Risks associated with preoperative anemia and perioperative blood transfusion in open surgery for intracranial aneurysms

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OBJECT Preoperative anemia may be treated with a blood transfusion. Both are associated with adverse outcomes in various surgical procedures, but this has not been clearly elucidated in surgery for cerebral aneurysms. In this study the authors assessed the association of preoperative anemia and perioperative blood transfusion, separately, on 30-day morbidity and mortality in patients undergoing open surgery for ruptured and unruptured intracranial aneurysms.

METHODS The authors identified 668 cases (including 400 unruptured and 268 unruptured intracranial aneurysms) of open surgery for treatment of intracranial aneurysms in the 2006–2012 National Surgical Quality Improvement Program, a validated and reproducible prospective clinical database. Anemia was defined as a hematocrit level less than 39% in males and less than 36% in females. Perioperative transfusion was defined as at least 1 unit of packed or whole red blood cells given at any point between the start of surgery to 72 hours postoperatively. The authors separately compared surgical outcome between patients with (n = 198) versus without (n = 470) anemia, and those who underwent (n = 78) versus those who did not receive (n = 521) a transfusion, using a 1:1 match on propensity score.

RESULTS In the matched cohorts, all observed covariates were comparable between anemic (n = 147) versus nonanemic (n = 147) and between transfused (n = 67) versus nontransfused patients (n = 67). Anemia was independently associated with prolonged hospital length of stay (LOS; odds ratio [OR] 2.5, 95% confidence interval [CI] 1.4–4.5), perioperative complications (OR 1.9, 95% CI 1.1–3.1), and return to the operating room (OR 2.1, 95% CI 1.1–4.5). Transfusion was also independently associated with perioperative complications (OR 2.4, 95% CI 1.1–5.3).

CONCLUSIONS Preoperative anemia and transfusion are each independent risk factors for perioperative complications in patients undergoing surgery for cerebral aneurysms. Perioperative anemia is also associated with prolonged hospital LOS and 30-day return to the operating room.

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KEY WORDS intracranial aneurysm; cerebral aneurysm; open surgery; anemia; transfusion; complications; outcome; morbidity; mortality; vascular disorders

ANEMIA is a clinically significant finding that has been shown to compromise surgical outcome in many specialties.1,6,14,24,27 Blood transfusion offers an immediate corrective measure in surgical candidates with anemia.14 However, transfusion is perhaps a hazardous intervention.19 Prior studies have examined anemia and blood transfusion in patients with traumatic brain injury32,38 and subarachnoid hemorrhage,23,25,28,31,35 but little is known about the role of anemia and transfusion as perioperative risk factors for patients who undergo neurosurgery.1,33 This study had two separate, although related, aims: to assess the independent association of preoperative

ABBREVIATIONS ACS = American College of Surgeons; ASA = American Society of Anesthesiologists; BMI = body mass index; CI = confidence interval; CPT = current procedural terminology; CVA = cerebrovascular accident; ICD-9 = International Classification of Diseases, Ninth Revision. LOS = length of stay; NSQIP = National Surgical Quality Improvement Program; OR = odds ratio.


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DISCLOSURE Dr. Selman has direct stock ownership in Osteoplastics and Surgical Theater.
anemia and perioperative blood transfusion separately on 30-day morbidity and mortality in patients undergoing open surgery for intracranial aneurysms.

**Methods**

**Data Source**

We used the American College of Surgeons’ (ACS) National Surgical Quality Improvement Program (NSQIP) database for data collection. The NSQIP began neurosurgical data collection in 2005 and now includes nearly 400 community and academic hospitals. The NSQIP contains de-identified data from randomly selected consenting patients for a total of 252 variables that include demographic variables, preoperative laboratory values, preexisting comorbidities, intraoperative variables, and 30-day postoperative morbidity and mortality. Data are collected prospectively by a trained surgical nurse at each participating institution. The ACS conducts an annual interrater reliability audit of the data collection at each site to ensure accurate data collection.\(^\text{2,21,34}\)

**Study Population**

Using the International Classification of Diseases, ninth revision (ICD-9) codes 430 and 437.3, we identified 962 patients who were surgically treated for intracranial aneurysms between 2006 and 2012 (Fig. 1). Patients who underwent craniotomy or skull base surgery for treatment, according to current procedural terminology (CPT) codes, were included in the study (n = 732). We excluded patients with missing preoperative hematocrit levels (n = 53). Patients with preoperative transfusion (n = 8) and septic shock (n = 3) were also excluded because they were infrequent, which would have strained the matching criteria. Thus, our study sample consisted of 668 patients who underwent craniotomy or skull base surgery for treatment of intracranial aneurysms, 268 (40.1%) of whom were treated for ruptured aneurysm.

