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The appropriateness of red blood cell use and the extent of overtransfusion: right decision? Right amount?

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BACKGROUND: Shrinkage of the donor pool coupled with an increasing demand for blood presents a major challenge to maintaining an adequate blood supply. Consequently it has become even more important to reduce inappropriate blood use, including decisions about when and how much blood to prescribe. This study aimed to ascertain the levels of inappropriate practice and factors associated with it.

STUDY DESIGN AND METHODS: The medical records of a randomly selected sample of hospital patients in Northern Ireland who received a red blood cell transfusion during 2005 (n = 1474) were reviewed, and inappropriate transfusion and overtransfusion criteria were applied. Logistic regression models were used to identify factors associated with inappropriate practice and overtransfusion.

RESULTS: In this study 23% of transfusions were considered inappropriate, occurring most commonly where the lowest hemoglobin (Hb) threshold for transfusion applied. Younger patients, those undergoing surgery, and those with lower comorbidity and higher Hb values were most likely to have an inappropriate transfusion. Among patients appropriately transfused, 19% were overtransfused. Females and those of lower weight (<65 kg) were most likely to be overtransfused.

CONCLUSION: While the choice of criteria used to judge decisions will influence the absolute level of inappropriate or overtransfusion reported, our findings suggest that a significant minority of clinicians are either unaware of or are reluctant to accept lower transfusion thresholds. To improve further improve transfusion practice we suggest that barriers to the implementation of recommended transfusion thresholds should be examined and guidance on an appropriate posttransfusion Hb level developed.

The main aim of modern transfusion services is to maintain an adequate, safe, and efficient supply of blood components for therapeutic use.[1] Increasing pressure on both the supply and the demand for blood has focused attention on ensuring that appropriate clinical use is made of available blood components. British red blood cell (RBC) transfusion guidelines suggest an upper hemoglobin (Hb) limit of 10 g/dL, above which an RBC transfusion is generally considered inappropriate and a lower limit of 7 g/dL, or 6 g/dL in some guidelines,[2,3] below which transfusion would always be indicated.[4-6] If a patient's Hb level falls between these upper and lower Hb limits, factors, such as comorbidity, blood loss, age, and the presence of symptoms of anemia, are used to guide the transfusion decision. However, clinical practice that is at variance with these guidelines is still reported, with inappropriate transfusion rates varying greatly (4%-66%) between studies, as shown by two recent systematic reviews.[7,8]

In considering whether the use of an RBC transfusion is appropriate or not, consideration should be given not only to the issue of "whether" to transfuse, but also to "how much" to transfuse (Fig. 1). As well as being wasteful of resource, overtransfusion can be dangerous, as illustrated

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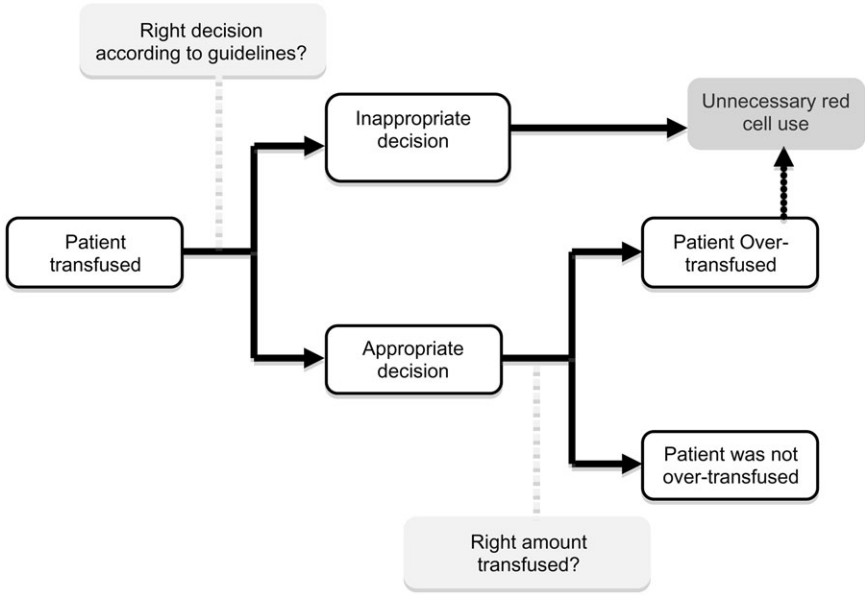

Fig. 1. Is the transfusions decision appropriate? Is the number of RBCs transfused appropriate? (See Table 2 for appropriateness and overtransfusion criteria.)

by the most recent Serious Hazards of Transfusion (SHOT) reports.[9,10] In 2008, one patient death was attributed to an excessive RBC transfusion; the category "transfusion-associated circulatory overload"[9] was added to the report. In 2009, 34 cases of transfusion-associated circulatory overload were reported; 32 of these were associated with the transfusion of RBCs, and there were four fatalities.[10] Few studies have examined this aspect of transfusion practice, but where it has been studied, levels of "overtransfusion" of the order of 24 to 75% have been reported.[11-14]

Our study aimed to assess whether RBC transfusion was being used appropriately, taking into account patient and disease considerations specified in current guidelines. The study was designed to estimate the degree of compliance with the current guidelines, to elucidate the degree if any of overtransfusion that was occurring, and to examine the patient, disease, and contextual factors that may be associated with the observed levels of compliance and overtransfusion.

