBCs to decrease the risk of immunosuppression and infection.

Analyses of this study found that the overall infection rate was somewhat (though not significantly) less when autologous transfusion methods (including ABD) were used than with allogeneic transfusions. Wound infection rates after autologous transfusions and when no transfusions occurred were significantly less than after allogeneic transfusions. The lower infection rate associated with autologous transfusion methods may be biased by recruitment of American Society of Anesthesiologists (ASA) Status 1 or 2 patients and the necessity of screening for infection before inclusion in an ABD program.

Studies pertaining to unwashed postoperative blood have not demonstrated an increased infection risk.[22,23] In this study, postoperative salvage was associated with the highest overall infection rate and wound infection rates in comparison to Cell Saver and ABD used alone. This technique involves the use of unwashed whole blood collected 5 to 6 hours before return. Therefore, it is possible that blood components were handled in ways that fostered microbial growth perioperatively in the recovery room. If a strict aseptic technique is not followed during the collection of shed blood, infection may result, especially if the blood is stored at ambient temperature for 5 to 6 hours. These findings are similar to those reported by Bierbaum et al.[11]

In conclusion, this European study suggests several recommendations:

First, predicted operative blood loss estimates and actual blood loss should converge within minimal margins of deviation. These blood loss estimates should be made at the time surgery is planned, not at the time of surgery itself. This will allow accurate estimation of blood needs and presurgery donation of adequate amounts of autologous blood, reduce the need for allogeneic "breakthrough" transfusions, minimize the amount of discarded blood, and enable erythropoietic activity well in advance of surgery. In turn, adequate blood management before surgery will buffer patients against postsurgical complications, both in general and specific to (allogeneic) transfusion.

Second, clinicians must focus on baseline Hb levels to determine the probability of transfusion, risk of allogeneic transfusion, eligibility for recombinant human erythropoietin therapy in combination with iron supplementation, and/or entry into an ABD program. This study, as well as that conducted by Faris et al.,[5] offers sensitive predictive models that can be readily integrated into surgical practice. Even before referring to probability plots, clinicians may want to adopt a clinical rule of thumb that baseline Hb levels at or exceeding 13.0 g per dL are essential for postsurgical recovery, reduction of complications, and improved patient status at discharge. The allogeneic transfusion trigger observed in the present study is higher than generally accepted guidelines. Adherence to these guidelines may well result in a decrease in the number of allogeneic transfusions.

Finally, many of the postoperative blood needs and complications during hip and knee arthroplasty can be influenced by good preoperative care, including initial Hb monitoring and preoperative adjustment, resolution of even minor infections, and allowance of sufficient time between the decision to operate and the actual surgery. The preoperative inconvenience owing to presurgery donation and waiting may be outweighed by the reduction in peri- and postsurgical complications. Considering that the majority of patients studied were elderly and at age-related risk adds strength to this argument.

In summary, the results of this study support the idea that a comprehensive blood management program for patients undergoing hip or knee arthroplasties minimizes the need for allogeneic transfusion. Further, such programs can optimize cost-benefit and risk ratios by decreasing infection rate and reducing discarded units if preoperative autologous donation is used. Such programs should include procedures that accurately select patients suitable for an ABD program; allow optimal collection and transfusion of appropriate amounts of autologous blood; assess operative procedures to limit and reduce blood loss; individualize blood management and transfusion practice; and optimize pre-, peri-, and postoperative Hb levels. This type of program would optimize patient management and reduce complications associated with anemia and blood transfusions in hip and knee arthroplasty patients.

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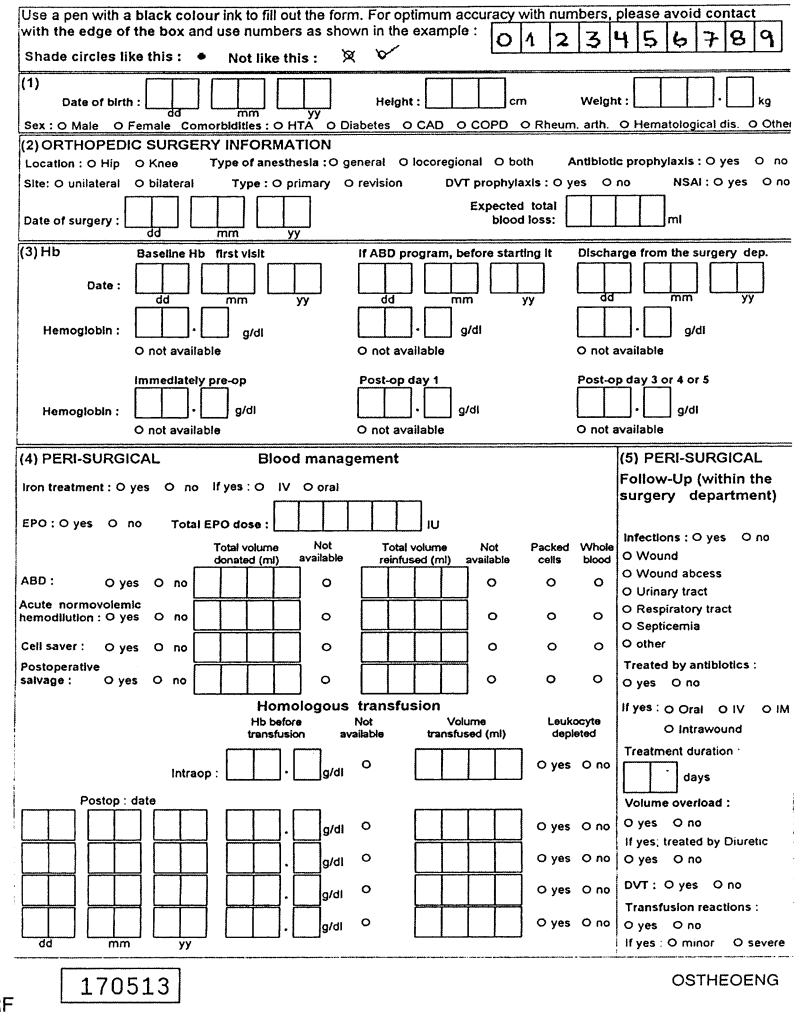
APPENDIX 1

OSTHEO CRF



APPENDIX 2

Total blood loss formulas

Total blood loss was calculated with the following formulas:[24,25]

Total RBC loss (mL) = [Uncompensated RBC loss (mL)] + [Compensated RBC loss (mL)]

Uncompensated RBC loss (mL) = [Initial RBC (mL)] − [Final RBC (mL)]

Compensated RBC loss = [Sum of RBCs received from the various sources of transfusion]

Initial RBC = [Estimated blood volume (mL)] × [Initial Hct level (%)] at Day –1

Final RBC (mL) = [Estimated blood volume (mL)] × [Final Hct level (%)] at Day +3

Estimated blood volume (mL) = Women: [Body surface area (m^2)] × 2430

Men: [Body surface area (m^2)] × 2530

Body surface area (m^2) = 0.0235 × [height (cm)]$^{0.42246}$ × [weight (kg)]$^{0.51456}$

And then, to obtain a result with blood loss at a Hct level of 35 percent

Total blood loss (mL) = [Total RBC loss (mL)]/0.35.

APPENDIX 3

Schematic representation of how missing data affect number of cases included in various analyses