**Anemia and Transfusion**

Our primary predictive variables of interest were anemia and transfusion. Anemia is defined variably in the literature.\(^\text{29}\) We used the WHO definition of anemia as hematocrit < 0.39% in males and < 0.36% in females.\(^\text{39,40}\)

We found that 198 patients in our study had preoperative anemia (Fig. 1). We also explored other definitions of anemia in sensitivity analyses, including hematocrit < 41% in males and < 36% in females. Transfusion was recorded in the NSQIP database for patients who received at least 1 unit of whole or packed red blood cells transfused at any time from the start of surgery to 72 hours after surgery. In our study population, 78 patients received perioperative transfusion (Fig. 1).

**Outcomes of Interest**

We focused on the following primary outcomes following surgery: 1) prolonged hospital length of stay (LOS), defined as LOS longer than the third quartile in the sample\(^\text{41-43}\) (17 days); 2) minor complications, including superficial surgical site infection, urinary tract infection, deep venous thrombosis, and/or thrombophlebitis; 3) major complications, consisting of deep-incision surgical site infection, organ or space surgical site infection, wound disruption, pneumonia, unplanned intubation, pulmonary embolism, greater than 48-hour postoperative ventilator-assisted respiration, progressive renal insufficiency, acute renal failure, cardiovascular accident with neurological deficit, coma longer than 24 hours, peripheral nerve injury, cardiac arrest requiring cardiopulmonary resuscitation, myocardial infarction, graft failure, prosthesis failure, flap failure, septic shock, and/or 30-day return to the operating room; 4) any complication, defined as having at least 1 minor or major complication; 5) return to the operating room, defined as any unplanned return to the operating room for a surgical procedure related to the primary procedure; 6) discharged with continued care, defined as being discharged to a skilled or unskilled care facility, exempting those who were initially admitted from such facilities; and 7) death within 30 days postoperatively.

**Patient History Covariates**

We analyzed all available preoperative and intraoperative factors in the NSQIP database that might have an effect on postoperative outcomes. Although the NSQIP does not include Hunt and Hess grade, we were able to approximate this for all patients with ruptured aneurysms (ICD-9 code 430) based on the preoperative variable recorded in the database. Patients who were “unconscious, or postured to painful stimuli, or were unresponsive to all stimuli entering surgery” were captured by the NSQIP under the variable “coma”; we assigned these patients a Hunt and Hess grade of V. Patients were considered to have “hemiplegia” in the NSQIP if they “had sustained acute or chronic neuromuscular injury resulting in total or partial paralysis on one side of the body, or if they had hemiplegia/hemiparesis upon arrival to the operating room, or if they had hemiplegia or hemiparesis associated with a CVA/Stroke.” We considered these patients to have Hunt and Hess Grade IV. We considered patients to have a Hunt and Hess grade of III if they had “impaired sensorium,” the definition of which in the NSQIP is as follows: patients who “were acutely confused and/or delirious and respond to verbal and/or mild tactile stimulation, or were noted to have developed an impaired sensorium if they have mental status changes, and/or delirium in the context of the current illness.” Patients who had chronic or long-standing mental status changes due to chronic mental illness or chronic dementing illnesses were not considered to have impaired sensorium. Unfortunately, the NSQIP does not provide any data on headache or nuchal rigidity, making it impossible to distinguish between patients with Hunt and Hess grades of I and II. Thus, we had to combine Hunt and Hess Grades I and II into 1 category; all patients who were not assigned as having Hunt and Hess grade of V, IV, or III were placed in this category.