MATERIALS AND METHODS

Study sample

The required sample of allogeneic RBC transfusion recipients was selected at random from all adults (≥18 years) issued with an RBC unit during one calendar year (2005) identified using hospital blood bank issues records. The number of patients included from each of the 11 hospitals in Northern Ireland was proportionate to that hospital's annual RBC usage to avoid oversampling within smaller hospitals. For each hospital, a list of eligible recipients was retrieved from the electronic blood bank system; each patient was assigned a unique random number, which was then used to sort the list. Patients were included sequentially from the sorted list until the required sample size was reached. Only the first transfusion episode identified for any individual was included in the study; thus any patient appeared only once in the study population. Transfusions were identified retrospectively to avoid influencing clinical behavior as a consequence of knowledge of the study. A sample size of 1474 individuals had a 95% probability of estimating the true population of inappropriately transfused patients to within ±3% (a confidence interval [CI] width of 6%) based on a worst-case scenario of 50% inappropriately transfused.

Transfusion episode

The number of units prescribed during each transfusion episode was required to assess whether overtransfusion had occurred. A transfusion episode was defined as the period between the first prescription of RBCs and the receipt of those RBCs by the patient. Where multiple prescriptions were placed for the same patient for the same condition, for example, in acute bleeding, all units received were considered to be part of a single transfusion episode.

Appropriateness of transfusion

The criteria used to assess the appropriateness of transfusion decisions were based on the clinical guidelines[15]

available at the time of the study and are described in Table 1. These guidelines were chosen as the Hb threshold range (7-10 g/dL) recommended therein was, and still is, in use in Northern Ireland.

Overtransfusion

Overtransfusion was defined as occurring when the posttransfusion Hb level was more than 2 g/dL above the relevant Hb transfusion threshold for that patient (Table 1). An estimate of the overall number of RBC units overtransfused was calculated using the sum of the differences between posttransfusion Hb and the target posttransfusion Hb and assuming that a 1 g/dL difference was achieved by the transfusion of one unit of RBCs.[11]

Bleeding status

The presence or absence of bleeding is specifically mentioned in transfusion guidelines as pertinent to the decision to transfuse. We defined four categories of bleeding, namely, no bleeding; bleeding in the absence of surgery (nonsurgical bleeding), for example, gastrointestinal hemorrhage; blood loss due to undergoing a surgical procedure (surgical bleeding); and bleeding as a complication of surgery (additional perioperative bleeding).

Comorbidity

Comorbidity was assessed using a count of the number of diseases present at the start of the transfusion episode. To take some account of the severity of conditions, we defined a subset of conditions that were those most commonly reported as causes of death in Northern Ireland, namely, cardiac, vascular, oncology, respiratory, gastrointestinal, liver, neurologic, urologic, and metabolic or endocrine conditions.[16] The variable "burden of disease" was a count of the number of these conditions present.

Data collection

The specified data items were chosen based on previously published studies of blood use and informal discussion with transfusion specialists (KB and KM; Table 2).[17-20] Study data were abstracted onto a study-specific case report form. Patient information was gathered from the medical records (demographic and clinical details) and laboratory records (hematologic data and number of units of RBCs transfused) of the selected patients.

A 10% sample of case notes and all case report forms were reviewed by a second abstractor (KB or KM) and any discrepancies were resolved by agreement. Laboratory variables assigned for each case were those recorded as close to the transfusion decision point as possible, that is, the last value recorded before transfusion.

TABLE 1. Hb thresholds above which a patient was considered to be: (A) inappropriately transfused (above the transfusion threshold) or (B) overtransfused (above the target posttransfusion Hb)

Transfusion Hb threshold (g/dL)	Appropriateness criteria	Target posttransfusion Hb threshold (g/dL)
<7	1. Under 65 years old and no cardiovascular or cerebrovascular conditions.*	9
<8	2. 65 years of age or older and no cardiovascular or cerebrovascular conditions.	10
<9	3. Cardiovascular or cerebrovascular conditions.	11
<10	4. Documented evidence of ongoing significant bleeding at the time of transfusion or current or recent (within 3 months) marrow failure or chemotherapy and/or radiotherapy.	12

* Cardiovascular or cerebrovascular conditions, including, for example, myocardial infarction, hypertension, atrial fibrillation, heart failure, and stroke.

