Factors Affecting Perioperative Transfusion Decisions in Patients with Coronary Artery Disease Undergoing Coronary Artery Bypass Surgery

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Background: A high proportion of patients having cardiac bypass surgery receive erythrocyte transfusions. Decisions about when to transfuse patients having surgery for coronary artery disease may impact on erythrocyte utilization and patient morbidity and mortality. There are no published data about the factors that influence physicians' decisions to transfuse erythrocytes to these patients. The objectives of this study were to determine the hemoglobin concentration for transfusion and the factors that influence physicians' perioperative transfusion decisions for coronary artery bypass patients.

Methods: The authors conducted a cross-sectional study using pretested, self-administered, mailed questionnaires sent in 2004 to all cardiac surgeons and anesthesiologists in Canada who participate in coronary artery bypass surgery. The questionnaire included four intraoperative and four postoperative vignettes. Factors assessed included patient age, sex, cardiac index, and myocardial ischemia.

Results: The response rates were 70% (345 of 489) for the intraoperative and 61% (297 of 489) for the postoperative case scenarios. The mean hemoglobin concentrations for transfusion were 7.0 g/dl for the intraoperative case scenarios and 7.2 g/dl for the postoperative case scenarios. Older age, the presence of myocardial ischemia, and a low cardiac index were factors that increased the hemoglobin concentration for transfusion ($P < 0.0001$). Physicians ranked myocardial ischemia as the most significant factor affecting their transfusion decisions.

Conclusions: Factors such as the presence of a low cardiac index, myocardial ischemia, and older age increase the hemoglobin concentrations at which physicians transfuse coronary bypass surgery patients. Future studies are required to elucidate whether transfusions based on these variables affect patient morbidity and mortality.

This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 5A.

Additional material related to this article can be found on the ANESTHESIOLOGY Web site. Go to http://www.anesthesiology.org, click on Enhancements Index, and then scroll down to find the appropriate article and link. Supplementary material can also be accessed on the Web by clicking on the "ArticlePlus" link either in the Table of Contents or at the top of the Abstract or HTML version of the article.

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RECENT reports suggest that 30–55% of patients undergoing coronary artery bypass surgery receive erythrocyte transfusions,[1–5] and that those who undergo transfusion receive a mean of 2.2–3.9 units.[3,6–9] Despite the high rate of erythrocyte utilization, the question of when to transfuse patients having coronary artery bypass surgery remains unclear. The decision about when to transfuse erythrocytes has important health and resource implications. Decisions not to transfuse patients may lead to unnecessary harm due to impaired oxygen delivery and impaired hemostasis.[10] Conversely, decisions to transfuse patients can also result in harms from various factors, including hemolytic transfusion reactions (*i.e.*, ABO-incompatible hemolytic transfusion reactions, delayed transfusion reactions, transfusion reactions due to incompatible solutions), transfusion-transmitted infections, transfusion-related acute lung injury, and bacterial contamination of blood components.[11–13] In addition, there are some additional potential harms that require further study, such as the effects of transfusion related immunomodulation and the effects of storage on erythrocytes, which may lead to increased infection, increased duration of stay in the hospital or intensive care unit, and multisystem organ failure.[14–17]

To optimize transfusion therapy in patients undergoing coronary bypass surgery, it is important to know the hemoglobin concentration at which physicians consider it necessary to transfuse these patients and the perioperative factors that physicians use to guide their transfusion decisions. By determining these factors, we can assess whether perioperative transfusion decisions are

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supported by evidence in the literature. If factors that influence transfusion decisions are not evidence based, additional research will be needed to establish whether transfusion based on these factors is beneficial or potentially wasteful or harmful. This will assist in improving transfusion behavior to optimize utilization and improve morbidity and mortality.

The purpose of our study was to determine the answer to these questions by surveying all anesthesiologists and surgeons participating in coronary artery bypass surgery in Canada.

Materials and Methods

Questionnaire Development

We used a cross-sectional study design using self-administered mailed questionnaires sent to cardiac surgeons and anesthesiologists in Canada. We developed the questionnaire according to previously published techniques.[18,19] The structure of the questionnaire was that of eight case scenarios that simulated patient encounters, with closed-ended questions (appendix; additional information regarding this is available on the ANESTHESIOLOGY West site at http://www.anesthesiology.org.). Four case scenarios dealt with the intraoperative setting, and four dealt with the postoperative setting in the intensive care unit. Only the perioperative period was considered because 60–80% of all erythrocytes that are transfused in coronary bypass surgery patients are transfused during this period.[20,21]