We used age, body mass index (BMI), and surgical time as continuous variables. We merged race categories into Caucasian versus all other races. We dichotomized both transfer and functional status, respectively, as admitted from home versus transferred from any facility and as independent versus dependent functional status. We merged...
the American Society of Anesthesiologists (ASA) classification into Grades 1 and 2 together and 3 and 4 together. We classified patients who had a history of transient ischemic attacks or cerebrovascular accidents (CVAs) with or without residual neurological deficits as having cerebrovascular comorbidities. Patients who required ventilator-assisted respiration during the 48 hours prior to surgery, had congestive heart failure that was diagnosed or was symptomatic within 30 days prior to surgery, self-reported angina in the month leading up to surgery, myocardial infarction within the 6 months prior to surgery, any history of percutaneous coronary intervention, prior cardiac surgery, angioplasty, or revascularization procedure for atherosclerotic peripheral vascular disease, or were experiencing rest pain or gangrene were considered to have cardiopulmonary comorbidities. Patients were defined as having renal comorbidities if they had renal disease or abnormal blood urea nitrogen or creatinine lab values. We defined cancer-related comorbidities as presenting with disseminated cancer, unintentional weight loss greater than 10% of body weight in the 6 months preceding surgery, or receiving chemotherapy or radiotherapy within 90 days prior to surgery. Self-reported patient history of abnormal bleeding, self-reported family history of bleeding disorders, vitamin K deficiency, and a comprehensive list of medications that pose a risk for bleeding abnormalities were captured through the NSQIP variable “bleeding disorders.” Patients with bleeding disorders or abnormal preoperative international normalized ratios, activated partial thromboplastin times, or platelet counts were considered to have bleeding risk factors. We investigated the presence of resident physicians in the operating room as a surrogate marker for academic institutions.

### Statistical Analyses

The two aims of the study required two separate sets of analyses. First, we assessed the independent effect of preoperative anemia on postoperative outcomes. Because patients cannot be randomly assigned to treatment groups, selection bias is an inherent limitation of observational...
studies, including our own. However, propensity score, defined as the chance that a patient has anemia given a set of baseline characteristics, allowed us to control for the non-random design of this study.\textsuperscript{30,21} We determined propensity score for each patient using multivariate logistic regression that included baseline variables with significant absolute standardized differences, including ruptured aneurysm and perioperative transfusion. We used a 1:1 greedy matching technique\textsuperscript{6} to match patients with anemia (aneurysm patients) to those without (nonanemic patients) according to their respective propensity scores. This allowed us to isolate the effect of anemia, in and of itself, from that of all other covariates (including ruptured aneurysm and perioperative transfusion) on postoperative outcomes.\textsuperscript{30} We used standardized differences to compare baseline characteristics in the unmatched and matched cohorts to ensure that a balanced distribution of covariates was achieved with propensity score matching. Unlike p values, the standardized difference does not depend on sample size, which is important in matched analyses because the inadvertently smaller size of the matched cohort may result in the false notion that improved covariate balance was achieved with matching.\textsuperscript{3} An absolute standardized difference of more than 0.20 was considered significant.\textsuperscript{4}

We also compared baseline characteristics according to anemia status using Pearson’s chi-square tests for categorical variables and ANOVA for continuous variables, to provide a measure of significant statistical difference before and after matching (reported as p values). However, these statistical measures were not used to assess covariate balance. Due to the matched nature of the data, we used conditional logistic regression analysis\textsuperscript{3,15} to model the relationship between anemia and adverse outcomes in the matched cohort. We repeated the above set of analyses, comparing patients according to transfusion status instead of anemia. To isolate the effect of transfusion from that of anemia, we matched patients who received a transfusion (transfused patients) to those who did not (nontransfused patients) on preoperative hematocrit level as well as on all pre- and intraoperative factors. Covariates that remained unbalanced in the matched cohort, having an absolute standardized difference greater than 0.20, were included in the final model. A p value < 0.05 was considered statistically significant. The SAS statistical program (version 9.2, SAS Institute) was used for all statistical analyses.

