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Odds of Transfusion for Older Adults Compared to Younger Adults Undergoing Surgery

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Attestation: Charles H. Brown IV has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

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Abstract

BACKGROUND—Recent randomized controlled trials have shown no benefit for transfusion to a hemoglobin >10 g/dL compared with lower hemoglobin thresholds in the perioperative period, even among older adults. Nevertheless, physicians may choose to transfuse older adults more liberally than younger adults. It is unclear whether older patients have higher odds than younger patients of being transfused in the perioperative period. Our objective in this study was to determine whether the odds of transfusion are higher in older patients than in younger patients in the perioperative period.

METHODS—We conducted this retrospective observational cohort study at a tertiary care academic medical center. We included adults who had undergone a surgical procedure as an inpatient at our institution from January 2010 to February 2012. The primary analysis compared the odds of transfusion for patients >65 years old with the odds of transfusion in younger patients based on multilevel multivariable logistic regression analyses including adjustment for comorbidities, surgical service, lowest in-hospital hemoglobin value, gender, and estimated surgical blood loss and accounted for clustering by the surgeon and procedure.

RESULTS—We included 20,930 patients in this analysis. In multilevel models adjusted for comorbidities, surgical service, estimated surgical blood loss, and lowest in-hospital hemoglobin value, with surgeon and procedure as random effects, patients >65 years old had 62% greater odds (odds ratio, 1.62; 95% confidence interval, 1.40–1.88; $P < 0.0001$) of being transfused than did younger patients. When patients were stratified by lowest in-hospital hemoglobin (7.00–7.99, 8.00–8.99, 9.00–9.99, and 10.00 g/dL), the odds of transfusion generally increased with each additional decade of age in every stratum, except for that containing patients in whom the lowest in-hospital hemoglobin did not decrease below 10 g/dL. When the odds of transfusion were compared between younger and older patients, significant differences were observed among surgical services ($P = 0.02$) but not among anesthesia specialty divisions ($P = 0.9$).

CONCLUSIONS—Older adults have greater odds of receiving red blood cell transfusion in the perioperative period than do younger patients, despite the lack of evidence supporting higher hemoglobin triggers in elderly patients. Further research is needed to determine whether transfusion practice in the elderly is an opportunity for education to improve blood management.

An increasing number of older adults (>65 years old [y/o]) present for surgery each year and demographic shifts in the U.S. population are expected to increase this trend.¹ Because postoperative morbidity and mortality are higher in this group,² physicians who provide perioperative care have focused on improving management of this vulnerable population.

A particularly contentious area of debate in the perioperative management of all patients, regardless of age, is the appropriate indication for blood transfusion. Transfusion practice in the perioperative period varies greatly among physicians, as shown by a wide range of hemoglobin transfusion triggers.^{3,4} Several recent randomized trials in multiple patient populations have shown either no difference in mortality,⁵ no difference in a composite

outcome of mortality and severe morbidity,⁶ or increased mortality⁷ with higher hemoglobin triggers (>9–10 g/dL), compared with lower hemoglobin triggers (7–8 g/dL). In the largest transfusion trial to date specifically focused on older adults (mean age 82 y/o) undergoing hip fracture repair, there was no difference in the primary composite outcome of death or inability to walk across the room unassisted between liberal and restrictive transfusion strategies.⁸ However, there is still controversy about the validity and generalizability of these findings, especially in the perioperative period.

Although no current evidence establishes that older patients benefit more from higher postsurgical in-hospital hemoglobin concentrations than do younger patients, it is unclear whether physicians have a greater propensity to transfuse older patients compared with younger patients and what factors might influence this decision. Several procedure-specific studies⁹ and studies with small sample sizes^{10,11} make note of increasing transfusion requirements among elderly patients, but potential explanatory variables, such as lowest hemoglobin concentration, comorbidities, and surgical blood loss have not been adequately considered. We hypothesized that among patients with similar lowest in-hospital hemoglobin concentrations, older patients would have higher odds of transfusion in the perioperative period than would younger patients. In addition, we examined characteristics of the patients, surgeons, anesthesiologists, and surgical procedures that might explain the increased odds of transfusion in older adults.

METHODS

All study procedures were approved by The Johns Hopkins Medical Institutions IRB, which waived the need for written informed consent.

Patients

All patients admitted to Johns Hopkins Hospital from August 2008 to February 2012 were retrospectively screened for inclusion in the cohort. Patients were included if they underwent surgery during their hospitalization after the implementation of computerized anesthesia records (Metavision®, iMdSoft, Needham, MA) in January 2010. These dates were chosen because study data were obtained from the computerized anesthesia records, which at the time of data analysis were available from January 2010 through February 2012. Patients were excluded if they were <21 y/o or if they underwent a peripartum-related procedure (ICD-9 diagnosis codes 630–680) or a procedure performed by an ophthalmologist or cardiac surgeon.

Data Sources

Patient demographics (age, gender), surgical procedure codes, and blood transfusion and hemoglobin data were collected with a blood management data acquisition portal (IMPACT Online®, Haemonetics Corp., Braintree, MA). Data available through this portal are extracted monthly from hospital information systems, and the extraction process was validated during implementation by comparing extracted data to source data for 30 patients. We validated data from an additional 50 randomly selected patients and found no errors among the variables used in this analysis. Comorbidity data were obtained by extracting up

to 30 ICD-9 discharge diagnoses from the hospital billing database (Datamart). Similarly, data from a random sample of 50 patients were assessed to gauge the accuracy of the ICD-9 comorbidities, and all listed codes reflected patient conditions. Surgical estimated blood loss data and anesthesia provider codes were obtained from computerized anesthesia records. The number of years since medical school graduation of the attending surgeon of record was obtained in April 2013 from publicly available data at the Maryland Board of Physicians (<https://www.mbp.state.md.us/bpqapp/>).