The four case scenarios were based on two ages (*i.e.,* 55 and 75 yr) for each sex. We included two plausible values for age, 55 and 75 yr, which represent approximately 1 SD above and below the mean age for cardiac bypass surgery (*i.e.,* approximately 65 yr with an SD of 10 yr).[1,4,7] Within each scenario, there were six variations, based on presence or absence of clinical myocardial ischemia and three categories of the cardiac index ($< 2 \, l \cdot min^{-1} \cdot m^{-2}$, 2–$2.5 \, l \cdot min^{-1} \cdot m^{-2}$, and $> 2.5 \, l \cdot min^{-1} \cdot m^{-2}$). The questionnaires were sent between April and July 2004. Because of a typographical error in the case scenarios dealing with the postoperative period, the portion of the questionnaire related to this period was sent out a second time (June and July 2004) to ensure the validity of the responses. The institutional review board (Research Ethics Board, St. Michael's Hospital, Toronto, Ontario, Canada) approved the study protocol.

The potential factors that may affect physicians' decisions to transfuse erythrocytes to coronary artery bypass surgery patients who were considered for inclusion in the questionnaire were identified by a comprehensive literature search of the MEDLINE (1966 to September 2003) and Cochrane Library (2003, Issue 3) databases. A study was included in the search if it (1) was published in English, (2) was an original report, and (3) had the objective to assess factors that predicted or were associated with increased transfusion rates of erythrocytes or whole blood in the perioperative period for patients undergoing coronary artery bypass surgery.

There were several variables identified in the literature search that resulted in increased transfusion rates. Older age and female sex were consistently associated with higher utilization of blood, so age and sex were incorporated into the scenarios.[1,2,4,7,22–27] Blood loss,[2,4,9] coronary ischemia,[22,23] and left ventricular dysfunction[2,4,7] have also been shown to be associated with increased transfusion rates, so these factors were also incorporated into the scenarios. We chose to include cardiac index rather than left ventricular function in the scenarios because cardiac index is more reflective of perioperative cardiac function. Although the literature consistently identifies blood loss as a factor associated with increased transfusion rates, we did not include it as a variable in the scenarios because it is widely accepted that transfusions are required for severe blood loss (as defined by factors such as rate of blood loss, amount of blood loss, and baseline hematocrit). Because the literature on the optimal hemoglobin concentration for transfusing patients with myocardial ischemia is conflicting[28–30] and our pilot testing identified myocardial ischemia as an important determinant in transfusion decisions, myocardial ischemia was included as a variable in the scenarios.

Given the design of the questionnaire, we were limited in the number of factors that we could vary in the scenarios because of questionnaire length. This forced us to hold several factors constant across the scenarios so that these factors would not confound responses based on the main variables that we chose to vary in the questionnaire. For example, because various comorbidities have been shown to affect transfusion decisions,[4,23,31] we designed the vignettes to reflect a patient without any additional comorbidities beyond coronary artery disease to ensure that transfusion decisions would not be confounded by the presence of various comorbidities. Similarly, the case scenarios described the patients as being hemodynamically stable and having normal mixed venous oxygen saturation because hemodynamic instability is associated with increased transfusion rates[2,7,23] and some physicians use mixed venous oxygen saturation to guide transfusion decisions.

To allow an assessment of whether physician variables may be associated with transfusion decisions, the questionnaire gathered information about the following physician characteristics: age, sex, academic affiliation, specialty, hospital, number of bypass patients per year at the hospital where the physician practiced, and number of surgeries for each physician per year.

The questionnaire also included a partially closed-ended question that asked physicians to choose from a list the three most important factors that influence their decisions to transfuse coronary artery bypass patients (appendix). The list contained hemoglobin concentration, age, sex, myocardial ischemia, cardiac index, blood
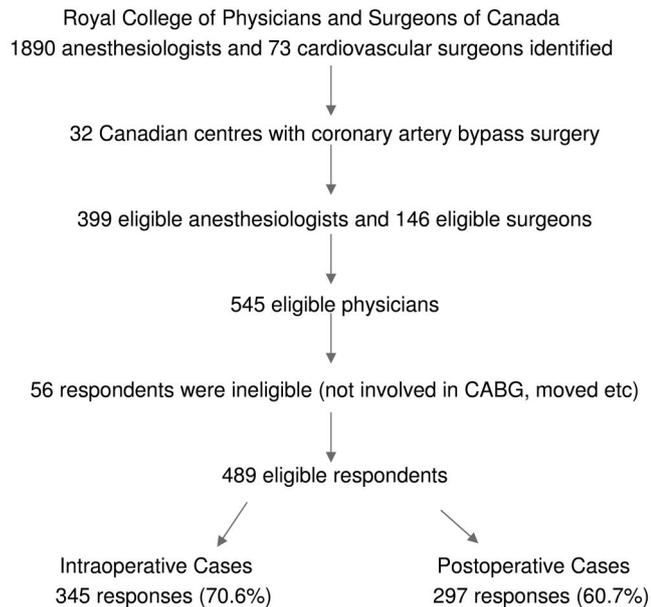
Royal College of Physicians and Surgeons of Canada
1890 anesthesiologists and 73 cardiovascular surgeons identified