TABLE 2. Study variables

Variable	Variable definition/code/unit of measurement
Patient characteristics	
Sex	Male or female
Age	At time of transfusion decision (years)
Weight	At time of transfusion decision (kg)
Bleeding status	No bleeding; medical (nonsurgical) bleeding; expected surgical loss; and additional (unexpected) perioperative bleeding
Presenting condition	The primary condition being treated at the time of transfusion. The conditions were classified as gynecology-obstetrics; cardiac; ear, nose, throat (ENT); gastrointestinal; hematology; liver; metabolic-endocrine; neurologic; musculoskeletal; respiratory; skin; urologic; vascular; and other
Cancer-related treatment	Indicated whether the treatment received was for cancer
Burden of disease score	A count of the total number of comorbidities associated with mortality (according to the Northern Ireland Mortality Statistics)
Clinical setting	
Patient setting	At time of transfusion decision: inpatient or outpatient
Grade of health professional prescribing transfusion	Consultant, specialist registrar, senior house officer, or junior house officer
Patient management	Surgery no more than 2 weeks before transfusion (surgical). No record of surgery in the 2 weeks before transfusion (medical).
Hematologic and biochemical parameters	
Pretransfusion Hb	Last recorded result before transfusion
Posttransfusion Hb	Earliest recorded Hb (g/dL) result after transfusion

Statistical analysis

Continuous data were summarized using a mean and standard deviation (SD), or median and range, as appropriate. Categorical data were summarized using proportions across each category of a given variable. Where appropriate Pearson's chi-square test of independence was used to identify whether there was a statistical association between categorical variables, the t test was used to investigate statistical differences between means and analysis of variance testing was used to compare multiple means.

Patients in receipt of an inappropriate transfusion could be considered as overtransfused; however, we excluded this group from this analysis to examine factors that may be influential in determining the amount of RBCs prescribed for those appropriately transfused. Multiple logistic regression analyses were used to examine the patient, clinical, and contextual factors independently associated with overtransfusion (0 = no; 1 = yes). Unadjusted and adjusted odds ratios (ORs), CIs, and p values are reported.

For the analysis of appropriateness, only unadjusted ORs are presented, as several of the explanatory variables (Hb, age, and comorbidity) were already included in the appropriateness criteria. Adjusting for any of these variables would therefore be likely to lead to overadjustment in the modeling.

For all analyses, robust standard errors for estimates were used to account for clustering of patient characteristics within hospitals.[21] A Hosmer and Lemeshow test was conducted to assess the goodness of fit of the overtransfusion adjusted model. In addition the area under the receiver-operating curve was calculated to give a measure of the model's ability to discriminate between patients who were overtransfused and those who were not.[22] The level of significance was taken to be a p value of less than 0.05. All analyses were conducted using computer software (STATA, Version 9.2, StataCorp, College Station, TX).

Ethics

Ethical approval was obtained through the Office for Research Ethics Committees in Northern Ireland (ORECNI) Reference Number 06/NIR03/46. All information was collected and stored anonymously on a password-protected computer within Queens University of Belfast.

RESULTS

A total of 1474 transfusion episodes were included in the study, accounting for the use of 3,804 units of RBCs, or 6.1% of all RBC issues in Northern Ireland during 2005. A median of 2 units (range, 1-28 units) was given per transfusion episode. The median age of transfusion recipients was 71 years (range, 19-100 years) and 53% were female. The mean pretransfusion Hb was 8.0 g/dL (SD, 1.4 g/dL), and the mean posttransfusion Hb was 10.3 g/dL (SD, 1.5 g/dL). The mean change in Hb per RBC unit transfused was 0.98 g/dL. A more detailed account of the epidemiology of RBC use within this sample has been described in a previous publication.[23]

Data quality was generally good, with missing data notable in three variables only: weight, 38% (558/1474) missing, more frequently among females (57%) and those in the oldest age group (31%); posttransfusion Hb, 13% (197/1474) missing, more frequently among outpatients (65%) and patients treated for hematologic conditions (34%); and the grade of the prescribing clinician, 14% (209/1474) missing.

A missing data category was created to account for missing weight and grade of prescriber information, allowing a more complete sample to remain in the modeling. We considered data imputation for those patients with missing posttransfusion Hb for the analysis of overtransfusion. However, given the number of variables that could have influenced the data imputation, we reasoned that the cleanest and most transparent way of dealing with this missing data was to exclude those patients from the overtransfusion regression analysis. Nevertheless, as the proportion of missing data overall was small, it is unlikely to change the outcome of the analyses.

Inappropriate transfusion

Based on the Hb thresholds defined in Table 3, 332 (23%; 95% CI, 20.4-24.7) of 1474 transfusion episodes were classified as inappropriate, accounting for the use of 735 units of RBCs (19%; 95% CI, 18.1-20.6). In an unadjusted analysis, inappropriate transfusions were observed more commonly among patients who were younger and with higher Hb values. Other factors associated with inappropriate transfusion were absence of comorbidity and undergoing surgery. Patients experiencing additional unexpected perioperative blood loss were less likely to be inappropriately transfused (Table 3).

