Transfusion rates vary significantly amongst Canadian medical centres

[Les taux de transfusion varient de façon significative dans les centres médicaux canadiens]

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Purpose: To document variation of transfusion practice following repair of hip fracture or cardiac surgery, as well as those requiring intensive care following a surgical intervention or multiple trauma (high risk patients).

Methods: We documented rates of allogeneic red cell transfusion in 41,568 patients admitted to 11 hospitals across Canada between August 1998 and August 2000 as part of a retrospective observational cohort study. In the subgroup of 7,552 patients receiving red cells, we also compared mean nadir hemoglobin concentrations from centre to centre.

Results: The overall rate of red cell transfusion was 38.7%, and ranged from 23.8% to 51.9% across centres among the 41,568 perioperative and critically ill patients. Women were more likely to be transfused (43.7% *vs* 35.3%, $P < 0.0001$), with higher rates of transfusion in eight of 11 centres. Compared to a chosen reference hospital having a crude transfusion rate near the median, the adjusted odds of transfusion ranged from 0.44 to 1.53 overall, from 0.42 to 1.22 in patients undergoing a hip fracture repair, from 0.72 to 3.17 in cardiac surgical patients undergoing cardiac surgery, and from 0.27 to 1.11 in critically ill and trauma patients. In the 7,552 transfused patients, the mean adjusted nadir hemoglobin was 74.0 ± 4.83 $g{\cdot}L^{-1}$ overall, and ranged from 66.9 ± 1.7 $g{\cdot}L^{-1}$ to 84.5 ± 1.6 $g{\cdot}L^{-1}$ across centres. Similar differences among centres were observed amongst hip fracture patients (71.2 ± 2.9 $g{\cdot}L^{-1}$ to 82.8 ± 1.7 $g{\cdot}L^{-1}$), cardiac surgical patients (65.7 ± 1.1 $g{\cdot}L^{-1}$ to 77.3 ± 1.0 $g{\cdot}L^{-1}$) and critically ill and trauma patients (66.1 ± 3.04 $g{\cdot}L^{-1}$ to 87.5 ± 2.5 $g{\cdot}L^{-1}$).

Conclusion: We noted significant differences in the rates of red cell transfusion and nadir hemoglobin concentrations in various surgical and critical care settings.

Objectif : *Documenter les variations dans la pratique des transfusions à la suite d'une réparation de fracture de la hanche ou d'une intervention chirurgicale cardiaque, de même que des transfusions chez des patients de soins intensifs à la suite d'une intervention chirurgicale ou d'un polytraumatisme (patients à haut risque).*

Méthode : *Nous avons vérifié les taux de transfusion allogéniques chez 41 568 patients admis dans 11 hôpitaux canadiens entre août 1998 et août 2000 dans le cadre d'une étude rétrospective de cohorte par observation. Dans le sous-groupe de 7 552 patients transfusés, nous avons aussi comparé la moyenne des concentrations d'hémoglobine minimales d'un centre à l'autre.*

Résultats : *Le taux global de transfusion de culots globulaires a été de 38,7 %, allant de 23,8 % à 51,9 % entre les centres parmi les 41 568 patients périopératoires et les grands malades. Les femmes étaient plus souvent transfusées (43,7 % vs 35,3 %, $P < 0,0001$), selon des taux plus élevés dans 8 centres sur 11. Comparées à celles d'un hôpital de référence choisi ayant un taux précis de transfusion près de la médiane, les probabilités de transfusion ajustées allaient de 0,44 à 1,53 globalement, de 0,42 à 1,22 chez les opérés à la hanche, de 0,72 à 3,17 chez les patients de cardiochirurgie et de 0,27 à 1,11 chez les grands malades et les polytraumatisés. Chez les 7 552 patients transfusés, la concentration minimale d'hémoglobine ajustée était de 74,0 ± 4,83 $g{\cdot}L^{-1}$ globalement et de 66,9 ± 1,7 $g{\cdot}L^{-1}$ à 84,5 ± 1,6 $g{\cdot}L^{-1}$ entre les centres. Des différences similaires ont été observées dans les centres parmi les patients avec fracture de la hanche (71,2 ± 2,9 $g{\cdot}L^{-1}$ à 82,8 ± 1,7 $g{\cdot}L^{-1}$), les patients de cardiochirurgie (65,7 ± 1,1 $g{\cdot}L^{-1}$ à 77,3 ± 1,0 $g{\cdot}L^{-1}$) et les grands malades et les polytraumatisés (66,1 ± 3,04 $g{\cdot}L^{-1}$ à 87,5 ± 2,5 $g{\cdot}L^{-1}$).*

Conclusion : *Les taux de transfusion de culots globulaires et les concentrations minimales d'hémoglobine diffèrent significativement en fonction de divers soins chirurgicaux et intensifs.*

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This study was in part sponsored by a grant from the Canadian Institutes of Health Research and an unrestricted grant from Ortho-Biotech, Canada.

Accepted for publication October 4, 2004.
Revision accepted February 15, 2005.