Variables

Patient age was the main exposure variable, and we decided a priori to examine primarily the effect of age (>65 years old vs ≤65 years old) on the odds of transfusion. We chose this age cutoff in concordance with commonly accepted practice and guidelines from the American Heart Association in reference to the elderly population.¹² However, we also a priori considered age as a continuous variable and as a categorical variable (20–39, 40–49, 50–59, 60–69, 70–79, and ≥80 y/o). We chose the reference category of 20 to 39 y/o for the categorical consideration of age after examining the data because nonparametric modeling demonstrated that the odds of transfusion began to increase after the age of 40 years.

To identify patient comorbidities, we used Clinical Classification Software (CCS) (<http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccsfactsheet.jsp>) from the Agency for Healthcare Quality and Research to categorize each ICD-9 diagnosis code into one of 260 clinically relevant diagnosis groups. ^a Using the CCS groups, we gave each patient a binary rating of yes/no for the following comorbidities: lipid disorders, anemia, delirium/dementia, heart valve disorders, hypertension, acute myocardial infarction, conduction disorders, coronary atherosclerosis, congestive heart failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease/asthma/other respiratory disease, liver disease, gastrointestinal disease, diabetes, and acute/chronic kidney disease. The corresponding CCS codes are listed in Appendix 1. We also used the Clinical Classification Software to group each ICD-9 procedure code into one of 231 clinically relevant procedure categories.^a

Estimated surgical blood loss was categorized into 250 mL increments because the distribution of blood loss was not normally distributed. The attending surgeon of record for each patient was classified into one of 9 surgical services: cardiac, general, gynecologic, neurosurgery, orthopedic, otolaryngology/plastic and reconstructive, thoracic, urology, and vascular. The attending anesthesiologist of record was classified into one of 6 divisions based on his/her primary appointment: general, cardiac, obstetric/regional, intensive care, neurosurgical, and pediatric.

Statistical Analysis

Baseline Comparison—We compared baseline characteristics of patients ≤65 y/o with characteristics of patients >65 y/o using *t* tests for continuous variables, χ^2 tests for

^aHCUP Clinical Classifications Software (CCS) for ICD-9-CM. Healthcare Cost and Utilization Project (HCUP). 2006–2009. Agency for Healthcare Research and Quality, Rockville, MD. Available at: www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp. Accessed August 1, 2012.

categorical variables, and rank-sum tests for ordinal and nonnormally distributed variables. To compare the number of units transfused, we generated categories (0, 1–2, 3 units). In all of our analyses, a P -value <0.05 was considered significant.

Regression Modeling—We used multilevel logistic regression models to examine the association between patient age and the odds of transfusion. Our a priori analyses are as follows: the primary analysis estimated the odds of transfusion separately for patients >65 and ≤ 65 y/o; as a secondary analysis, we estimated how the odds of transfusion changed as a function of age based on decades of age and also linearly by year of age. After examining the data, it appeared that transfusion practices among individual surgeons, anesthesiologists, and procedures might be similar, and thus, patients nested within surgeons, anesthesiologists, and procedures were likely not independent of one another. Failure to account for this similarity or “clustering” could lead to inaccurate standard error (SE) estimations with the potential for incorrect inferences.¹³ Therefore, our analyses used random intercept multivariable logistic regression models that included a random intercept for surgeon, anesthesiologist, and procedure. However, the results indicated that after accounting for surgeon and procedure, the degree of clustering of outcomes within anesthesiologists was minimal, and this random intercept was dropped from the model. In addition, the analyses initially included random slopes for age at the level of the surgeon, anesthesiologist, and procedure, but these results also indicated that the contributions of the random slopes were minimal, so they were dropped from the model.

Potential confounders selected a priori that were included as fixed effects in the final model included gender, surgical service, the presence or absence of each comorbidity, lowest hemoglobin concentration, and estimated surgical blood loss.

A series of hypothesis-generating analyses were considered after examining the data. These analyses examined factors that might influence transfusion decisions for older adults and included: presence of specific comorbidities, surgeon years after medical school, surgical service, and anesthesiologist specialty division. Each of these factors was added to the model as a main effect and interaction with age.

Multiple Imputation for Missing Data—Of the 20,930 patients included in the study, 4352 had missing estimated blood loss values in the anesthesia computerized record. There are multiple explanations for this missingness, although the most common reason has been shown to be minimal blood loss, which is not accurately documented in a computerized record that requires numeric input.¹⁴ We performed multiple imputation to impute missing values for estimated blood loss. We first constructed a regression model using age, procedure code, lowest hemoglobin value, difference between initial and lowest hemoglobin value, IV fluid administered during anesthesia, and intraoperative transfusion of packed red blood cell units. We then created 5 new datasets with imputed values using the “PROC MI” command in SAS and applied the multilevel regression models described above to each imputed dataset. Finally, we combined the results of these regression analyses using the “PROC MIANALYZE” command in SAS to generate final estimates.¹⁵

Stata ver.12.0 (StataCorp, College Station, TX) was used for data analysis. SAS ver. 9.2 (SAS Institute, Cary, NC) was used for multiple imputation analysis.