The level of inappropriate transfusion observed varied by the primary condition being treated. Using gastrointestinal disorders as the reference category, patients treated primarily for a cardiac condition had the lowest level of inappropriate transfusion (OR, 0.32; 95% CI, 0.1-1.01). This group also had significantly lower Hb levels (7.6 g/dL; $p < 0.001$) and significantly higher comorbidity (3.3 serious comorbidities; $p < 0.001$).

The highest levels of inappropriate transfusion were found among patients with urologic (30%) or gynecologic conditions (30%; OR, 1.51; 95% CI, 1.04-2.20 and OR, 1.50; 95% CI, 1.17-1.93, respectively; Table 3). These two groups

TABLE 3. Logistic regression analysis of the appropriateness of transfusion: patient characteristics (inappropriate transfusion: 0 = no; 1 = yes)*

	Inappropriate transfusion†		Unadjusted risk		
Clinical factors	Yes	No	OR	95% CI	p value
Sex—reference category: male					
Male	154 (22)	534 (78)		Reference category	
Female	178 (23)	608 (77)	1.02	0.82-1.26	0.89
Age—reference category: at least 18 years old but not greater than 45 years old					
18≥, years, <45	60 (31)	135 (69)		Reference category	
45≥, years, <60	83 (35)	153 (65)	1.22	0.82-1.81	0.32
60≥, years, <70	67 (23)	220 (77)	0.69	0.39-1.21	0.19
70≥, years, <80	64 (17)	319 (83)	0.45	0.28-0.74	0.002
80≥ years	58 (16)	315 (85)	0.41	0.27-0.64	<0.001
Patient weight (kg)—reference category: at least 65 kg but not greater than 85 kg					
<65 kg	87 (22)	303 (78)	0.99	0.73-1.35	0.97
65≥, kg, <85	82 (22)	284 (78)		Reference category	
≥85 kg	36 (23)	124 (77)	1.01	0.68-1.48	0.98
Missing	127 (23)	431 (77)	1.02	0.67-1.56	0.93
Pretransfusion Hb—reference category: at least 7 g/dL but not greater than 8 g/dL‡					
Hb < 7 g/dL		295 (100)		Perfectly predicts appropriateness	
7≥, Hb, <8 g/dL	69 (15)	407 (85)		Reference category	
8≥, Hb, <9 g/dL	88 (20)	345 (80)	1.50	1.14-1.98	0.004
9≥, Hb, <10 g/dL	95 (50)	95 (50)	5.90	3.76-9.26	<0.001
Hb 10 ≥ g/dL	78 (100)			Perfectly predicts appropriateness	
Burden of disease—reference category: no other comorbidity					
No other comorbidity	35 (38)	56 (62)		Reference category	
1	91 (36)	163 (64)	0.89	0.54-1.49	0.66
≥2	206 (18)	923 (82)	0.36	0.20-0.64	0.001
Bleeding—reference category: medical, no bleeding					
Medical, no bleeding	142 (23)	475 (77)		Reference category	
Medical, bleeding	69 (16)	360 (84)	0.64	0.48-0.86	0.003
Surgical, bleeding	109 (34)	214 (66)	1.70	1.14-2.55	0.009
Surgical, additional perioperative bleeding	12 (11)	93 (89)	0.43	0.24-0.79	0.006
Presenting condition—reference category: gastrointestinal					
Gastrointestinal	95 (22)	334 (78)		Reference category	
Gynecology	38 (30)	89 (70)	1.50	1.17-1.93	0.002
Hematology	46 (21)	176 (79)	0.92	0.64-1.32	0.64
Cardiac	9 (8)	100 (92)	0.32	0.11-0.91	0.03
Respiratory	15 (17)	73 (83)	0.72	0.49-1.06	0.09
Orthopedic	53 (28)	139 (72)	1.34	0.89-2.02	0.16
Urologic	33 (30)	77 (70)	1.51	1.04-2.19	0.03
Vascular	19 (23)	63 (77)	1.06	0.60-1.87	0.84
Other	24 (21)	91 (79)	0.93	0.59-1.45	0.75
Cancer-related hospital admission—reference category: not cancer related					
No	218 (21)	834 (79)		Reference category	
Yes	114 (27)	308 (73)	1.41	1.09-1.84	0.009

* Adjusted for clustering by hospital.
† Data are reported as number (%).
‡ Excluding patients with an Hb level of less than 7 or more than 10 g/dL: patients with this Hb value predict the appropriateness category perfectly.

tended to have higher pretransfusion Hb values, 8.1 and 8.2 g/dL ($p < 0.001$), while gynecology patients were younger (45 years old; $p = 0.001$) with low comorbidity (1.4 comorbidities; $p < 0.0001$). Patients being treated for cancer also had a higher risk of inappropriate transfusion (OR, 1.41; 95% CI, 1.09-1.84). This group tended to be younger with 59% compared to 45% below the age of 70 years of age ($p < 0.001$). They also had a significantly higher pretransfusion Hb level, 8.2 g/dL compared to 7.9 g/dL ($p < 0.001$), with only 11% of patients in the cancer group having an Hb level below 7 g/dL (compared to 24% of noncancer patients [$p < 0.001$]).