DESPITE a number of blood conservation strategies and ongoing concerns regarding transfusion-transmitted infections, red blood cells (RBC) remain an important life-saving therapy in perioperative and critical care.[1] Indeed, a significant proportion of the entire blood supply is administered to critically ill patients, following multiple trauma and in the perioperative setting, particularly following hip fracture repair or cardiac surgery. Brien *et al.*[2] documented that 56% of all red cells were administered to surgical patients, while a study by Ghali[3] documented that 69% of red cells are transfused into surgical patients.

Exploring practice variation in various clinical settings has become an important tool in the assessment of health services. If significant practice variation is documented, this should provide the impetus to explore reasons for such variation, which may include the lack of high quality evidence, or where evidence is solid, problems in the dissemination or uptake of the existing evidence. In transfusion medicine, significant practice variation has been documented within specific disease categories,[4,5] clinical settings and surgical procedures,[6] including hip[7–10] and knee[7,9,10] arthroplasty and coronary revascularization [or coronary artery bypass grafting (CABG)].[11–13] Controlling for population differences, blood loss and pump time, a prospective audit conducted on CABG patients[13] identified that transfusion factors such as the nadir and discharge hematocrits accounted for significant variation in blood use among 18 tertiary care hospitals. In similar patients, Surgenor and colleagues[11] found that there were significant differences in the percentage of patients transfused between hospitals. Hébert *et al.* found a significant variation in transfusion practice (in terms of nadir hemoglobin concentrations) among six Canadian intensive care units (ICUs) after controlling for the effects of disease severity, diagnosis, age and gender. Thus, significant differences in the approach to allogeneic red cell transfusions have been consistently observed among institutions. However, there are few recent studies exploring practice variation, despite the publication of clinical trials addressing this issue and significant improvements in blood safety.[14,15] Therefore, we examined transfusion practice across 11 Canadian academic and community hospitals caring for the critically ill, as well as patients undergoing cardiac surgical procedures and hip fracture repair.

Methods

Study design and patient population

Clinical information was collected as part of a large retrospective observational cohort examining clinical outcomes before and after the implementation of a universal pre-storage leuko-reduction program involving Canada's entire blood supply.[16] In the leuko-reduction study, we identified all consecutive patients in three distinct high-risk categories: 1) patients requiring intraoperative repair of a hip fracture; 2) patients following cardiovascular surgery requiring cardiopulmonary bypass; and 3) postoperative and multiple trauma patients admitted to an ICU.

Patients were identified from the health records of participating hospitals as well as clinical databases at all participating institutions. We excluded patients who: were less than 16 yr of age; had been previously included in this study; died within the first 24 hr of hospital admission; did not survive 24 hr following the completion of the index surgical procedure or time of admission to the ICU. For the evaluation of nadir hemoglobin concentrations in transfused patients, we also excluded patients admitted with a diagnosis of infection prior to the first transfusion, patients who had previously been diagnosed with a hematological malignancy, or were considered brain dead.

We examined variation in allogeneic RBC transfusion practice amongst 41,568 patients seen at 11 major Canadian hospitals.

Data collection

The original study was approved by the Ethics Review Board at each participating centre. Using the eligibility criteria listed above, we identified all patients between June of 1998 and September of 2000 using either electronic hospital health records databases or information collected from the leuko-reduction study. In the original leuko-reduction study, we collected information from patient medical charts using a standardized case report form and a detailed procedures manual. All personnel performing data abstraction participated in a training session to ensure quality of the data, and were subsequently given a dummy protocol in order to mask the intent of the initial study. Patient information abstracted and relevant to the current study included patient indication for transfusion (i.e., repair of hip fracture, cardiac surgery or admission to the ICU following surgery or multiple trauma), gender, date of birth, date of hospital admission, medical centre at which the patient was seen, nadir hemoglobin level, total number of transfusions administered, leuko-reduction status of blood products administered (i.e., prior to or following the implementation of universal leuko-reduction), date of hospital discharge, vital status at discharge and length of stay in hospital. Information for patients who did not receive allogeneic red cells included the procedure or diagnosis, the centre, patient age and gender, dates of

TABLE Patient demographics

Patient group/ measure	*All patients (n = 41,568)*	*Transfused patients (n = 7,552 of 41,568 patients)*
Repair of hip fracture		
Total # (% of total)	3,945 (9.5%)	836 (11.1%)
% female	71.8%	74.9%
Median site level (range)	10% (4.1%-32.9%)	17.4% (0.7%-33.7%)
Cardiac surgery		
Total # (% of total)	11,812 (28.4%)	3,584 (47.5%)
% female	29.1%	41.7%
Median site level (range)	40.6% (4%-55.3%)	52.1% (7.2%-75.1%)
ICU admission		
Total # (% of total)	25,811 (62.1%)	3,132 (41.5%)
% female	39.8%	41.4%
Median site level (range)	67.1% (37.4%-91.9%)	51.5% (13.3%-87.6%)
Age in yr (mean ± SD)		
Overall	62.3 ± 18.7	67.4 ± 14.6
Repair of hip fracture	77.8 ± 15.3	77.8 ± 16.5
Cardiac surgery	65.1 ± 11.6	68.3 ± 10.3
ICU admission	58.6 ± 20.3	63.5 ± 16.7

ICU = intensive care unit.

admission, surgery and hospital discharge and survival status at hospital discharge.