RESULTS

Patient and Transfusion Characteristics

Data were available for 150,184 inpatients at Johns Hopkins Hospital, of whom 20,930 met the inclusion criteria, as shown in Figure 1. Baseline characteristics of patients are shown in Table 1. Compared with younger patients, patients >65 y/o were more likely to be men, to be diagnosed with comorbid conditions, and to be admitted to different surgical services. The percentage of patients who received a red blood cell transfusion was significantly higher for patients >65 y/o than for younger patients (27.4% vs 16.5%; $P < 0.0001$). There were significantly more units transfused (by tertiles) for patients >65 y/o (73.1% received 0 units, 13.8% received 1–2 units, and 13.1% received 3–4 units) than for patients ≤65 y/o (83.6% received 0 units, 8.3% received 1–2 units, and 8.1% received ≥3 units; $P < 0.001$). When only the patients who actually received transfusions were considered, the number of units transfused did not differ significantly between patients >65 y/o (51.2% received 1–2 units, and 48.8% received ≥3 units) and patients ≤65 y/o (50.8% received 1–2 units, and 49.2% received ≥3 units; $P = 0.81$).

In addition, among all patients, the initial, lowest, and last hemoglobin values were clinically similar, although statistically lower, among patients >65 y/o compared with those ≤65 y/o, as shown in Table 1. Among patients who actually received transfusions, differences between patients >65 y/o and younger patients for the first hemoglobin, lowest hemoglobin, and last hemoglobin were also not clinically significant (first hemoglobin: 11.4 ± 1.9 vs 11.3 ± 2.2 g/dL, $P = 0.48$; lowest hemoglobin: 7.8 ± 1.1 vs 7.5 ± 1.2 g/dL, $P < 0.001$; last hemoglobin before discharge: 9.6 ± 1.2 vs 9.4 ± 1.3 g/dL, $P < 0.001$).

Transfusion in Older Adults

Across all levels of hemoglobin values, the overall odds of transfusion were higher for patients >65 y/o than for younger patients in unadjusted models (odds ratio [OR], 1.87; 95% confidence interval [CI], 1.74–2.02; $P < 0.0001$) and in adjusted models (OR, 1.62; 95% CI, 1.40–1.88; $P < 0.0001$) (Table 2). Next, we compared transfusion practices for patients with similar lowest in-hospital hemoglobin values by stratifying patients by their lowest in-hospital hemoglobin value. As shown in Table 2, the multilevel adjusted odds of transfusion were higher for patients >65 y/o than for younger patients in each stratum of lowest hemoglobin concentration below 10 g/dL (for 7.00–7.99 g/dL: OR, 2.18; 95% CI, 1.66–2.85; $P < 0.0001$; for 8.00–8.99 g/dL: OR, 1.69; 95% CI, 1.30–2.19; $P < 0.0001$; for 9.00–9.99 g/dL: OR, 2.03; 95% CI, 1.44–2.87; $P < 0.0001$). Above 10 g/dL hemoglobin, the odds of transfusion did not differ between older and younger adults.

The increased probability of transfusion with increasing age is shown graphically in Figure 2. Among patients with similar lowest in-hospital hemoglobin concentrations, exploratory data analysis (via locally weighted scatterplot smoothing) revealed a linear association between patient age and odds of transfusion after the age of 40 years. To further explore this

finding, we calculated the odds of transfusion with each increasing decade of age compared with the reference group of patients 20 to 39 y/o (Table 2) and found that in multilevel adjusted models, the odds of transfusion increased with each decade of age. When patients were stratified by lowest in-hospital hemoglobin, the odds of transfusion generally increased with each decade of age for patients with hemoglobin below 9 g/dL, compared with odds of transfusion in the reference group of patients. For patients with a lowest in-hospital hemoglobin between 9 and 10 g/dL, the odds of transfusion were significantly higher than those for the reference group only for patients >70 y/o. Beyond 10 g/dL, the odds of transfusion for patients >65 y/o were not greater than those of younger patients.

Characteristics that Influence Transfusion Behavior: Patient, Surgeon, Anesthesiologist, and Procedure

Patient Characteristics—To identify characteristics that might better determine transfusion behavior in the overall population and in older adults specifically, we considered characteristics of patients, anesthesiologists, surgeons, and procedures. First, among patients, the higher prevalence of comorbidities in older adults was an important factor in transfusion decisions because the addition of overall comorbidity information to the crude model attenuated the adjusted OR of transfusion in older adults compared with younger adults.

We next examined the effect of the presence or absence of particular comorbidities on odds of transfusion in older adults (Fig. 3). Generally, the higher odds of transfusion for older adults compared with younger adults were similar in the presence or absence of particular comorbidities (P interaction >0.05). However, among patients with cerebrovascular disease, peripheral vascular disease, and cardiac conduction abnormalities, the odds of transfusion for older adults were significantly different compared with patients without these comorbidities; with the important result that in patients with these comorbidities, the odds of transfusion in older adults were no different than for younger adults. (For patients with cerebrovascular disease, OR, 0.75; 95% CI, 0.42–1.31; P = 0.31 versus without cerebrovascular disease, OR, 1.70; 95% CI, 1.47–1.98; P < 0.0001; P interaction = 0.005; for patients with peripheral vascular disease, OR, 1.14; 95% CI, 0.86–1.53; P = 0.36 versus without peripheral vascular disease, OR 1.79; 95% CI, 1.52–2.10; P < 0.0001; P interaction = 0.006; and for patients with cardiac conduction abnormalities, OR, 1.17; 95% CI, 0.86–1.58; P = 0.32 versus without cardiac conduction abnormalities, OR 1.76; 95% CI, 1.50–2.07; P < 0.0001; P interaction = 0.02) In other words, the presence of these specific comorbidities significantly modified the decision to transfuse older adults, such that age was no longer significantly associated with the odds of transfusion, and younger and older adults were transfused similarly. However, the odds of transfusion for older adults with acute myocardial infarction were significantly higher than the odds of transfusion for younger adults with acute myocardial infarction (OR, 2.63; 95% CI, 1.40–4.97; P = 0.003) and compared with those patients without acute myocardial infarction (OR, 1.59; 95% CI, 1.37–1.84; P = 0.02; P interaction = 0.003).