↓

32 Canadian centres with coronary artery bypass surgery

↓

399 eligible anesthesiologists and 146 eligible surgeons

↓

545 eligible physicians

↓

56 respondents were ineligible (not involved in CABG, moved etc)

↓

489 eligible respondents

↙ ↘

Intraoperative Cases   Postoperative Cases
345 responses (70.6%)   297 responses (60.7%)

Fig. 1. Participants. CABG = coronary artery bypass surgery.

loss, mixed venous oxygen saturation, lactic acidosis, comorbid illnesses, and a category labeled "other" to permit any factors that were not included in the list.

The questionnaire was pretested to assess face and content validity, comprehensibility, time to completion, and ambiguity. The questionnaire was initially pilot tested by 12 resident physicians, and several modifications were made based on their feedback. Subsequently, the revised questionnaire was pilot tested by 3 individuals (a nurse practitioner and 2 residents) before being finalized.

Study Participants

All cardiac surgeons and anesthesiologists involved in coronary artery bypass surgery in Canada were eligible to participate in the survey. A list of anesthesiologists and cardiovascular surgeons practicing in Canada in 2003 was obtained from the Royal College of Physicians and Surgeons of Canada (Ottawa, Ontario, Canada) (fig. 1). Thirty-two Canadian adult medical centers that perform coronary artery bypass surgery were identified through the Canadian Cardiovascular Society's Web site.†† To determine which of the physicians identified from the Royal College of Physicians and Surgeons of Canada participated in coronary artery bypass surgery and whether any physicians not registered with the Royal College of Physicians and Surgeons of Canada participated in coronary artery bypass surgery, each center was given a list of its anesthesiologists and surgeons to review and was asked to identify those participating in coronary artery bypass surgery at their centers and add the names of physicians who were missing from the list.

†† Canadian Cardiovascular Society. Available at: http://www.ccs.ca. Accessed October 15, 2004.

The eligible survey population was 399 anesthesiologists and 146 surgeons (n = 545).

Survey Administration

We adopted several techniques to try to maximize the response rate[18,32]: developing a respondent-friendly questionnaire, using colored ink, personalizing communications (*i.e.*, using real stationary, the respondents' names, and ink signatures), providing stamped self-addressed envelopes, sending a prepaid financial token of appreciation not conditional on response [$5 Canadian], and making up to five contacts with each subject.

Statistical Analysis

The mean hemoglobin concentrations selected for transfusion were calculated for each case scenario. We used the Student t test to assess the effect of binary physician variables on the dependent variable (hemoglobin concentration), and P values were calculated based on the method of Satterthwaite, assuming unequal variances. Linear regression was used for continuous physician variables. For univariate analysis of patient variables on the hemoglobin concentration (cardiac index, myocardial ischemia, age, sex), paired Student t tests were used. Analysis of variance was used to determine the effect of the hospital variable on the hemoglobin concentration.

A mixed effects regression model was developed for the multivariable analysis. All patient and physician variables were included in the regression model. The dependant variable comprised 24 hemoglobin concentrations for each respondent. We modeled dependence between hemoglobin concentrations on the same respondent through use of a compound symmetric covariance structure for the model.[33] Univariate analysis revealed that the hemoglobin concentrations differed according to the hospital where a physician practiced. Therefore, we controlled for clustering secondary to the hospital by including a random effect for hospital in the mixed effects regression model.

Interaction terms, chosen based on their clinical plausibility, were also included in the multivariable model. A global assessment of all interaction terms using the likelihood ratio test comparing models with and without interaction terms was used. The P value was not significant for the intraoperative case scenarios; thus, interaction terms were only included for the postoperative case scenarios.

The proportions of missing data for the intraoperative and postoperative case scenarios were only 1.3% (210 of 16,368) and 1% (146 of 13,968), respectively, so we used complete case analysis for most analyses (except for regression).[34] We used linear regression to impute missing values for the mixed effects regression model.