Statistical analysis

We compared baseline variables of transfused and non-transfused patients by evaluating measures of central tendency and dispersion. As an initial exploration of gender differences, we compared the proportion of patients receiving transfusions overall and by condition using a stratified Chi-square. To explore centre effects, we calculated rates and unadjusted odds ratios (OR; along with 95% confidence intervals) for each centre and for each major diagnostic grouping (ICU, cardiac surgery and hip fracture) within each centre. As a second step, we used logistic regression to calculate the adjusted odds of transfusion for each centre using centre J as a reference while adjusting for diagnostic grouping, age and gender. Site J was chosen because it was a large centre with a crude transfusion rate close to the median of the 11 sites, both overall and within each patient subgroup.

Nadir hemoglobin values in patients receiving allogeneic red cells were also used in the evaluation of centre effects. Adjusted mean values and 95% confidence intervals for nadir hemoglobin concentrations were calculated for all centres using analysis of covariance, in all transfused patients and within each of the three major diagnostic subgroups of interest. Explanatory variables included centre, gender, age, the presence of one of 12 major co-morbid conditions (ischemic heart disease, congestive heart failure, AIDS, severe immunosuppression, metastatic cancer, severe dementia, chronic renal failure, severe lung disease, disabling stroke, severe cirrhosis/hepatic failure, diabetes, mellitus and obesity), and severity of illness using APACHE II scores in the ICU patient subgroup.

All statistical analyses were carried out using SAS, version 8.1 (SAS Institute Inc., Cary, NC, USA).

Results

A total of 41,736 consecutive patients from 11 centres were identified between June 1st, 1998 and September 30th 2000. One hundred and sixty eight patients (0.4%) were excluded from the analysis of transfusion rates due to incomplete or incorrect data regarding patient type ($n = 159$), age ($n = 5$) and gender ($n = 4$). During this time interval, we enrolled 3,945 (9.5%) hip fracture patients, 11,812 (28.4%) cardiac surgical patients and 25,811 (62.1%) postoperative and critically ill patients (Table). Average ages and the proportion of women within each diagnostic group were comparable across centres. In a subset of 7,552 transfused patients, additional information was available on nadir hemoglobin levels and the number of transfusions administered during the first 30 days of hospitalization. In this subset, 35 (0.5%) patients had missing information on the presence of co-morbid illnesses; for these cases we assumed that there were no relevant co-morbid illnesses.