Surgeon Characteristics—The multilevel logistic regression models quantified the variation that was observed in the odds of transfusion across surgeon. Based on the results of

the models, there was substantial variability in the odds of transfusion, as indicated by the large standard deviation (SD) of the random intercept for surgeon (estimated SD of the random intercept: 0.37). To characterize this variability in another way, for a male patient who is >65 y/o with no comorbidities, a lowest in-hospital hemoglobin concentration of 8.0 g/dL, and estimated blood loss between 250 and 500 mL, the average probability of transfusion in this patient is 30%, and for 95% of surgeons for which our sample represents, the probability of transfusion in this patient would range between 17% and 47%. It is important to note that the variability among surgeons changed according to the lowest hemoglobin values of the patients. At the low hemoglobin concentration of 7.00 to 7.99 g/dL, the variability of transfusion among all surgeons was smallest, as indicated by a small SD of the random intercept (SD: 0.05). However, as lowest in-hospital hemoglobin concentration increased, the variability in surgical decision to transfuse patients increased substantially, as indicated by the increasing SD of the random intercept, for lowest hemoglobin concentration of 8.00 to 8.99 g/dL, SD: 0.29; for lowest hemoglobin concentration of 9.00 to 9.99 g/dL, SD: 1.17; for lowest hemoglobin concentration of >10 g/dL, SD: 1.09.

When we examined variability among individual surgeons in transfusing older adults versus younger adults, we found that individual surgeons were relatively consistent in their practice of transfusing older patients more than younger patients, as demonstrated by the low SD of the random slope for age (SD: 0.02).

Exploring the differences among surgeons further, we did find substantial variability among surgical services (Table 3). Compared with other services, the orthopedic service had the highest odds of transfusion for older adults (OR, 2.24; 95% CI, 1.52–3.29; $P < 0.0001$). The odds of transfusion were not significantly higher for older adults than for younger adults in the urology, gynecologic, and vascular surgical services. The number of years since a surgeon's medical school graduation was also considered a characteristic that might influence the decision to transfuse older adults more than younger adults. Surgeons who had been out of medical school for fewer (OR, 1.41; 95% CI, 1.13–1.74; $P < 0.0001$) or > (OR, 1.89; 95% CI, 1.54–2.31; $P < 0.0001$) 18 years (the median number for our sample) had higher odds of transfusing older adults than younger adults (Table 3). There was no statistically significant difference in transfusion behavior for older adults between the older and younger surgeons ($P = 0.08$).

Anesthesiologist Characteristics—Our multilevel logistic regression models also quantified the variation in the odds of transfusion across anesthesiologists. The estimated SD of the random intercept for anesthesiologist was 0.001 indicating little variability among anesthesiologists in the odds of transfusion across all patients. Similarly, the models estimated little variability in the odds of transfusion for older adults compared with younger adults across anesthesiologists (random slope SD of 0.001). We also examined whether there was variability among the different divisions of anesthesiologists and found that the ORs across divisions were similar when transfusion of older adults was compared with transfusion of younger adults ($P = 0.9$; Table 3). Although patients undergoing cardiac surgery were excluded from this analysis, patients >65 y/o who underwent noncardiac surgery but were cared for by cardiac anesthesiologists did not have greater odds of

transfusion than did younger patients. In every other anesthesia division except pediatrics, the odds of transfusion were significantly higher for older adults than for younger adults.

Procedure Characteristics—Finally, we considered the association between surgical procedure and the odds of transfusion. There was substantial variability in the odds of transfusion across different procedures, as indicated by the large SD of the random intercept for procedure (estimated SD of the random intercept [SD: 0.21]). Similar to other characteristics that we examined, there was little variability among procedures in the specific odds of transfusion for older adults compared with younger adults, as demonstrated by the low variability in random slope for age in a multilevel model (SD: 0.01).

Comparison of Models

To quantify the importance of patient variables such as age, blood loss, hemoglobin concentration, and comorbidities (fixed effect variables) compared with the effects of individual surgeon and procedure (random effects variables), we calculated the area under the curve (AUC) and SE for each of several models. For the fixed effects only model, the AUC (SE) was 0.9674 (0.0019), implying that this model was highly discriminating for predicting which patients would be transfused. Incorporating the individual surgeon as a random effect slightly improved the AUC (SE) to 0.9718 (0.0011), and further incorporating the individual procedure as a second random effect improved the AUC (SE) to 0.9731 (0.0011). Comparison of the AUC in each model thus demonstrates that the random effects of surgeon and procedure only slightly add to the discriminating ability of the base model, thereby emphasizing the importance of characteristics such as age, blood loss, hemoglobin concentration, and comorbidities in determining transfusion decisions.

DISCUSSION

In this study, we observed that older patients had increased odds of red blood cell transfusion in the perioperative period, even among patients with similar lowest in-hospital hemoglobin concentrations and after adjusting for comorbidities, surgical blood loss, surgeon, and procedure. The results of this study are notable for the consistency of the findings across all levels of lowest in-hospital hemoglobin lower than 10 g/dL, as well as a “dose” effect of age, such that each increasing decade of age was generally associated with increased odds of transfusion.