The question that asked physicians to rank the three most significant factors that influenced their transfusion

Table 1. Characteristics of Physicians for the Intraoperative and Postoperative Case Scenarios

Characteristic	Intraoperative (n = 338)	Postoperative (n = 288)
Age, mean ± SD, y	46.4 ± 8.6	46.6 ± 8.4
Male sex, n (%)	286 (85)	249 (86)
Anesthesiologists, n (%)	241 (71)	198 (69)
Academic center, n (%)	299 (89)	257 (90)
Years in practice, median (IQR)	13 (6–20)	14 (6–20)
Involved in preoperative transfusion decisions, n (%)	208 (62)	170 (59)
Involved in intraoperative transfusion decisions, n (%)	321 (96)	269 (94)
Involved in postoperative transfusion decisions, n (%)	215 (64)	188 (66)
Cases/physician, median (IQR)	100 (60–100)	100 (65–160)
Cases/center, median (IQR)	850 (400–1,200)	858 (600–1,200)

Data are expressed as mean ± SD, n (percentage), and median (interquartile range [IQR]).

decisions was analyzed as follows. Each factor that was ranked first was given three points. Factors ranked second and third were given two points and one point, respectively. The number of points was then summed for each factor.

A *P* value less than 0.05 was considered significant for all analyses. All *P* values were two tailed. The statistical software package SAS®, version 8.2 (SAS Institute, Cary, NC), was used for data analyses.

Given the total population available to be surveyed (n = 545), the confidence interval half-length for response rates of 60% and 70% was 0.03, reflecting a high level of precision for the results.[18]

Results

Of the 545 anesthesiologists and surgeons who were mailed a survey questionnaire, 56 respondents either were not involved in coronary artery bypass surgery or had relocated, leaving 489 eligible respondents. The response rates were 70% (345 of 489) for the intraoperative case scenarios and 61% (297 of 489) for the postoperative case scenarios (fig. 1). Responses were received from anesthesiologists from all 32 cardiac centers and from cardiac surgeons from 30 of 32 centers (94%). There were no differences between respondents and nonrespondents in their sex or the province in which they practiced.

A number of respondents were excluded from the analyses. For the intraoperative case scenarios, 2 respon-

dents were not involved in intraoperative transfusion decisions and did not complete the case scenarios. Five other respondents were excluded, 3 because they answered only one question in each case scenario and 2 because they completed only the demographics portion of the questionnaire. Thus, there were 338 responses that were included in the analysis of the 489 eligible respondents (69%) for the intraoperative case scenarios.

For the postoperative case scenarios, we excluded respondents who indicated they were not involved in postoperative transfusions decisions and did not complete the postoperative case scenarios (n = 6), respondents who answered only one question in each case scenario (n = 3), and respondents who only completed the demographics portion of the questionnaire (n = 2). Thus, there were 286 responses that were included in the analysis of the postoperative case scenarios of the 489 eligible respondents (58%).

Table 1 depicts the characteristics of the study groups. The majority of physicians were male (85%) and belonged to an academic center (90%).

The analyses of the female and male case scenario did not demonstrate significant differences from each other (results not shown); therefore, we only present the results of the univariate and multivariable analyses for the female case scenarios.

Hemoglobin Concentrations for Transfusion

For the scenarios of a 55-yr-old female, the mean hemoglobin concentrations for erythrocyte transfusion were 7.0 ± 0.8 g/dl for the intraoperative scenarios and

Table 2. Mean Hemoglobin Concentrations for Transfusion for the 55-Year-old Female Patient According to Cardiac Index and Presence of Myocardial Ischemia

Variable	Intraoperative Mean Hemoglobin Concentration ± SD, g/dl	Postoperative Mean Hemoglobin Concentration ± SD, g/dl	P Value
Cardiac index > 2.5	6.95 ± 0.79	7.20 ± 0.70	< 0.001
Cardiac index < 2	7.88 ± 1.02	8.04 ± 0.92	< 0.001
MI and cardiac index > 2.5	7.81 ± 1.04	8.08 ± 0.93	0.002
MI and cardiac index < 2	8.47 ± 1.08	8.71 ± 0.94	< 0.001

Data are expressed as mean ± SD. Units for cardiac index = $l \cdot min^{-1} \cdot m^{-2}$.

MI = myocardial ischemia.

Table 3. Mean Hemoglobin Concentrations for Transfusion for the 75-Year-old Female Patient According to Cardiac Index and Presence of Myocardial Ischemia

Variable	Intraoperative Mean Hemoglobin Concentration ± SD, g/dl	Postoperative Mean Hemoglobin Concentration ± SD, g/dl	P Value
Cardiac index > 2.5	7.39 ± 0.84	7.55 ± 0.71	< 0.001
Cardiac index < 2	8.22 ± 1.04	8.33 ± 0.95	0.007
MI and cardiac index > 2.5	8.06 ± 1.04	8.30 ± 0.93	< 0.001
MI and cardiac index < 2	8.65 ± 1.01	8.86 ± 0.91	< 0.001

Data are expressed as mean ± SD. Units for cardiac index = $l \cdot min^{-1} \cdot m^{-2}$.

MI = myocardial ischemia.