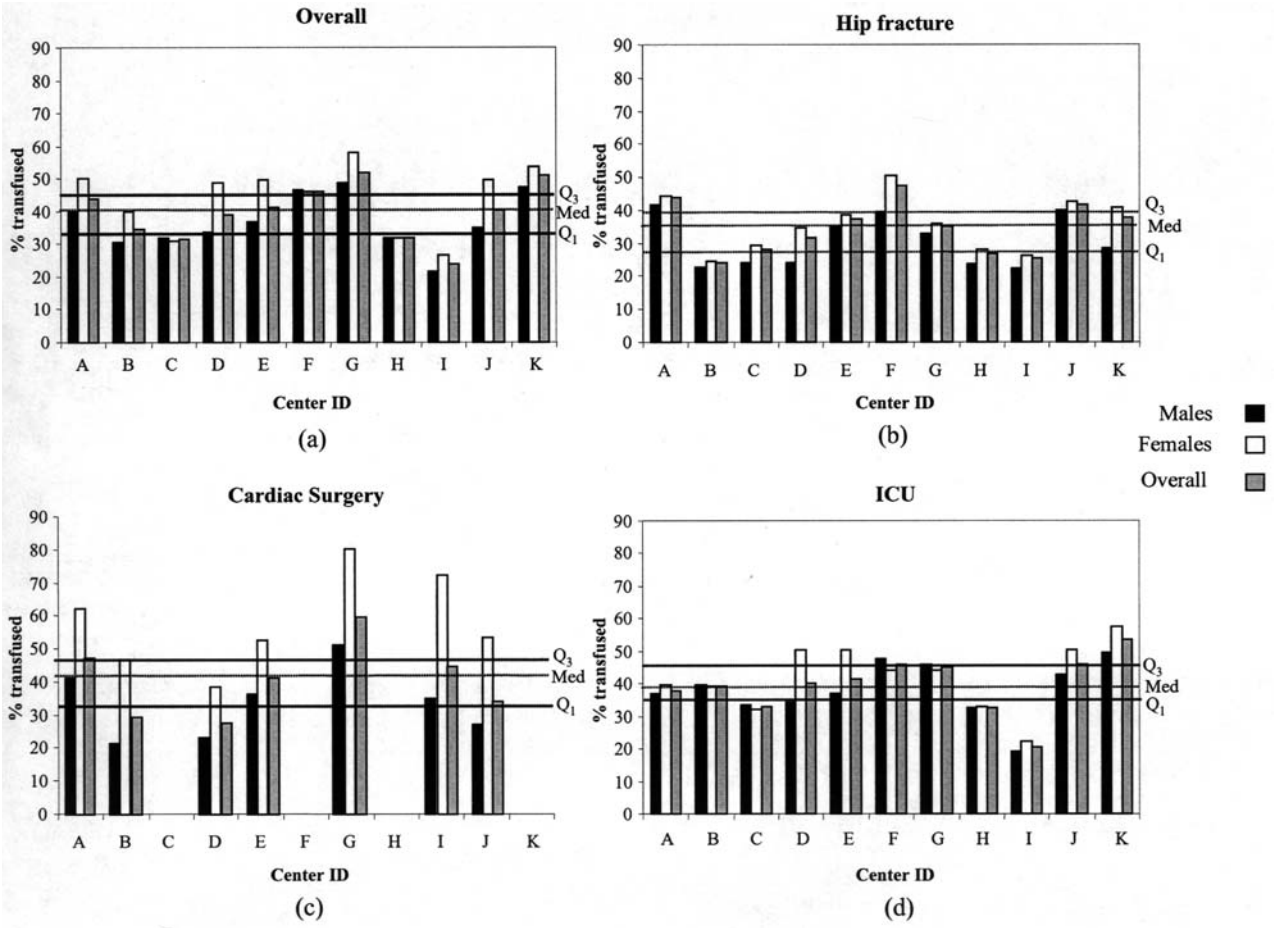

FIGURE 1 Gender-specific and overall crude rates of transfusion across the 11 centres included in the study for the four groups of patients of interest: (a) overall (n = 41,568), (b) repair of hip fracture patients (3,945), (c) cardiac surgery patients (n = 11,812) and (d) patients receiving post-surgical or post-traumatic intensive care unit care (n = 25,811). The horizontal dashed lines indicate the median, first quartile and third quartile transfusion rates amongst the 11 hospitals studied. ICU = intensive care unit.

Overall

The overall unadjusted rate of transfusion was 38.7%, and varied from 23.8% to 51.9% across centres. Transfused patients were older than non-transfused patients (67.4 ± 14.6 yr *vs* 60.6 ± 19.4 yr). Women were transfused more often than men (43.7% *vs* 35.3%, $P < 0.0001$; Figure 1), and the proportion of women administered red cells was higher than that of males in eight of 11 centres. As compared to centre J (OR = 1), we observed a range of adjusted odds of transfusion from 0.44 to 1.53 (Figure 2). The adjusted OR were significantly lower in centres B, C, H and I, and significantly higher in centres F, G and K. As a second index, we noted that the median number of transfusions per patient ranged from two to three units per patient across centres (Figure 3).

Hip fracture repair patients

The overall rate of transfusion amongst the 3,945 patients undergoing hip fracture repair was 34.4%, and varied from 24.3% to 47.6% across centres. Transfused patients were older than non-transfused patients (77.8 ± 16.5 yr *vs* 76.1 ± 15.5 yr), and females were transfused more frequently than males (35.5% *vs* 31.6%, $P = 0.0214$; Figure 1). After adjustment for the effects of age and gender, the odds of transfusion relative to centre J ranged from 0.42 to 1.22. Centres B, C, D, G, H and I were associated with significantly lower odds of transfusion, while no centre was associated with significantly higher odds. The median number of transfusions per patient ranged from two units to three units across centres (Figure 3).