Results

Anemia Compared With No Anemia

In the general cohort, ruptured aneurysms, emergency cases, and perioperative transfusion were more common among anemic patients (Table 1). In patients with subarachnoid hemorrhage, there was no difference in the Hunt and Hess grade between anemic and nonanemic patients. It is evident by the large number of variables with significant standardized differences that baseline characteristics were not balanced in the general cohort among patients with anemia compared with those without anemia. We matched 147 patients with anemia to 147 patients without anemia. In the matched cohort, no absolute standardized differences remained significant (Table 1). Thus we were able to fully control for the differences in the baseline characteristics between patients with and without anemia in our matched cohort. In the general cohort, all observed outcomes were more frequent in anemic patients except for 30-day mortality (Table 2). In the matched cohort, prolonged LOS, complications, and 30-day return to the operating room continued to be more frequent in anemic patients (Table 2).

Transfusion Compared With No Transfusion

In the general cohort, patients who underwent perioperative transfusion were more likely to undergo surgery for ruptured aneurysms, undergo emergency operations, and have bleeding risk factors (Table 3). Hunt and Hess grade was also significantly different for patients who had subarachnoid hemorrhage, with transfused patients presenting with a higher grade. The average preoperative hematocrit level for patients who received transfusion was 4% lower than for those who did not. Covariate balance was achieved by matching 67 patients who underwent transfusion to 67 patients who did not (Table 3). Exempting minor complications, all adverse events were significantly more frequent in the transfused patients in the general cohort (Table 4), although in the matched cohort the disparity was less remarkable.

Adverse Outcomes

In the general cohort, anemia was associated with 2–3 times the odds for all adverse events compared with nonanemic patients, but not 30-day mortality (Table 5). In the matched cohort, anemia continued to be associated with prolonged LOS (odds ratio [OR] 2.5, 95% confidence interval [CI] 1.4–4.5), complications (OR 1.9, 95% CI 1.1–3.1), and return to the operating room (OR 2.2, 95% CI 1.1–4.5). In the general cohort, transfusion was associated with all adverse outcomes except minor complications (Table 5). In the matched cohort, transfusion continued to be associated with more than twice the odds for complications (OR 2.4, 95% CI 1.1–5.3). Sensitivity analyses using different cutoffs for anemia confirmed similar study findings.

Discussion

The propensity score in retrospective studies minimizes selection bias to the same effect of randomization in prospective studies.\textsuperscript{3,4} We used matching on propensity score to control for the presence of comorbidities in anemic and transfused patients. The match was successful in that we were able to successfully match 74% of anemic with nonanemic patients and 71% of transfused with nontransfused patients, achieving covariate balance in both matched cohorts.

Anemia and transfusion were each found to be independently associated with adverse postoperative outcomes in patients undergoing open surgery for management of intracranial aneurysms. Anemia, in and of itself, was found to double the odds for prolonged LOS, complications, and 30-day return to the operating room, while transfusion was found to more than double the odds for perioperative complications.

Interpretation of Results in the Context of the Literature

Preoperative anemia is a clinically significant finding
and may be a marker of underlying disease. Similarly, patients who receive a transfusion have a more severe medical condition. Thus, the association between anemia or transfusion and adverse outcomes in the general cohorts may be, at least in part, reflective of overall poor health of these patients. However, this association persists after matching on propensity scores, which allow us to balance the burden of comorbidities between anemia and no anemia and transfused and nontransfused patients. This tells us that anemia and transfusion are, in and of themselves, risk factors for adverse outcomes.

To the best of our knowledge, this is the first study to

<table>
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<th>Matched Cohort</th>
<th>Absolute Standardized Difference†</th>
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<td>Difference</td>
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<td></td>
<td>Difference‡</td>
<td>Difference†</td>
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<td>V</td>
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LFT = liver function test; SIRS = systemic inflammatory response syndrome; WBC = white blood cell.
* All significant p values are in bold.
† Significant standardized differences (> 0.20) are bolded.
‡ Only for patients with subarachnoid hemorrhage.
assess the effect of anemia and transfusion on 30-day outcomes of patients undergoing surgery for cerebral aneurysms. The only prior study that provides some overlap with our targeted population and aim is the 2014 Alan et al. study. The population targeted by that study was patients undergoing elective cranial surgery, thus adding value to their presentation, risk factors, and outcomes from those undergoing elective cranial surgery, but anemia was associated with prolonged hospital LOS. This result suggests that patients with aneurysms are different in their presentation, risk factors, and outcomes from those undergoing elective cranial surgery, thus adding value to this paper.