7.2 ± 0.7 g/dl for the postoperative scenarios ($P < 0.0001$; table 2). The distribution of hemoglobin concentrations for transfusion differed for the intraoperative and postoperative scenarios and for age (tables 2 and 3 and fig. 2). For the postoperative *versus* the intraoperative period and for 75 *versus* 55 yr olds, the distributions of the hemoglobin concentrations for transfusion were shifted to the right, representing more aggressive transfusion practices for the postoperative period and for older patients.

The mean hemoglobin concentrations for transfusion increased for the scenario where the patient was described to have myocardial ischemia and a reduced cardiac index (tables 2 and 3). The presence of each of these factors accounted for an increase in the hemoglobin concentrations selected for transfusion of approximately 1.0 g/dl. The presence of both myocardial ischemia and a cardiac index less than $2 \ l \cdot min^{-1} \cdot m^{-2}$ resulted in an increment in the hemoglobin concentration for transfusion of approximately 1.5 g/dl for both the 55- and 75-yr-old patient scenarios. Older age resulted in a 0.5-g/dl increase in the hemoglobin concentration for transfusion.
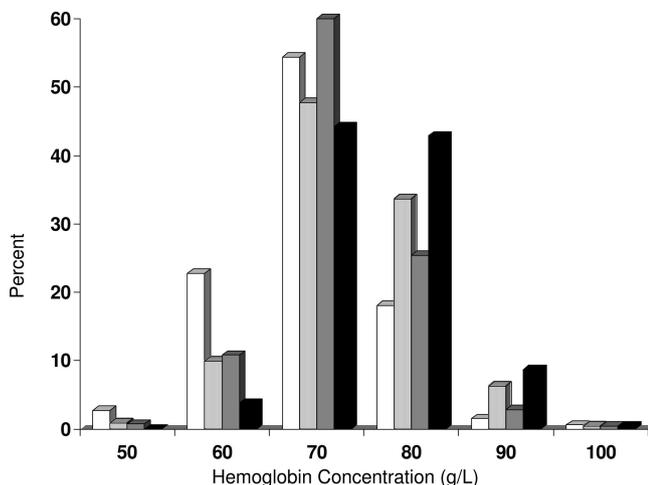

Fig. 2. The mean hemoglobin concentration at which physicians would transfuse erythrocytes for 55- and 75-yr-old patients in the intraoperative (IO) and postoperative periods (PO). *Open bars* = 55-yr-old woman, IO; *light gray/hatched bars* = 75-yr-old woman, IO; *dark gray bars* = 55-yr-old woman, PO; *black bars* = 75-yr-old woman, PO.

Univariate Analyses

The univariate analyses identified seven variables that significantly affected the hemoglobin concentration for transfusion: age of the patient in the scenario, presence of myocardial ischemia, cardiac index, number of cardiac cases per individual physician, and hospital ($P < 0.001$). Patient sex and physician specialty, sex, age, academic affiliation, and years of practice did not significantly affect the hemoglobin concentration.

Regression Analysis

The results from the regression models (tables 4–6) show that physicians chose higher hemoglobin concentrations for transfusion with older patient age, presence of myocardial ischemia, and lower cardiac indices. The model also identified that for the intraoperative scenarios, the academic affiliation of the physician affected hemoglobin concentrations for transfusion, with physicians working in academic institutions selecting lower hemoglobin concentrations than physicians in community settings. For the postoperative case scenarios, there were four interaction terms that were significant (table 6). Physicians selected higher hemoglobin concentrations for transfusion with increasing age and myocardial ischemia, increasing age and declining cardiac index, presence of myocardial ischemia and declining cardiac index. This indicates the effect of age was dependent on the presence of myocardial ischemia and cardiac index and that the effect of myocardial ischemia was also dependent on the level of cardiac index. In addition, physician involvement in the postoperative transfusion decisions was associated with decreased hemoglobin concentrations for the postoperative case scenarios (table 5).

Factors Physicians Identified as Being Most Significant in Their Transfusion Decisions

Myocardial ischemia was the most highly ranked factor influencing intraoperative and postoperative transfusion decisions. Hemoglobin concentration and blood loss were the second- and third-ranked factors for intraoperative transfusion decisions; their order was reversed for postoperative transfusion decisions. The cardiac index and mixed venous oxygen saturation were also com-