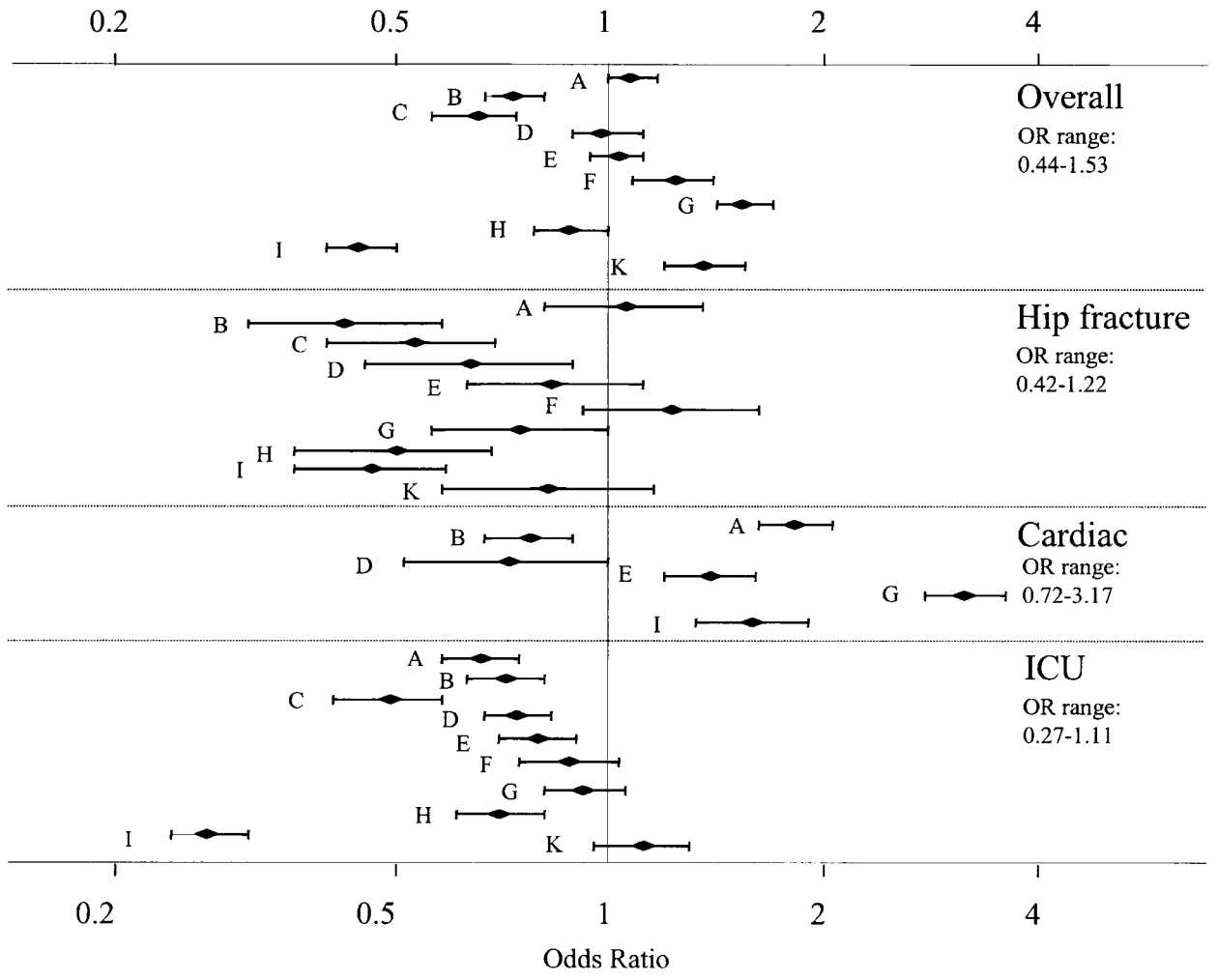

FIGURE 2 Between-centre variation in the odds of transfusion both overall, and within the three patient subgroups of interest. Site J was selected as the reference site for all comparisons, and statistical adjustments for the effects of age, gender and indication were made. ICU = intensive care unit.

Cardiac surgical patients

The 11,812 cardiac surgical patients were gathered from seven of 11 centres participating in this study. The proportion of cardiac surgical patients that received one or more transfusions at these sites was 43.8% overall, and ranged from 28.1% to 60.5% across centres. Transfused patients were older than non-transfused patients (68.3 ± 10.3 yr *vs* 62.9 ± 11.7 yr), and females were transfused more frequently than males (61.3% *vs* 36.6%, $P < 0.0001$; Figure 1). After adjustment for the effects of age and gender, the degree of variation across hospitals relative to centre J ranged from adjusted odds of 0.72 to 3.17. Centre B was associated with significantly lower odds of transfusion relative to site J, while sites A, E, G and I were associated with significantly higher adjusted odds of transfusion. The median number of transfusions per patient ranged from two units to three units across centres (Figure 3).

ICU patients

Amongst the 25,811 patients admitted to ICU for postoperative and trauma care, 36.9% received one or more red cell units, with rates varying between 20.4% and 53.4% between sites. Transfused patients were older than non-transfused patients (63.5 ± 16.7 yr *vs* 56.8 ± 20.9 yr), and females were transfused more frequently than males (40.1% *vs* 34.9%, $P < 0.0001$; Figure