To our knowledge, little evidence supports a more liberal transfusion practice for older adults based on age alone. The primary outcomes from several large randomized clinical trials (TRICC–30 day mortality, TRACS⁶–30 day mortality and severe morbidity, and FOCUS⁸–60 day mortality and inability to walk independently) in varied surgical populations failed to demonstrate that a liberal transfusion strategy improved the primary outcome compared with a restrictive strategy. Similarly, transfusion guidelines from the American Society of Anesthesiologists,¹⁶ the Society for Critical Care Medicine,¹⁷ and the American Association of Blood Banks¹⁸ stress the importance of considering the overall clinical situation and patient symptoms, but none of these guidelines state that patient age should be considered a primary factor in the decision to transfuse. However, our findings show that the odds of transfusion in the perioperative period increase with each decade of

age, thereby exposing older adults to potentially harmful effects of blood transfusion, such as acute lung injury, cardiac overload, infections, hemolytic reactions, and immunomodulation.^{19–23}

We explored several factors that might have influenced the more liberal strategy for transfusion in older adults, including characteristics of the patient, surgeon, anesthesiologist, and procedure. First, we found that several patient comorbidities were important in modifying the odds of transfusion for older adults compared with younger adults. Cerebrovascular disease, peripheral vascular disease, and cardiac conduction abnormalities all eliminated the importance of age in increasing the odds of transfusion, suggesting that clinicians consider these diseases more important than age in deciding whether to transfuse an individual patient. However, in the absence of these diseases, age is a strong consideration in the decision to transfuse. Given that older adults are more at risk for cerebrovascular disease, conduction abnormalities, and peripheral vascular disease, a potential explanation for the increased odds of transfusion in older adults is that clinicians suspect one of these comorbidities might be present in the older adults, but not the younger adults, and thus transfuse based on the suspected presence of the particular comorbidity.

Characterization of surgical attributes demonstrated that there was a nonsignificant trend ($P = 0.08$) toward older surgeons compared with younger surgeons having higher odds of transfusing older patients. This result indicates that blood management efforts may have affected transfusion decisions for younger surgeons preferentially. However, there was significant variability among surgical services in the decision to transfuse older adults, implying that there might be a greater culture of transfusing older adults in individual surgical specialties, such as orthopedic surgery. We also found that variability in transfusion rates by surgeon for patients of any age was smallest when the patient's lowest in-hospital hemoglobin was 7 to 8 g/dL. These results imply that at lower hemoglobin levels, surgical decision making about transfusion is more uniform, but as the lowest hemoglobin approaches 10 g/dL, the decision to transfuse takes on increased variability. However, there was no difference in the odds of transfusing older adults compared with younger adults among anesthesiology divisions. This finding is consistent with an integrated practice pattern of anesthesiologists, who may take care of different types of patients on any given day, in spite of primary appointment in a particular division.

We also explored variability in the odds of patients being transfused among individual surgeons and anesthesiologists. Among patients at any age, we found significant variability in the odds of transfusion among surgeon and procedure, but not anesthesiologist. In particular, the variability among surgeons was 3 times the variability among procedures, both of which were greater than the variability among anesthesiologists. The variability among individual surgeons is highlighted in the results section, in which the probability of transfusion for a hypothetical patient (a >65 y/o man with no comorbidities, a lowest in-hospital hemoglobin concentration of 8.0 g/dL, and estimated blood loss between 250 and 500 mL) ranged between 17% to 47% depending on the individual surgeon. Our finding of variability in surgical decision-making for patients at any age is consistent with prior literature.³ However, for older adults compared with younger adults, we found that the odds of transfusion were similarly greater across individual surgeons and anesthesiologists,

indicating that both surgeons and anesthesiologists had similar behavior in deciding to transfuse older versus younger adults, and in each case, the odds of transfusion for older adults were significantly higher.

We compared the ability of several models to predict which patients would be transfused and found that the model which included only fixed effects (age, blood loss, hemoglobin concentration, surgical service, and comorbidities) had a high discriminating ability to predict transfusion in individual patients. To evaluate variability among individual surgeons and procedures in transfusion practice, we added random effects for surgeon and procedure to the baseline model, and these changes only slightly improved the model's discriminating ability, thus demonstrating the relatively significant importance of patient characteristics (compared with variability among surgeons or procedures) in determining odds of transfusion for individual patients.

Taken as a whole, our results show that patient characteristics in the perioperative period (including age) are highly predictive of likelihood of transfusion. However, there is variability among surgeons, and so the high absolute rate of transfusion in older adults is partly due to the tendency of particular surgeons to transfuse patients of any age at higher rates compared to their colleagues. In terms of older adults compared with younger adults, several individual patient comorbidities and the specific surgical service affected the odds of transfusion for older adults compared with younger adults, but generally, both surgeons and anesthesiologists were similar in deciding to transfuse older adults with greater odds than younger adults. Thus, reducing unnecessary blood transfusions in older adults might require efforts directed at general transfusion decision-making, in addition to efforts directed at transfusion decision-making in older adults.

Our results differ qualitatively from a previous report by Frank et al.,³ that showed variability in hemoglobin transfusion triggers among both surgeons and anesthesiologists. Our results may be explained by incorporation of important variables, such as patient comorbidities, estimated blood loss, and lowest hemoglobin concentration into our models, thus explaining previously observed variability by patient and surgical characteristics. Indeed, the discriminating ability of our fixed effects only model was high, indicating that our chosen covariates were important in predicting odds of transfusion in individual patients. Furthermore, unlike that study,³ we considered transfusion over the entire hospitalization rather than just in the operating room, and any decisions made by the anesthesiologist in the operating room may have been subsumed by transfusion decisions that occurred in the postoperative period.