Overall, surgical patients were more likely to be inappropriately transfused than medical patients (OR, 1.56; 95% CI, 1.17-2.08; Table 4). However, when the nature of surgical bleeding was considered, it was observed that inappropriate transfusions occurred more frequently among those patients without bleeding complications (OR, 1.7; 95% CI, 1.14-2.55), while those with additional perioperative bleeding were observed to have more appropriate transfusions (OR, 0.43; 95% CI, 0.24-0.79).

There appeared to be a higher proportion of inappropriate transfusions (31%) among the patients in whom the transfusion was prescribed by a consultant compared to other grades of clinician, specialist registrar (21%), senior house office (17%), and junior house officer (21%; $p = 0.0001$). However, missing prescriber data (13% [197/1474] of information regarding prescriber grade) makes it

TABLE 4. Logistic regression analysis of the appropriateness of transfusion: setting characteristics (inappropriate transfusion: 0 = no; 1 = yes)

	Inappropriate transfusion*		Unadjusted risk†		
Clinical factors	Yes	No	OR	95% CI	p value
Patient setting—reference category: medical					
Medical	211 (20)	835 (80)		Reference category	
Surgical	121 (28)	307 (72)	1.56	1.17-2.08	0.002
Treatment setting—reference category: outpatient					
Outpatient	41 (26)	118 (74)		Reference category	
Inpatient	291 (22)	1024 (78)	0.82	0.59-1.13	0.22
Grade of prescribing clinician—reference category: JHO					
JHO	35 (22)	125 (78)		Reference category	
SHO	63 (17)	300 (83)	0.75	0.39-1.45	0.39
SpR	38 (21)	147 (79)	0.92	0.53-1.62	0.78
Consultant	143 (31)	313 (69)	1.63	1.13-2.36	0.009
Multiple prescriber	2 (11)	16 (89)	0.45	0.08-2.58	0.37
Missing	51 (17)	241 (83)	0.78	0.45-1.26	0.29

* Data are reported as number (%).
† Adjusted for clustering by hospital.
JHO = junior house officer; SHO = senior house office; SpR = specialist registrar.

TABLE 5. Overtransfusion among appropriately transfused patients*

Appropriateness criteria (g/dL)	Patients overtransfused	Units overtransfused†	Median difference between pretransfusion Hb and appropriate Hb thresholds (range)‡	Median units transfused
7	21/36 (58%)	32	0.4 (0.1-2.6) to 2.4 (2.1-4.6)	3 (1-8)
8	26/57 (46%)	33	0.9 (0.1-3.7) to 2.9 (2.1-5.7)	2 (1-5)
9	95/463 (21%)	96	1.3 (0.1-5.0) to 3.3 (2.1-7.0)	2 (1-16)
10	47/435 (11%)	46	2.2 (0.1-6.0) to 4.2 (2.1-8.0)	2 (1-28)
Overall	189/991	207	1.6 (0.1-6.0) to 3.6 (2.1-8.0)	2 (1-28)

* Appropriately transfused patients and patients with posttransfusion Hb recorded only.
† This was calculated by summing the difference between the overtransfusion threshold Hb and the posttransfusion Hb, with each 1 g/dL difference estimated to be one unit of RBCs.
‡ This was calculated by subtracting the pretransfusion Hb from the Hb thresholds: appropriate transfusion threshold to target posttransfusion Hb threshold (Table 1).

difficult to draw firm conclusions about the level of inappropriate prescribing by clinician grade.

Inappropriate transfusions were most common among the group of patients for whom the lowest transfusion threshold (Hb 7 g/dL) applied. A total of 143 patients (79%; 95% CI, 72.9-84.9) of a possible 182 patients in this group were inappropriately transfused. As the transfusion threshold increased, the number of inappropriate transfusions fell from 63 of 128 patients (49%; 95% CI, 40.3-58.2) in the 8 g/dL threshold group to 88/595 patients (15%; 95% CI, 12.0-17.9) in the 9 g/dL group and 38 of 569 patients (7%; 95% CI, 4.77-9.05) in the 10 g/dL threshold group.

Overtransfusion

Of the 1142 patients classified as appropriately transfused, 151 (receiving 396 units of RBCs) had a missing posttransfusion Hb result, prohibiting an assessment of potential overtransfusion. These patients were predominantly in the highest Hb threshold group (96/151; 64%), being treated for a hematologic condition (60/151; 40%) and not undergoing a surgical procedure (142/151; 95%).