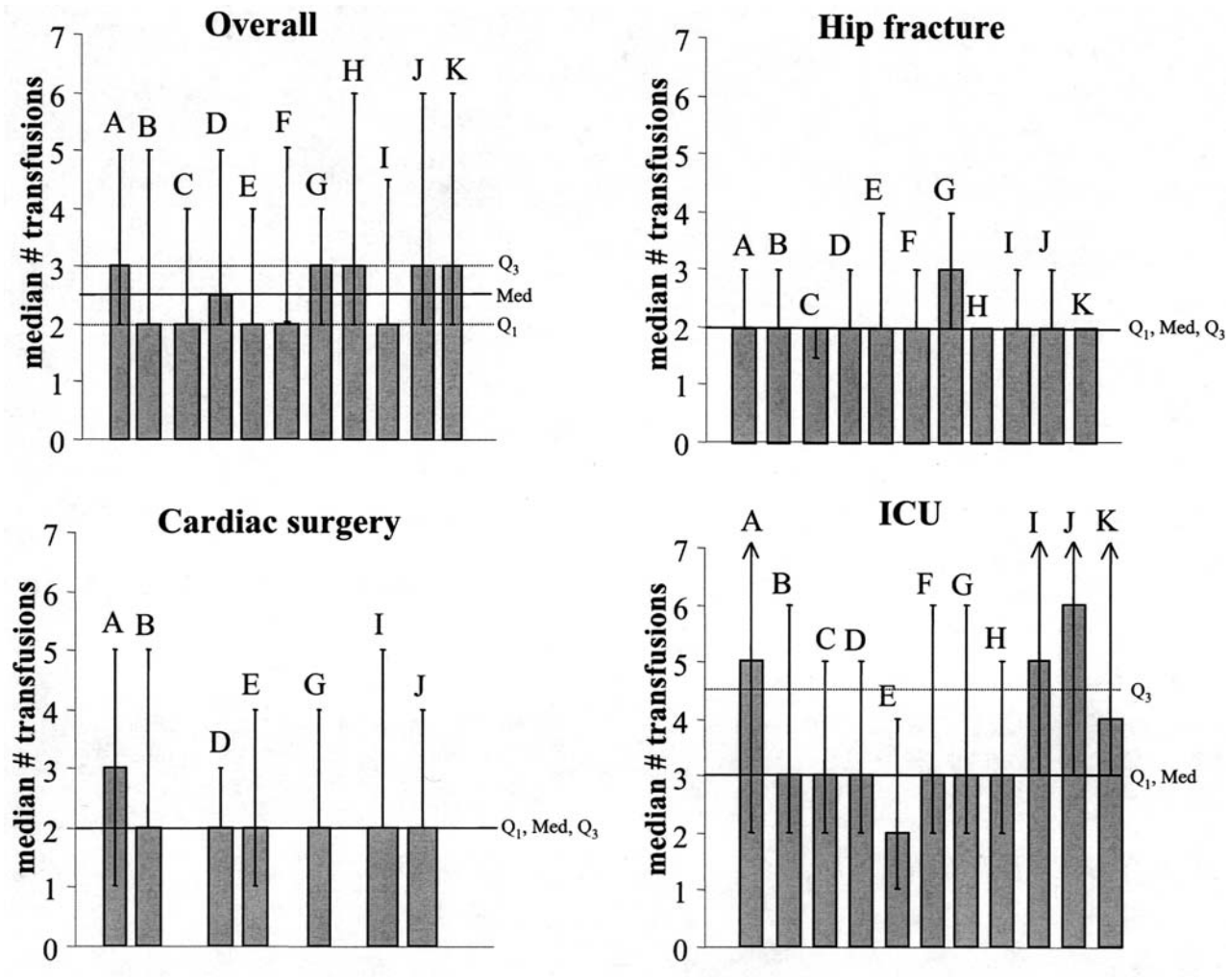

FIGURE 3 Distribution of the median number of transfusions amongst transfused patients at each of the 11 participating centres, along with their associated interquartile ranges. ICU = intensive care unit.

1). After adjustment for the effects of age and gender, the adjusted odds of transfusion as compared to centres J ranged from 0.27 to 1.11. Centres A, B, C, D, E, H and I had significantly lower odds of transfusion relative to centre J, while the remaining centres had comparable odds of transfusion (Figure 2). The median number of transfusions per patient ranged between two units and six units across centres (Figure 3).

Nadir hemoglobin levels within patient groups

In the subset of 7,552 patients receiving red cell transfusions, the mean adjusted nadir hemoglobin was 74.0 ± 4.83 $g{\cdot}L^{-1}$, with a range of 66.9 ± 1.7 $g{\cdot}L^{-1}$ to 84.5 ± 1.6 $g{\cdot}L^{-1}$ (Figure 4). Following hip fracture repair, the mean nadir hemoglobin was 77.6 ± 11.6 $g{\cdot}L^{-1}$ and ranged from 71.2 ± 2.9 $g{\cdot}L^{-1}$ to 82.8 ± 1.7 $g{\cdot}L^{-1}$ (Figure 4). Amongst cardiac surgical patients, the mean nadir hemoglobin concentration was 72.5 ± 10.7 $g{\cdot}L^{-1}$, and ranged from 65.7 ± 1.1 $g{\cdot}L^{-1}$ to 77.3 ± 1.0 $g{\cdot}L^{-1}$ (Figure 4). In postoperative and trauma patients admitted to an ICU, the mean nadir hemoglobin was 74.8 ± 13.5 $g{\cdot}L^{-1}$ and ranged from 66.1 ± 3.04 $g{\cdot}L^{-1}$ to 87.5 ± 2.5 $g{\cdot}L^{-1}$ (Figure 4). Centres C and F consistently demonstrated some of the higher mean levels across diagnostic groups, while centres D and E demonstrated lower mean levels. The remaining centres fell into the middle range, with relative positions changing marginally within each diagnostic grouping.