The current study has several potential limitations. Because the association between chronological age and odds of transfusion might be confounded by differences in perioperative characteristics between older and younger patients, we adjusted our analyses to account for lowest in-hospital hemoglobin concentration, patient comorbidities, and surgical blood loss. Further, we accounted for the fact that patients who undergo specific procedures with specific surgeons and specific anesthesiologists may be similar to each other by using statistical techniques appropriate to this clustering of data (i.e., multilevel modeling). Nevertheless, the data are limited in several ways. First, the patients represent practice at

only 1 institution. Second, comorbidity information was obtained through discharge codes and was categorized as the presence or absence of a comorbidity. Thus, our analysis does not account for the severity of individual comorbidities, only the presence or absence of that comorbidity. In addition, it is difficult to differentiate preexisting morbidities from those that result from anemia or transfusion. Although discharge codes may not be as accurate as data obtained from chart abstraction, we did not use discharge diagnoses as our primary exposure (age) or outcome (transfusion); we used them only to adjust the multivariable model. Third, we do not have data on postsurgical blood loss, such as drain output. However, all of our analyses were adjusted for intraoperative blood loss and for lowest hemoglobin value, which may account for differences between elderly and younger patients in postoperative bleeding. Furthermore, because we do not know the relationship between the times of transfusion and the lowest hemoglobin values, we are unable to call the lowest in-hospital hemoglobin value a true transfusion “trigger.” Thus, an accurate interpretation of our data would be that elderly patients have increased odds of transfusion after accounting for the lowest hemoglobin value, whether that value is measured before transfusion or later in the hospital course. Interestingly, the first, lowest, and last hemoglobin concentrations were similar among patients >65 y/o compared with younger patients, indicating that hemoglobin concentration, while important, does not explain the increased odds of transfusion in older adults. Our dataset was missing estimated blood loss values for 21% of patients, and these missing values were imputed. Previous work has shown that imputed values for blood loss might be biased because of a lower likelihood of intraoperative transfusion for patients in whom estimated blood loss was missing.²⁴ However, our imputation model accounted for this potential bias by incorporating several pertinent variables, including actual transfusion, IV fluids, and hemoglobin change; therefore, any bias was likely to be small. In addition, we categorized blood loss in the final regression model, so small biases in imputed blood loss values were likely subsumed within the final categorization of the variable. Finally, we do not account for symptoms in the decision to transfuse. This is an important limitation and emblematic of the larger issue that we do not have the precise rationale for transfusion for each patient. Conceivably, older adults might have more symptoms of anemia that might be improved with transfusion. Although older patients may experience more symptoms of anemia, and other unmeasured variables may be present, transfusion decisions have been shown to be driven largely by hemoglobin concentrations rather than by symptoms, although the reasons for transfusion decisions in this study population are not known.²⁴

In conclusion, our results reveal that older adults have significantly higher odds of transfusion than do younger adults in the perioperative period, even after controlling for lowest in-hospital hemoglobin concentration, comorbidities, surgical blood loss, surgeon, and procedure. Because there is little or no evidence supporting higher hemoglobin transfusion triggers in elderly patients, further research is needed to determine if transfusion practice in the elderly is an opportunity for education to improve blood utilization in the perioperative setting.

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Appendix 1. Classification of Comorbidities Based on Clinical Classification Software Codes

Diabetes: CCS codes 49, 50
Disorders of lipid metabolism: CCS code 53
Anemia: CCS codes 59, 61, 62
Delirium/dementia: CCS code 653
Heart valve disorders: CCS code 96
Hypertension: CCS codes 98, 99
Acute myocardial infarction: CCS code 100
Conduction disorders/dysrhythmias: CCS codes 105, 106
Coronary atherosclerosis: CCS code 101
Congestive heart failure: CCS code 108
Cerebrovascular disease: CCS codes 110–113
Peripheral vascular disease: CCS codes 114–117

Chronic obstructive pulmonary disease/asthma/other respiratory: CCS codes 127, 128, 132–134
Liver disease: CCS codes 149–151
Gastrointestinal disease: CCS codes 139, 140, 144, 146
Acute/chronic kidney disease: CCS codes 156–158

CCS = clinical classifications software.

Figure 1.

Patient flowchart demonstrating the data initially available, followed by exclusion criteria that were applied to generate the analyzed patient cohort.

Figure 2.

Lowess-smoothed curve showing unadjusted estimated probability of transfusion by average age of patient (years), stratified by the lowest in-hospital hemoglobin value.

Figure 3.

Adjusted odds ratio of transfusion for patients >65 years old compared with patients ≤65 years old. * $P < 0.05$ for the comparison of the odds ratio of transfusion for patients with the comorbidity compared with patients without the comorbidity.