A study conducted in a mixed surgical population found increased risk for adverse events in anemic patients with preoperative cardiovascular comorbidities. We took cardiovascular comorbidities into account in our study, matching patients on this variable. Thus, in our matched cohorts between anemia and prolonged LOS, complications, and return to the operating room, and between transfusion and complications, suggests that preoperative anemia and perioperative transfusion, separately, are a priori risk factors for adverse outcomes.

Severity of anemia may affect the outcome of surgery. We did not address this question in our study because stratification of patients according to severity of anemia would have resulted in a low number of patients in each category, compromising the power of the statistical analyses. Similarly, the risk of complications may increase with each additional unit of transfusion. We were unable to determine the number of units of transfused whole or packed red blood cells from the NSQIP database beyond the fact that the transfusion included at least 1 unit of whole or packed red cells. In a report characterizing blood use in cerebrovascular surgery, Couture and colleagues found that patients with ruptured and unruptured intracranial aneurysms are transfused with an average of 2.4 units intra- or postoperatively. In another study of 472 cases of intracranial surgery, including 54 patients with aneurysms, Cataldi et al. similarly reported that transfused patients most commonly received 1 or 2 units of autologous or allogeneic blood. There is little reason to believe that patients in our sample differed in the number of transfused units compared with the above-mentioned studies.

We are unable to determine from the NSQIP database the reason why each patient received a transfusion perioperatively. We used surrogate variables to approximate the potential risk of significant bleeding occurrence perioperatively that prompted transfusion. In the matched cohort,
Anemia and transfusion in intracranial aneurysms

The optimal target hemoglobin level is unknown in neurosurgical patients, with literature focused on patients with traumatic brain injury and subarachnoid hemorrhage. The 2012 Guidelines from the American Heart and the American Stroke Associations does not make recommendations for when to initiate transfusion in patients with aneurysmal subarachnoid hemorrhage.10 Physician preference and institutional trends are thus major decisive factors in the type of treatment provided to patients with different types of aneurysms.10,31 Three studies assessing the frequent use of transfusion in patients with subarachnoid hemorrhage

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<td>Diabetes mellitus (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.5</td>
<td>8.5</td>
</tr>
<tr>
<td>Hypertension requiring medication (%)</td>
<td>53.3</td>
<td>53.3</td>
</tr>
<tr>
<td>Comorbidities (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiopulmonary (%)</td>
<td>23.5</td>
<td>23.5</td>
</tr>
<tr>
<td>Cerebrovascular (%)</td>
<td>17.4</td>
<td>17.4</td>
</tr>
<tr>
<td>Renal</td>
<td>21.1</td>
<td>21.1</td>
</tr>
<tr>
<td>Cancer-related (%)</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Bleeding risk factors (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.4</td>
<td>9.4</td>
</tr>
<tr>
<td>Steroid use for chronic condition (%)</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Prior operation w/in 30 days (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Sepsis or SIRS (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.9</td>
<td>7.9</td>
</tr>
<tr>
<td>Abnormal WBC count (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29.9</td>
<td>29.9</td>
</tr>
<tr>
<td>Abnormal LFTs (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>12.2</td>
<td>12.2</td>
</tr>
<tr>
<td>Mean preop hematocrit ± SD (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>39 ± 5</td>
<td>39 ± 5</td>
</tr>
<tr>
<td>Resident in operating room (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>82.7</td>
<td>82.7</td>
</tr>
<tr>
<td>Mean total operation time ± SD (min)</td>
<td>259 ± 99</td>
<td>259 ± 99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>General Cohort</th>
<th>Matched Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nontransfused (n = 521)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfused (n = 78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p Value*</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Absolute Standardized Difference†</td>
<td>0.49</td>
<td>0.38</td>
</tr>
<tr>
<td>Nontransfused (n = 67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfused (n = 67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p Value</td>
<td>0.86</td>
<td>0.86</td>
</tr>
<tr>
<td>Absolute Standardized Difference</td>
<td>0.03</td>
<td>0.03</td>
</tr>
</tbody>
</table>