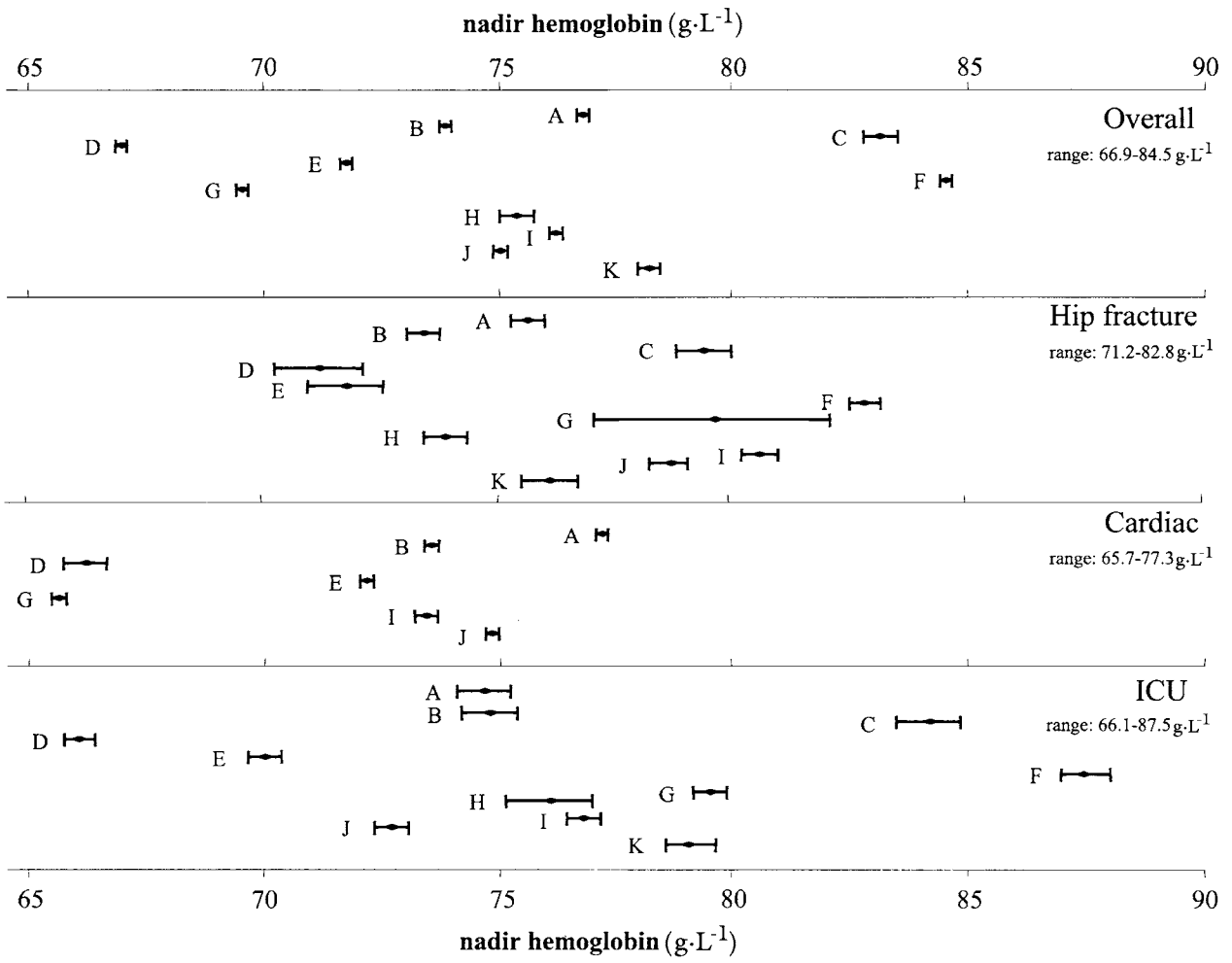

FIGURE 4 Adjusted, group-specific mean nadir hemoglobin levels for transfused patients at each of the participating centres in this study, along with their 95% confidence intervals. Adjustments were made for the effects of age, gender, hospital, and the presence/absence of 12 different co-morbidities listed earlier. ICU = intensive care unit.

Discussion

In this study, we documented variation in crude rates and adjusted odds of red cell transfusion between hospitals, both overall and in each of the three major diagnostic groups. The adjusted odds of transfusion varied most amongst patients having undergone cardiac surgery and to a lesser degree amongst patients who underwent hip fracture repair and postoperative and trauma patients requiring ICU care. Furthermore, it is noted that the adjusted odds of transfusion varied most between patients undergoing cardiac surgery. This suggests that there exist factors in this procedure that amplify the impact of RBC mass on transfusion, such as the hemodilution effects of cardiopulmonary bypass. This makes cardiac surgery a useful field for the study of this topic. Other transfusion-related indices including the median number of units transfused and nadir hemoglobin concentrations consistently documented practice variation between centres, overall and within each major diagnostic grouping. In addition, similar trends were observed when comparing amongst the different indices, with the exception of nadir hemoglobin concentrations.