By our criteria, 189 of 991 evaluable patients (19%; 95% CI, 16.7-21.7) were overtransfused (Table 5). Using an unadjusted analysis, overtransfusion was more common among females, nonsurgical patients, and patients of lower weight (Table 6). The association of overtransfusion with weight is likely to be confounded by the association with sex, because females were generally lighter (mean, 64.1 kg vs. 74.3 kg for females and males, respectively, $p < 0.0001$). This size and blood volume differential is likely to account for the finding that females tended to have a greater mean change in Hb per unit transfused than males, 1.10 g/dL compared to 0.86 g/dL, respectively. This relationship is further supported by the observed mean increase in Hb per unit transfused by weight group: less than 65 kg group 1.31 (SD, 0.6) g/dL, 65 to 85 kg group 1 (SD, 0.55) g/dL, and more than 85 kg group 0.83 (SD, 0.41) g/dL. By this argument, lighter females are more likely to exceed the Hb definition of overtransfusion than heavier males with the same pretransfusion Hb level given a similar volume of blood.

The sum of the differences between the posttransfusion Hb and the overtransfusion Hb threshold for all evaluable patients was equivalent to 207 RBC units. Thus,

TABLE 6. Multiple logistic regression analysis of overtransfusion (overtransfused transfusion: 0 no; 1 yes)*

Clinical factors	Overtransfused patients†		Unadjusted analysis				Adjusted analysis			
	Yes	No	OR	95% CI		p value	OR	95% CI		p value
Sex—reference category: male										
Male	62 (13)	405 (87)				Reference category				
Female	127 (24)	397 (76)	2.09	1.53	2.86	<0.001	1.88	1.35	2.61	<0.001
Age—reference category: at least 18 years old but not greater than 45 years old										
18≥, years, <45	21 (18)	97 (82)				Reference category				
45≥, years, <60	24 (18)	112 (82)	0.99	0.48	2.04	0.98	1.30	0.55	3.03	0.55
60≥, years, <70	31 (16)	160 (84)	0.89	0.52	1.54	0.69	1.14	0.61	2.12	0.68
70≥, years, <80	48 (18)	223 (82)	0.99	0.77	1.28	0.96	1.18	0.79	1.74	0.42
80≥ years	65 (24)	210 (76)	1.42	0.73	2.79	0.30	1.60	0.93	2.76	0.09
Patient weight (kg)—reference category: at least 65 kg but not greater than 85 kg										
<65 kg	67 (26)	195 (74)	2.31	1.49	3.58	<0.001	1.70	1.07	2.69	0.02
65≥, kg, <85	33 (13)	222 (87)				Reference category				
≥85 kg	8 (7)	105 (93)	0.51	0.39	0.68	<0.001	0.51	0.35	0.76	0.001
Missing	81 (22)	289 (78)	1.95	1.31	2.90	0.001	1.69	1.04	2.72	0.03
Pretransfusion Hb—reference category: less than or equal to 7 g/dL										
Hb < 7 g/dL	62 (23)	209 (77)				Reference category				
7≥, Hb, <8 g/dL	44 (12)	318 (88)	0.47	0.35	0.63	<0.001	0.47	0.34	0.65	<0.001
8≥, Hb, <9 g/dL	66 (23)	224 (77)	0.99	0.67	1.47	0.97	1.08	0.77	1.53	0.63
9≥, Hb, <10 g/dL	17 (25)	51 (75)	1.12	0.65	1.94	0.68	1.43	0.72	2.88	0.31
Burden of disease—reference category: no comorbidity										
None	8 (20)	33 (80)				Reference category				
One	33 (24)	103 (76)	1.32	0.59	2.98	0.50	1.10	0.46	2.64	0.82
≥2	148 (18)	666 (18)	0.92	0.42	2.01	0.82	0.71	0.23	2.17	0.55
Bleeding—reference category: no bleeding										
Medical, none	95 (26)	271 (74)				Reference category				
Medical, bleeding	48 (15)	278 (85)	0.49	0.30	0.92	0.006	0.34	0.19	0.60	<0.001
Surgical, bleeding	37 (18)	172 (82)	0.61	0.36	1.05	0.08	0.81	0.58	1.14	0.22
Surgical, additional perioperative bleeding	9 (10)	81 (90)	0.31	0.12	0.81	0.02	0.31	0.10	0.92	0.04
Presenting condition—reference category: gastrointestinal										
Gastrointestinal	62 (20)	245 (80)				Reference category				
Gynecology	14 (20)	55 (80)	1.01	0.59	1.71	0.98	0.68	0.36	1.31	0.25
Hematology	27 (23)	89 (77)	1.20	0.58	2.50	0.63	0.63	0.31	1.28	0.20
Cardiac	11 (12)	80 (88)	0.54	0.24	1.23	0.14	0.45	0.17	1.22	0.12
Respiratory	19 (30)	45 (70)	1.67	0.83	3.36	0.15	1.01	0.46	2.18	0.99
Orthopedic	20 (15)	113 (85)	0.70	0.41	1.18	0.18	0.37	0.19	0.74	0.005
Urologic	11 (16)	57 (84)	0.76	0.39	1.51	0.44	0.69	0.31	1.50	0.35
Vascular	10 (17)	48 (83)	0.82	0.41	1.67	0.59	0.74	0.34	1.63	0.46
Other	15 (18)	70 (82)	0.85	0.43	1.66	0.63	0.76	0.34	1.69	0.50
Cancer-related hospital admission—reference category: no										
No	136 (18)	606 (82)				Reference category				
Yes	53 (21)	196 (79)	1.20	0.80	1.81	0.37	0.98	0.77	1.26	0.90
Treatment setting—reference category: outpatient										
Outpatient	7 (18)	33 (82)				Reference category				
Inpatient	182 (19)	769 (81)	1.12	0.59	2.11	0.74	2.05	0.77	5.44	0.15