LFT = liver function test; SIRS = systemic inflammatory response syndrome; WBC = white blood cell.
* All significant p values are in bold.
† Significant standardized differences (> 0.20) are in bold.
‡ Only for patients with subarachnoid hemorrhage.
suggested that transfusion was associated with worse outcomes, including greater risk for vasospasm, thrombotic events, and death.23,25,35 However, a small randomized trial in patients with subarachnoid hemorrhage found that maintaining higher hemoglobin levels via transfusion may be safe and feasible.28 A recent systematic review of neurocritically ill patients concluded that sufficient evidence does not exist to allow distinction between the efficacy of a lower or higher threshold of transfusion in these patients.13 In other surgical specialties, transfusion at lower hemoglobin trigger points did not result in poorer outcomes.8,22,37

Clinical Implications
Our findings suggest that preoperative anemia should not be disregarded as a benign finding. This conclusion is consistent with most,23,33,35 but not all prior studies1,28 investigating various subpopulations of neurosurgical and neurocritically ill patients. In emergency cases, perioperative transfusion may offer an immediate measure to correct low preoperative hematocrit, but as we demonstrated, transfusion also compromises the outcome of surgery. In elective cases, postponement of surgery in the interest of thorough investigation for the underlying cause of anemia and more conservative intervention measures such as nutritional supplementation, ferrous sulfate, or erythropoietin11 may avert the adverse surgical outcomes.

Awareness of the risks associated with perioperative transfusion, and the desire to avoid transfusion whenever possible, can also affect surgeon attentiveness to maintaining intraoperative hemostasis. In a comparison of 103 neurosurgical patients who were Jehovah’s Witnesses (6 of whom had aneurysms or arteriovenous malformations) to a valid control group, Suess and colleagues demonstrated that intraoperative blood loss and transfusion were more common in the control group.36 Nevertheless, outcome of surgery was similar, although an operation in Jehovah’s Witness patients lasted on average 30 minutes longer, suggesting that when made aware of the inability to rely on transfusion, surgeons were more attentive to intraoperative hemostasis.36

Study Limitations
This study has several limitations. Given the institutional differences in management of patients with cerebral

<table>
<thead>
<tr>
<th>Variable*</th>
<th>General Cohort</th>
<th>Matched Cohort</th>
<th>p Value</th>
<th>General Cohort</th>
<th>Matched Cohort</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total hospital LOS (days)</td>
<td>Nontransfused (n = 521)</td>
<td>Transfused (n = 78)</td>
<td>p Value</td>
<td>Nontransfused (n = 67)</td>
<td>Transfused (n = 67)</td>
<td>p Value</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>11 ± 11</td>
<td>24 ± 40</td>
<td>&lt;0.01</td>
<td>15 ± 12</td>
<td>25 ± 47</td>
<td>0.14</td>
</tr>
<tr>
<td>Median</td>
<td>7</td>
<td>17</td>
<td>&lt;0.01</td>
<td>12</td>
<td>16</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prolonged LOS of ≥17 days (%)</td>
<td>73.5</td>
<td>92.3</td>
<td>&lt;0.01</td>
<td>37.3</td>
<td>49.3</td>
<td>0.16</td>
</tr>
<tr>
<td>Minor complication (%)</td>
<td>9.8</td>
<td>16.7</td>
<td>0.18</td>
<td>17.9</td>
<td>13.4</td>
<td>0.48</td>
</tr>
<tr>
<td>Major complications (%)</td>
<td>25.0</td>
<td>61.5</td>
<td>&lt;0.01</td>
<td>41.8</td>
<td>61.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Any complications (%)</td>
<td>27.5</td>
<td>65.4</td>
<td>&lt;0.01</td>
<td>43.3</td>
<td>62.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Return to the operating room w/in 30 days (%)</td>
<td>8.8</td>
<td>19.2</td>
<td>&lt;0.01</td>
<td>16.4</td>
<td>16.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Discharged w/ continued care (%)†</td>
<td>24.9</td>
<td>61.5</td>
<td>&lt;0.01</td>
<td>45.2</td>
<td>56.0</td>
<td>0.42</td>
</tr>
<tr>
<td>30-day mortality (%)</td>
<td>3.5</td>
<td>16.7</td>
<td>&lt;0.01</td>
<td>7.5</td>
<td>16.4</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* Please see Table 2 for definitions of adverse outcomes.
† Data were only available for patients undergoing surgery in 2011 and 2012.