Table 1

Patient Characteristics

	65 y/o (n = 15640)	>65 y/o (n = 5290)	Total (N = 20930)	P
Demographics				
Age (y) mean $\pm$ SD	48.8 $\pm$ 11.6	73.3 $\pm$ 6.2	55.0 $\pm$ 15.0	< 0.0001
% Male	48.5	55.3	50.2	< 0.0001
Comorbidities ^a (%)				
Cerebrovascular disease	2.2	5.3	3.0	< 0.0001
Delirium, dementia, or other cognitive disorders	0.9	5.2	1.9	< 0.0001
Hypertension	36.5	65.4	43.8	< 0.0001
Acute myocardial infarction	1.9	2.8	2.1	0.0001
Coronary atherosclerosis	5.6	21.0	9.5	< 0.0001
Congestive heart failure	2.0	5.7	2.9	< 0.0001
Cardiac valve disease	3.8	10.3	5.5	< 0.0001
Conduction abnormalities	8.0	22.3	11.6	< 0.0001
Lipid metabolism disorders	17.0	33.9	21.3	< 0.0001
Peripheral vascular disease	9.6	21.3	12.6	< 0.0001
Lung disease	18.7	22.0	19.5	< 0.0001
Liver disease	7.4	8.6	7.7	0.0032
Gastrointestinal disease	5.5	8.0	6.1	< 0.0001
Kidney disease	7.0	13.0	8.5	< 0.0001
Diabetes	13.2	24.8	16.1	< 0.0001
Anemia	13.3	13.6	13.4	0.53
Surgical service ^b (%)				
OLHNS/plastic	14.0	11.7	13.5	< 0.0001
General/trauma/transplant	28.0	27.8	28.0	
Gynecologic	7.1	2.8	5.99	
Neurosurgery	18.7	15.8	17.9	
Orthopedic	9.6	11.8	10.2	
Thoracic	4.3	7.2	5.1	
Urology	15.1	15.5	15.2	
Vascular	3.1	7.3	4.2	
Surgeon years since medical school graduation (%)				
<18 y	51.2	44.8	50.4	< 0.0001
>18 y	48.8	55.2	49.6	
Anesthesia division				
General	48.0	46.9	47.7	< 0.0001
Cardiac	6.1	7.8	6.5	
Obstetric/regional	17.8	18.6	18.0	
ICU	9.2	10.4	9.5	
Neurosurgical	17.7	15.7	17.2	

	65 y/o	>65 y/o	Total	P
	(n = 15640)	(n = 5290)	(N = 20930)	
Pediatric	1.3	0.6	1.1	
Estimated blood loss (mL) median (IQR)	200(80–400)	200(100–500)	200(100–400)	< 0.0001
Transfusion (%)	16.5	27.4	19.3	< 0.0001
Hemoglobin values in-hospital (g/dL), (mean ± SD)				
Initial	12.57 ± 1.95	12.33 ± 1.87	12.51 ± 1.93	< 0.0001
Lowest	10.4 ± 2.18	9.89 ± 2.06	10.28 ± 2.16	< 0.0001
Last	10.99 ± 1.84	10.64 ± 1.67	10.90 ± 1.89	< 0.0001

OLHNS = otolaryngology head and neck surgery; ICU = intensive care unit; IQR = inter quartile range.

^aICD-9 discharge codes were used to identify comorbidities, and Clinical Classification Software was used to combine comorbidities into clinically meaningful diagnosis categories.

^bSurgical service was defined according to the primary appointment of the primary surgeon of record.

Table 2

Odds Ratio of Transfusion for Patients >65 Y/O Compared With Patients 65 Y/O, Overall and by Strata of Lowest In-Hospital Hemoglobin

Patient age (N)	% Transfused	Crude			Adjusted ^d		
		OR	95% CI	P	OR	95% CI	P
		Overall					
>65 vs 65 y/o (5205 vs 15500)	27.4 vs 16.5	1.87	(1.74–2.02)	<0.001	1.62	1.40–1.88	<0.0001
Age by decade							
20–40 y/o (3417)	14.3	REF			REF		
40–50 y/o (3588)	14.5	1.02	(0.89–1.16)	0.80	1.29	1.01–1.65	0.04
50–60 y/o (5220)	16.7	1.21	(1.07–1.36)	0.002	1.36	1.08–1.71	0.008
60–70 y/o (5095)	21.6	1.65	(1.46–1.85)	<0.001	1.82	1.44–2.30	<0.001
70–80 y/o (2494)	28.2	2.36	(2.07–2.68)	<0.001	2.58	1.98–3.35	<0.001
>80 y/o (891)	34.2	3.12	(2.64–3.70)	<0.001	3.29	2.35–4.60	<0.001
Stratified by lowest in-hospital hemoglobin value							
7.0–7.99 g/dL (2156)							
>65 vs 65 y/o (736 vs 1420)	80.3 vs 66.1	2.10	(1.70–2.59)	<0.001	2.18	1.66–2.85	<0.001
Age by decade							
20–40 y/o (256)	56.6	REF			REF		
40–50 y/o (335)	59.7	1.13	(0.82–1.58)	0.45	1.23	0.83–1.82	0.31
50–60 y/o (484)	69.8	1.77	(1.29–2.43)	<0.001	1.98	1.35–2.92	<0.001
60–70 y/o (570)	74.0	2.18	(1.60–2.97)	<0.001	2.47	1.65–3.68	<0.001
70–80 y/o (365)	83.0	3.74	(2.59–5.41)	<0.001	4.05	2.54–6.46	<0.001
>80 y/o (146)	82.9	3.71	(2.26–6.09)	<0.001	3.93	2.13–7.23	<0.001
8.0–8.99 g/dL (2454)							
>65 vs 65 y/o (838 vs 1616)	43.9 vs 31.3	1.72	(1.45–2.04)	<0.001	1.69	1.30–2.19	<0.0001
Age by decade							
20–40 y/o (287)	23.7	REF			REF		
40–50 y/o (348)	24.4	1.04	(0.72–1.50)	0.83	1.33	0.82–2.14	0.24
50–60 y/o (558)	32.6	1.56	(1.13–2.16)	0.007	1.32	0.85–2.07	0.22
60–70 y/o (711)	38.7	2.03	(1.49–2.78)	<0.001	1.84	1.18–2.87	0.007
70–80 y/o (395)	46.8	2.84	(2.03–3.97)	<0.001	3.28	2.01–5.34	<0.001