Table 4. Multivariable Analysis of Simulated Patient Characteristics

Variable	Intraoperative Parameter Estimate* (95% CI)	P Value	Postoperative Parameter Estimate* (95% CI)	P Value
Intercept	86.5 (77.7 to 95.4)	< 0.0001	84.8 (76.2 to 93.4)	< 0.0001
Sex, F:M	0.14 (−0.09 to 0.38)	0.25	0.25 (−0.2 to 0.7)	0.32
Age, 55:75 yr	−3.13 (−3.4 to −2.4)	< 0.001	−1.92 (−2.4 to −1.4)	< 0.001
Cardiac index, > 2.5:2–2.5	−2.12 (−2.4 to −1.8)	< 0.001	−1.74 (−2.3 to −1.1)	< 0.001
Cardiac index, > 2.5:< 2	−7.47 (−7.7 to −7.1)	< 0.001	−5.61 (−6.2 to −5.0)	< 0.001
Cardiac index, 2–2.5:< 2	−5.35 (−5.6 to −5.1)	< 0.001	−3.87 (−4.5 to −3.3)	< 0.001
Myocardial ischemia, no:yes	−6.8 (−7.0 to −6.6)	< 0.001	−5.4 (−5.9 to −4.8)	< 0.001

Data are expressed as parameter estimate with 95% confidence interval (CI). Units for cardiac index = $l \cdot min^{-1} \cdot m^{-2}$.

* The term *parameter estimate* refers to how much the outcome (*i.e.*, the hemoglobin concentration at which the decision is made to transfuse) changes for every one unit or category change in the specified variable. A negative (−) parameter estimate indicates that the hemoglobin concentration selected for transfusion increases per unit/category change in the variable. A positive (+) parameter estimate indicates that the hemoglobin concentration selected for transfusion decreases per unit/category change in the variable. For example, when the cardiac index decreases from 2.5 to 2–2.5 $l \cdot min^{-1} \cdot m^{-2}$, when age increases from 55 to 75 yr, and in the presence of myocardial ischemia, the hemoglobin concentration for transfusion increases.

monly selected as significant factors, whereas comorbid illnesses were infrequently selected.

Discussion

Our survey identified that physicians would transfuse healthy young patients undergoing coronary artery bypass surgery at a hemoglobin concentration of 7.0 g/dl and would transfuse patients more aggressively in the presence of older age, low cardiac index, and myocardial ischemia and in the postoperative *versus* the intraoperative period. The finding that a hemoglobin concentration of 7.0 g/dl was selected in patients without comorbid illnesses is consistent with previous reports.[30,35] Of particular interest was the finding that a reduced cardiac index and the presence of myocardial ischemia each resulted in a 1.0-g/dl increase in the hemoglobin concentration for transfusion for the scenario responses. In the open-ended question about significant factors affecting transfusion decisions, the respondents selected myocardial ischemia as the most significant factor influencing their transfusion decisions.

Based on results from previous studies, it is unclear at

what hemoglobin concentration physicians should be transfusing patients with myocardial ischemia, left ventricular dysfunction, and increasing age. Recent reports describe conflicting data regarding the hemoglobin concentration at which to transfuse patients with acute coronary syndromes.[28–30] One study reports a decreased mortality with transfusions below a hemoglobin concentration of 8.3 g/dl and an increased mortality with transfusions above this concentration.[25] Other studies have found a reduction in mortality among patients transfused at a hemoglobin concentration less than 10 g/dl compared with those transfused at higher hemoglobin concentrations.[28] Our study found that in the presence of myocardial ischemia, physicians selected hemoglobin concentrations for transfusion of 7.8 and 8.0 g/dl for the intraoperative and postoperative case scenarios, respectively. The question of whether a hemoglobin concentration of 8.0 g/dl is associated with optimal outcomes in coronary artery bypass surgery patients with myocardial ischemia has not been answered and must be addressed, because physicians indicate that they are selecting a hemoglobin concentration for transfusion that is lower than suggested in previous reports.

Table 5. Multivariable Analysis of Physician Characteristics

Variable	Intraoperative Parameter Estimate* (95% CI)	P Value	Postoperative Parameter Estimate* (95% CI)	P Value
Specialty, A:CV	−0.28 (−2.6 to 2.0)	0.81	0.09 (−2.0 to 2.1)	0.92
Sex, F:M	1.70 (0.6 to 50.1)	0.14	20.2 (−6.2 to 46.7)	0.13
Academic institution, no:yes	3.26 (0.08 to 6.4)	0.04	2.5 (−0.4 to 5.4)	0.10
Age	0.02 (−0.2 to 0.3)	0.80	0.08 (−0.1 to 0.3)	0.45
Years in practice	−0.008 (−0.2 to 0.2)	0.95	−0.05 (−0.3 to 0.2)	0.65
Cases/physician	−0.01 (−0.02 to 0.002)	0.08	−0.007 (−0.02 to 0.004)	0.22
Preoperative†, no:yes	−0.10 (−1.9 to 1.7)	0.91	−0.06 (−1.8 to 1.6)	0.94
Intraoperative†, no:yes	−1.62 (−5.8 to 2.5)	0.44	2.4 (−1.1 to 5.9)	0.17
Postoperative†, no:yes	1.40 (−0.7 to 3.4)	0.19	2.7 (0.7 to 4.7)	0.01

Data are expressed as parameter estimate with 95% confidence interval (CI).