### Table 5. Preoperative anemia and perioperative transfusion as predictors of adverse outcomes after surgery for intracranial aneurysms in the general and matched cohorts*

<table>
<thead>
<tr>
<th>Variable†</th>
<th>General Cohort</th>
<th>Matched Cohort‡</th>
<th>General Cohort</th>
<th>Matched Cohort‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged LOS (&gt;17 days)</td>
<td>3.2 (2.2–4.6)</td>
<td>2.5 (1.4–4.5)</td>
<td>4.2 (2.6–6.5)</td>
<td>1.6 (0.8–3.2)</td>
</tr>
<tr>
<td>Minor complications</td>
<td>2.4 (1.5–4.0)</td>
<td>2.5 (1.2–5.2)</td>
<td>1.5 (0.8–2.9)</td>
<td>0.7 (0.3–1.8)</td>
</tr>
<tr>
<td>Major complications</td>
<td>2.4 (1.7–3.5)</td>
<td>1.6 (1.0–2.7)</td>
<td>4.9 (3.1–7.7)</td>
<td>2.3 (1.1–4.8)</td>
</tr>
<tr>
<td>Any complications</td>
<td>2.5 (1.8–3.6)</td>
<td>1.9 (1.1–3.1)</td>
<td>5.0 (3.1–7.9)</td>
<td>2.4 (1.1–5.3)</td>
</tr>
<tr>
<td>Required continued care§</td>
<td>2.0 (1.2–3.2)</td>
<td>2.3 (0.7–7.3)</td>
<td>4.3 (2.2–8.6)</td>
<td>NA¶</td>
</tr>
<tr>
<td>30-day return to the operating room</td>
<td>2.7 (1.6–4.4)</td>
<td>2.2 (1.1–4.5)</td>
<td>2.4 (1.3–4.3)</td>
<td>1.0 (0.4–2.5)</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>1.5 (0.8–2.8)</td>
<td>0.6 (0.2–1.5)</td>
<td>5.5 (2.8–10.9)</td>
<td>3.0 (0.8–11.1)</td>
</tr>
</tbody>
</table>

* All data given as ORs (95% CIs). Odds ratios that are statistically significant are bolded.
† Please see Table 2 for definitions of adverse outcomes.
‡ Conditional logistic regression.
§ Data were available only for patients undergoing surgery in 2011 and 2012.
¶ Not able to calculate due to the low number of patients discharged with continued care in the matched cohort.
aneurysms, and that the NSQIP collects data from nearly 400 institutions nationwide, our study sample is likely heterogeneous. We are unable to take into account the surgical complexity of aneurysm repair for each patient, although we did include length of surgery, assuming that more complex surgeries may take longer to complete. The NSQIP does not provide data on the subtype of anemia, duration prior to surgery, exact etiology, and whether patients were symptomatic. However, we have access to data about the possible etiologies of anemia, including sex, pulmonary and renal comorbidities, alcohol use, steroid use for a chronic condition, chronic diseases, and prior surgery within 30 days. The NSQIP also does not distinguish between patients receiving allogeneic, autologous, or cell-saver blood products; these are all pooled under the category “transfusion.” Lastly, due to the retrospective nature of this study, it is not possible to establish direct causation between either anemia or transfusion and adverse surgical outcomes. Although the propensity score facilitates randomization with respect to the observed covariates, unavai

Author Contributions
Conception and design: A Seicean, Alan, Bambakidis. Acquisition of data: A Seicean. Analysis and interpretation of data: A Seicean, Alan, S Seicean, Neuhauser. Drafting the article: Alan, Neuhauser. Critically revising the article: A Seicean, Alan, Selman, Bambakidis. Reviewed submitted version of manuscript: all authors. Statistical analysis: A Seicean, S Seicean. Study supervision: Bambakidis.

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