* Adjusted for clustering by hospital.
† Data are reported as number (%).

7.7% (95% CI, 6.8%-8.8%) of the 2763 units of RBCs prescribed for these patients could be considered to be excessive.

A multiple logistic regression analysis was conducted to identify factors that were independently associated with overtransfusion. Variables were selected for inclusion in the model on the basis of the unadjusted analysis. Bleeding status rather than patient management (medical or surgical) was used to evaluate the role of blood loss. Grade of prescribing clinician was omitted from the final model, as there were no associations identified when this variable was included (analysis not shown).

Several variables were shown to be independently associated with overtransfusion (Table 6). Female sex (OR, 1.88; 95% CI, 1.35-2.60) and patients weighing less than 65 kg (OR, 1.70; 95% CI, 1.07-2.69) were at higher risk of overtransfusion. Patients with Hb levels between 7 and 8 g/dL (OR, 0.47; 95% CI, 0.34-0.65), weighing 85 kg or more (OR, 0.51; 95% CI, 0.35-0.76), being treated for an orthopedic condition (OR, 0.37; 95% CI, 0.19-0.74), or with medical bleeding (OR, 0.34; 95% CI, 0.19-060) or additional perioperative surgical bleeding (OR, 0.31; 95% CI, 0.10-0.92) were at lower risk. In the final adjusted model, the Hosmer-Lemeshow test ($\chi^2 = 7.65$, $p = 0.47$, d.f. = 8) and the area under the receiver operating curve (C = 0.72) demonstrated that the model fitted the data well.

DISCUSSION

Right decision?

The absolute level of inappropriate RBC transfusion recorded in our study (23%) falls within the midrange of results reported in other studies of 4 to 66%.[8] Different study time periods, practice guidelines, study designs, and in particular the influence of the specific appropriateness criteria are likely contributors to the variation in results reported and also make it difficult to compare absolute levels of inappropriate transfusion across studies.[7,8] Had we applied criteria specified by, for example, the American Society of Anesthesiologists,[2,3] we would have reported a higher estimate of the level of inappropriate transfusion as this guideline recommends a lower transfusion threshold (6 g/dL), compared to the regional transfusion guidelines promoted within Northern Ireland (7 g/L).[5,24]

Variables associated with higher levels of inappropriate transfusion in our study were a higher pretransfusion Hb level and younger age and lower levels of comorbidity. The latter association is likely to be confounded by the relationship with age, as comorbidity tends to increase with age ($r = 0.51$, $p < 0.0001$). More restrictive Hb thresholds were applied for younger patients, those without significant comorbidity, and those in whom bleeding was not a problem, and these were the groups that by our criteria had the highest level of inappropriate transfusion. This is in keeping with the findings of others who have concluded that restrictive transfusion policies are associated with increased levels of inappropriate transfusion observed.[7,8] While the influence of age and Hb should have been taken into account as they were constituent parts of the criteria used to define appropriate practice, there were still differences detected across groups of patients defined by these variables. This would suggest that clinicians give more weight to these factors when considering transfusion than do guideline writers.

Variation in the level of inappropriate transfusion observed among different clinical specialties is likely to be explained at least in part by the characteristics of the patients typically treated in those specialties. The higher levels of inappropriate transfusion found among younger patients, patients in the gynecology and obstetrics population, and the relatively younger patients undergoing cancer treatment are consistent with hypothesis. Patients in the aforementioned specialties also had the highest pretransfusion Hb levels of the study population.

Surgical patients were more likely to receive an inappropriate RBC transfusion. When taking into account bleeding status, surgical patients without bleeding complications were at the highest risk of receiving an inappropriate transfusion. As information on the actual amount of blood loss recorded in the clinical records was inconsistent, it is not possible to establish whether those with less blood loss were those that were being transfused inappropriately. Despite evidence of the positive influence of the Maximum Surgical Blood Ordering Schedule on transfusion practice,[25] it is possible that some blood cross matched under the Maximum Surgical Blood Ordering Schedule is transfused because it is available rather than clinically required.[26,27]

The high level of appropriate practice in cardiac specialties may be due to the use of specialist practice protocols that incorporate transfusion guidelines, combined with the higher Hb threshold for transfusion (9 g/dL) for patients with cardiac conditions. Similar levels of compliance have been observed in other highly specialized areas with closely monitored patients, for example, only 3% of patients were inappropriately transfused in a study set in intensive care.[28]

Right amount?