* The term *parameter estimate* refers to how much the outcome (*i.e.*, the hemoglobin concentration at which the decision is made to transfuse) changes for every one unit or category change in the specified variable. A negative (−) parameter estimate indicates that the hemoglobin concentration selected for transfusion increases per unit/category change in the variable. A positive (+) parameter estimate indicates that the hemoglobin concentration selected for transfusion decreases per unit/category change in the variable. † Involvement in transfusion decisions in the preoperative, intraoperative, and postoperative settings.

A = anesthesiologists; CV = cardiac surgeons.

Table 6. Multivariable Analysis of Significant Interaction Terms* for the Postoperative Case Scenarios

Variable	Parameter Estimate† (95% CI)	P Value
Age and MI, no:yes	−1.21 (−1.7 to −0.7)	< 0.001
Age and cardiac index, > 2.5:< 2	−0.65 (−1.2 to −0.04)	0.04
MI and cardiac index, > 2.5:< 2	−2.22 (−2.8 to −1.6)	< 0.001
MI and cardiac index, 2–2.5:< 2	−1.94 (−2.5 to −1.3)	< 0.001

Data are expressed as parameter estimate with 95% confidence interval (CI). Units for cardiac index = $l \cdot min^{-1} \cdot m^{-2}$.

* Interaction terms apply when two variables are correlated such that their effect on an outcome is not just the sum of their individual contributions. † The term *parameter estimate* refers to how much the outcome (*i.e.*, the hemoglobin concentration at which the decision is made to transfuse) changes for every one unit or category change in the specified variable. A negative parameter estimate indicates that the hemoglobin concentration selected for transfusion increases per unit/category change in the variable. A positive (+) parameter estimate indicates that the hemoglobin concentration selected for transfusion decreases per unit/category change in the variable. For example, in the presence of myocardial ischemia (MI) and with a decrease in the cardiac index from 2.5 to less than $2 \, l \cdot min^{-1} \cdot m^{-2}$, the hemoglobin concentration for transfusion increases by a factor of 2.22.

The optimum level of hemoglobin chosen for transfusion has also not been determined for patients with left ventricular dysfunction. On one hand, transfusions can exacerbate the left ventricular dysfunction leading to pulmonary edema.[30] On the other hand, low hemoglobin levels can contribute to mortality. A hemoglobin concentration of 9.0 compared with 14.0 g/dl has been associated with increased mortality in patients with heart failure.[36] Our study shows that anesthesiologists and surgeons believe that patients with a low cardiac index (less than $2 \, l \cdot min^{-1} \cdot m^{-2}$) should be transfused more aggressively in the intraoperative and postoperative settings, consistent with a previous small study demonstrating that response to blood transfusion is determined by the pretransfusion cardiac index.[37] However, whether the hemoglobin concentrations for transfusion that physicians in our survey selected (7.9 and 8.0 g/dl intraoperatively and postoperatively, respectively) optimize transfusion outcomes has yet to be established.

In the presence of either myocardial ischemia or a declining cardiac index both intraoperatively and postoperatively, physicians increased the hemoglobin concentration for transfusion by 1.0 g/dl, and in the presence of both factors, they increased the hemoglobin concentration for transfusion by 1.5 g/dl. A 1.0-g/dl increase in hemoglobin concentrations for transfusion represents a large difference that can have a significant impact on erythrocyte utilization. A previous study has demonstrated that an increase in the hemoglobin concentration for transfusion of 1.0 g/dl in patients undergoing coronary bypass surgery is associated with a 20% increase of erythrocyte use.[38] Optimum utilization of blood components is essential given that periodic shortages of blood occur and that the cost of blood continues to increase.[39] This further emphasizes the need to establish whether transfusing coronary bypass surgery patients more aggressively in the presence of myocardial ischemia or low cardiac index is a clinically appropriate strategy.

The influence of age on hemoglobin thresholds represents a more contentious issue. Although there is a suggestion that the minimum hemoglobin needed to maintain adequate oxygen transport increases with age,[40] several small studies have shown that older individuals can tolerate hemodilution to a hematocrit of less than 30%.[41–43] To our knowledge, there have not been any clinical studies that show that older patients should be more aggressively transfused than younger patients. The results of a trial of transfusions in critically ill patients did not demonstrate a difference in mortality for patients aged older than 55 yr who were transfused at a hemoglobin concentration of less than 7.0 g/dl compared with a hemoglobin concentration of less than 10.0 g/dl.[35] However, it is well established that age is a predictor for increased transfusion rates.[1,4] In our study, although higher hemoglobin concentrations for transfusion were selected as age increased in the case scenarios, when physicians were asked directly about the significant factors that affected their transfusion decisions, they did not consider age to be an important factor. Perhaps physicians used age as a marker of comorbidity when responding to the case scenarios, accounting for their tendency to transfuse the 75-yr-old patient more aggressively than the 55-yr-old patient. The question of whether age, independent of comorbidities, should affect the hemoglobin concentration for transfusion needs to be answered because, with an aging population, transfusions based on age alone may significantly impact erythrocyte utilization.