A few different patterns of use emerged from examination of hemoglobin concentrations and rates of transfusion. Three centres (D, E and G) consistently demonstrated low mean nadir hemoglobin levels and mid-level or high odds of transfusion. This pattern

might suggest that the centres had higher rates of transfusion, in patients with increased severity of illness or undergoing more complex procedures resulting in greater degrees of blood loss than other centres. Conversely, centre C, associated with high mean nadir hemoglobin levels and lower odds of transfusion may reflect lower rates of transfusion in a more stable, lower risk population centre. Many of the remaining centres were associated with high mean nadir hemoglobin levels and high odds of transfusion, perhaps suggesting a very liberal use of red cells at such centres. Given that only selected patients were included in the analysis of nadir hemoglobin concentrations, the qualitative patterns are largely speculative. There are, however, consistent centre-specific variations in transfusions in major perioperative consumers of red cells.

Prior studies have documented the independent effects of both gender and age on the likelihood of transfusion.[17–19] The increased risk of transfusion in women has been shown by some to be independent of smaller blood volume as compared to men,[20] while others have shown that the gender effect disappeared following inclusion of blood volume as an additional covariate in a multivariate analysis.[21] Further research regarding this matter is needed. Regarding the effect of age, older patients are thought to be sicker than younger patients and, consequently, are transfused at a higher rate. However, the effects of both age and comorbidities on transfusion needs are confounded by indication, thus complicating observational research of this issue.

In a systematic review published in 1998 as part of background documents for the Canadian Medical Association guidelines on red cells and blood product usage, Hébert and colleagues identified 189 articles that addressed questions related to clinical transfusion practice.[22,23] They only identified only a few studies that described overall utilization of red cells between and within different disciplines as well as patterns of use over time.[2,3,24–27] There were also a significant number of studies describing red cell utilization in selected patient populations. In a 1992 survey conducted in 61 Toronto area hospitals, 65% of the allogeneic red cells used were administered to patients undergoing operative procedures categorized as digestive and abdominal, cardiovascular and musculoskeletal.[24] Brien *et al.*[2] documented that 56% of all red cells were administered to surgical patients, while a study by Ghali[3] documented that 69% of red cells are transfused into surgical patients. In cardiac surgery, the proportion of patients receiving red cells ranges from 50% to 80%.[8,24,28]

In addition, there were few recent studies which systematically attempted to identify and characterize the source of practice variation. Several investigators identified practice variation as being an inter-institutional phenomenon. The first such study undertook a secondary analysis of a large database conducted in 1978[29] and observed a striking variation among hospitals in Connecticut. The authors inferred that physician habits and personal preferences determined institutional variation in blood utilization. However, others criticized the study for failing to control for the effects of case mix.[30] Subsequently, significant practice variation was also documented within specific disease categories,[4,5] clinical settings and surgical procedures,[6,31] including hip[7–10] and knee[7,9,10] arthroplasty and coronary revascularization (or CABG).[11–13] Controlling for population differences, blood loss and pump time, a prospective audit conducted on CABG patients[13] identified transfusion factors such as the nadir and discharge hematocrits as accounting for significant variation in blood use among 18 tertiary care hospitals. In similar patients, Surgenor and colleagues[11] found that there were significant differences in the percentage of patients transfused between hospitals. Hébert *et al.* found a significant variation in transfusion practice (in terms of nadir hemoglobin concentrations) among six Canadian ICUs after controlling for the effects of disease severity, diagnosis, age and gender. Thus, significant differences in the approach to allogeneic red cell transfusions have been consistently observed among institutions.

Retrospective chart reviews and self-administered surveys have also attempted to determine if physicians account for significant variations. In the SANGUIS study, transfusion rates were found to depend more on physicians than the patient population or type of procedure or hospital.[6] Wide variation was found among 43 hospitals in ten European countries[31] and between hospitals within the same country. Some factors found to influence this variation were age, gender, preoperative hematocrit and blood loss, all factors related to patients. In observational studies in cardiac surgery, patient characteristics associated with transfusions of red cells include a long list of demographic factors such as age and gender, diagnostic characteristics such as procedure and co-morbid illnesses, factors related to blood volume such as preoperative hematocrit and body mass index, as well as other factors such as the use of antifibrinolytics and preoperative use of antiplatelet agents.[32] Surveys of physicians have also explored factors that might influence practice.[33] There are, however, few studies that attempt to dissect physician-based factors and institutional factors that might explain practice variation while considering the confounding influence of all other characteristics.

This study documented practice variation in three major diagnostic groups among 11 Canadian centres while controlling for a few important factors that might influence the administration of red cells. However, like many other studies, we were unable to secure information on a number of important variables such as specific procedures, co-morbid illnesses and indicators of severity of illnesses. In addition, we were unable to identify physician-based factors that might have affected transfusion practice within the same institution.

In conclusion, we documented inter-institutional practice variation in three major populations of patients who frequently receive red cells. We suggest that future studies should attempt to characterize the source of variation. In addition, if variation truly exists, future studies should define optimal transfusion practice in a variety of clinical settings by conducting randomized controlled trials.

Acknowledgements

The authors thank Nadine Shehata for her expert opinion during the preparation of this manuscript, as well as Nancy Cleary for her superb secretarial assistance.

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