Guidance is lacking on a desirable posttransfusion target Hb range. The unnecessary risk to patients of prescribing multiple units (particularly pairs of RBCs) based on habit and not on evidence or patient need has been highlighted[29] and reassessment after transfusion of each unit is recommended before prescribing further units.[11,30]

In common with other reports,[11] our study found that the posttransfusion target Hb was consistently around 10 g/dL regardless of the pretransfusion Hb and the appli-

cable Hb threshold. Interestingly, the mean Hb level at which transfusion was initiated was similar (8 g/dL) in each "threshold group" and a median of 2 units was transfused per episode; thus the mean posttransfusion Hb result of 10 g/dL could be predicted. This traditional target of 10 g/dL (30% hematocrit [Hct]) may be perpetuating overtransfusion, particularly among patients with a low Hb threshold (7 or 8 g/dL) where a lower posttransfusion target may be acceptable.

Applying our definition of overtransfusion based on the Hb transfusion threshold, we found that 19% of patients who had an otherwise appropriate transfusion were overtransfused. If the patients who were inappropriately transfused, and therefore by definition overtransfused, were included, the figure increases to at least 521 of 1142 (46%).

When attempting to compare the absolute levels of overtransfusion observed with those reported in other studies, similar problems to those encountered when comparing levels of inappropriate transfusion are apparent. Mold and Allard,[13] using a similar approach to that employed in our study, found much higher levels of overtransfusion (51.5%). However, their study was limited in size (54 patients), was conducted over 1 month only, and was restricted to general medical patients. In our study, 20.7% of medical patients were judged to be overtransfused. Joshi and coworkers[12] found 24% of patients undergoing elective primary total hip arthroplasty were overtransfused (discharge Hct were above 36%), a much higher level than that observed for orthopedic surgical patients in our study (12% overtransfused). Grey and Finlayson[11] noted that 75% of patients in their audit of severe iron deficiency anemia had posttransfusion Hb levels in excess of 10 g/dL, which they suggested indicated excessive transfusion.

The elderly (>80 years old), females, and those of lower weight were at the highest risk of overtransfusion. As previously mentioned, lighter females are more likely to exceed the target Hb than heavier males with the same pretransfusion Hb level when a similar volume of blood is transfused. Overtransfusion was also more commonly observed among patients with missing weight values. As noted, within the missing weight category there were a higher proportion of females (57%) and those aged over 80 years old (31%), which may explain the higher risk of overtransfusion observed, as these patients were typically lighter in weight.

Patients with medical bleeding or bleeding complications of surgery were less likely to be overtransfused. It is reasonable to assume that active bleeding reduced the chance of our posttransfusion Hb target being exceeded.

Limitations

The retrospective collation of data from clinical records is time-consuming, and inevitably leads to a delay in providing results. However, the guidelines in Northern Ireland and the United Kingdom have remained unchanged since our study was undertaken, and in the absence of other drivers of change, the results are still likely to be relevant.

Retrospective analysis of medical records can readily access details such as age and sex. However, other important factors pertinent to the transfusion decision are much less likely to be documented, for example, the ability to tolerate anemia, anticipated future blood loss, and patient beliefs as well as the physician's education, experience, and personality.[31-33] Such missing information may contribute to misclassification of behavior,[34] accounting for some of the observed differences among studies. In addition, poor documentation of transfusion events is highly correlated with inappropriate transfusions.[35]

The choice of a posttransfusion Hb target that delineates overtransfusion is also likely to influence the levels of overtransfusion reported. Our choice of a 2 g/dL target zone may be construed as generous and thus underestimate the actual level of overtransfusion. However, it is likely to reflect clinical thinking that must consider not only the level of Hb that is safe, but also the likelihood that the cause of the low Hb is reversible by means other than transfusion, the rate at which this might occur, and whether any significant harm is likely to ensue as a result of waiting for physiologic recovery where this is expected.

CONCLUSION

Our study adds to those that report ongoing inappropriate and overtransfusion. While variation in the absolute rates observed is likely to reflect differences in the definitions of "appropriate" applied, we concur with other authors who suggest that a significant proportion of clinicians appear to be uncomfortable with the transfusion thresholds suggested by current guidelines. In addition, we suggest that the lack of guidance on appropriate posttransfusion target Hb ranges is likely to compound the variation in transfusion practice observed.

Increasing awareness of the interaction between body size, sex, and the effects of transfusion of a standard RBC unit on Hb levels may help to limit overtransfusion. However, more fruitful issues for further research are likely to be an assessment of the barriers to the implementation of current guidelines on transfusion thresholds, and the development of a concept of a "safe" Hb range that takes into account a patient's likely physiologic response to anemia to assess the appropriateness of RBC transfusion.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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