The lower hemoglobin concentrations for transfusion for the intraoperative *versus* the postoperative period that were noted in this study are largely consistent with previous reports that describe transfusion policies as part of their study.[1,2,25,27] The rationale for the lower hemoglobin concentration for intraoperative transfusions is that during surgery, while patients are on cardiopulmonary bypass, oxygen requirements are reduced. Postoperatively, higher hemoglobin concentrations may have been selected because of anticipated increases in the oxygen-carrying capacity that patients would require for increased metabolic function after awakening.

There are a number of limitations to this study. The responses from scenario-based questionnaires may not

correlate with actual physician behavior.[44,45] We attempted to minimize this limitation by developing scenarios that closely simulated real patients. The factors that were included in the scenarios were based on a systematic literature review of variables that have been found to be associated with increased transfusion rates. The scenarios were then pilot tested to ensure that they were relevant to physicians. The case scenarios stipulated that the patient had no comorbidities in order to keep this factor constant so that we could assess the influence of other factors on transfusion decisions. The exclusion of comorbidities from the scenarios may limit the generalizability of our findings to patients with significant comorbidities.[46] However, when respondents were asked to indicate the major factors that influence their transfusion decisions, they rarely selected comorbid illness. By excluding blood loss as a factor, we were also unable to explore the aspects of blood loss (*e.g.*, rate of loss, amount of loss) that may be of most importance in precipitating transfusion decisions. In addition, because coronary artery bypass surgery is increasingly being offered to octogenarians and nonagenarians, decisions based on a 75-yr-old patient scenario may not apply to the these older patients. Last, although it is plausible that factors affecting transfusion decisions in this Canadian study would apply to other countries, because studies addressing risk factors for transfusion are largely consistent across different countries,[1,2,4] it is possible that local factors in other countries may influence transfusion decisions.

We have identified that physicians are more aggressive in transfusing (*i.e.*, transfuse at a higher hemoglobin concentration) older patients, patients with myocardial ischemia, patients with left ventricular dysfunction, and patients in the postoperative *versus* the intraoperative period. Because decisions to either transfuse or not transfuse coronary bypass surgery patients may result in increased morbidity and mortality and may significantly affect erythrocyte utilization,[38,47,48] it is essential to determine whether physician transfusion practices as suggested by our results improve clinical outcomes in this patient population. In particular, our findings suggest that further studies are needed to establish the optimal hemoglobin concentration at which to transfuse coronary bypass surgery patients experiencing left ventricular dysfunction or myocardial ischemia and to determine whether older age should influence the hemoglobin concentration for transfusion.

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‡‡ This case scenario represents one of eight scenarios. Subsequent scenarios differed by age (*i.e.*, 75 yr), sex (*i.e.*, male), and perioperative period (intraoperative *vs.* postoperative). Units for cardiac index = $1 \cdot min^{-1} \cdot m^{-2}$.

Appendix

Case Scenario 1‡‡

A 55-yr-old female is having primary elective coronary artery bypass surgery. She has no preoperative morbidity. Her heart rate is 90 beats/min and her blood pressure is 110/70 mmHg. She is euvolemic and has a mixed venous oxygen saturation of 70%. Below what hemoglobin concentration would you transfuse red cells in the following intraoperative scenarios? (Check one in each scenario.)

Case Scenario	Hemoglobin Concentration, g/dl					
	5.0	6.0	7.0	8.0	9.0	10.0
1. (a) Cardiac index > 2.5						
(b) Cardiac index between 2 and 2.5						
(c) Cardiac index < 2						
2. If she has intraoperative myocardial ischemia and						
(a) Cardiac index > 2.5						
(b) Cardiac index between 2 and 2.5						
(c) Cardiac index < 2						

The Ranking Question

Please rank the three most significant factors that affect your decision to transfuse red blood cells in the intraoperative setting. Place the numbers that appear next to these three factors in their respective ranking boxes.

Factor	Rank
1. Intraoperative blood loss	
2. Age	□ Most significant
3. Sex	
4. Cardiac index	
5. Intraoperative hemoglobin concentration	□ Second
6. Myocardial ischemia	
7. Lactic acidosis	
8. Mixed venous oxygen saturation	□ Third
9. Comorbid illness; please specify	
10. Other; please specify	