Patient age (N)	% Transfused	Crude			Adjusted ^a		
		OR	95% CI	P	OR	95% CI	P
		Overall					
>80 y/o (155)	51.0	3.35	(2.21–5.08)	< 0.001	4.01	2.21–7.28	< 0.001
9.0–9.99 g/dL (2862)	14.1						
>65 vs 65 y/o (822 vs 2040)	20.4 vs 11.5	1.98	(1.59–2.46)	< 0.001	2.03	1.44–2.87	< 0.001
Age by decade							
20–40 y/o (414)	8.2	REF			REF		
40–50 y/o (466)	8.6	1.05	(0.65–1.69)	0.84	1.19	0.61–2.30	0.61
50–60 y/o (676)	12.9	1.65	(1.09–2.51)	0.02	1.07	0.57–2.00	0.83
60–70 y/o (736)	15.4	2.03	(1.35–3.04)	< 0.001	1.51	0.81–2.81	0.20
70–80 y/o (418)	19.6	2.73	(1.78–4.18)	< 0.001	2.24	1.14–4.40	0.02
>80 y/o (152)	30.3	4.85	(2.96–7.94)	< 0.001	5.21	2.37–11.5	< 0.001
> 10g/dL (12,271)	1.0						
>65 vs 65 y/o (2610 vs 9661)	1.4 vs 0.9	1.63	(1.10–2.42)	< 0.001	1.06	0.52–2.14	0.88
Age by decade							
20–40 y/o (2223)	0.5	REF			REF		
40–50 y/o (2266)	0.6	1.15	(0.53–2.48)	0.73	0.84	0.29–2.41	0.74
50–60 y/o (3276)	0.9	1.59	(0.81–3.13)	0.18	1.09	0.42–2.83	0.86
60–70 y/o (2877)	1.4	2.66	(1.40–5.08)	0.003	1.39	0.51–3.81	0.52
70–80 y/o (1230)	1.4	2.56	(1.23–5.42)	0.01	1.53	0.44–5.29	0.51
>80 y/o (399)	1.8	3.29	(1.29–8.41)	0.01	1.69	0.33–8.69	0.53

CI = confidence interval; OR = odds ratio; REF = reference category.

^aMultilevel adjusted model incorporated surgical procedure and individual surgeon as random intercept terms. Fixed effect covariates included gender, estimated surgical blood loss, lowest in-hospital hemoglobin value, surgical service, cerebrovascular disease, delirium or dementia, hypertension, acute myocardial infarction, coronary atherosclerosis, congestive heart failure, cardiac valve disease, conduction disease, lipid disorders, peripheral vascular disease, lung disease, liver disease, kidney disease, diabetes, and anemia. Patients with missing data for any part of the model (except for imputed values) were not included in the adjusted model with the assumption of missing completely at random.

Odds Ratio of Transfusion for Patients >65 Y/O Compared With Patients 65 Y/O, by Surgical and Anesthesia Characteristics

Table 3

	Crude			Adjusted ^a			P interaction
	OR	95% CI	P	OR	95% CI	P	
Surgical service							0.015
OLHNS/plastic	1.48	1.31–1.68	< 0.001	2.41	1.25–4.63	0.008	
General/trauma/transplant	1.72	1.62–1.82	< 0.001	1.74	1.35–2.26	< 0.001	
Gynecologic	1.64	1.37–1.96	< 0.001	1.83	0.63–5.36	0.26	
Neurosurgery	1.69	1.55–1.85	< 0.001	1.69	1.14–2.49	0.008	
Orthopedic	3.32	3.04–3.62	< 0.001	2.24	1.52–3.29	< 0.001	
Thoracic	1.11	0.96–1.28	0.16	2.08	1.13–3.82	0.02	
Urology	2.38	2.13–2.66	< 0.001	1.49	0.97–2.27	0.07	
Vascular	1.03	0.91–1.17	0.63	0.55	0.1–2.75	0.47	
Surgeon years since medical school graduation							0.08
<18 y	1.81	1.62–2.01	< 0.001	1.41	1.13–1.74	< 0.001	
>18 y	1.97	1.78–2.19	< 0.001	1.89	1.54–2.31	< 0.001	
Anesthesia division							0.90
General	1.92	1.72–2.14	< 0.001	1.79	1.44–2.23	< 0.001	
Cardiac	1.39	1.07–1.80	0.02	1.10	0.66–1.84	0.72	
Obstetric/regional	1.99	1.67–2.36	< 0.001	1.86	1.29–2.66	< 0.001	
ICU	1.96	1.54–2.48	< 0.001	1.75	1.05–2.91	0.03	
Neurosurgical	1.79	1.50–2.15	< 0.001	1.75	1.23–2.50	0.002	
Pediatric	4.05	1.45–11.3	0.008	1.10	0.66–1.84	0.72	

CI = confidence interval; OR = odds ratio; OLHNS = otolaryngology head and neck surgery.

^aMultilevel adjusted model incorporated surgical procedure and individual surgeon as random intercept terms. Fixed effect covariates included gender, estimated surgical blood loss, lowest in-hospital hemoglobin value, surgical service, cerebrovascular disease, delirium or dementia, hypertension, acute myocardial infarction, coronary atherosclerosis, congestive heart failure, cardiac valve disease, conduction disease, lipid disorders, peripheral vascular disease, lung disease, liver disease, gastrointestinal disease, kidney disease, diabetes, and anemia.