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Variation in Transfusion Practices and the Association with Perioperative Adverse Events in Patients Undergoing Open Abdominal Aortic Aneurysm Repair and Lower Extremity Arterial Bypass in the Vascular Quality Initiative

Zachary Osborne¹, Kristine Hanson¹, Benjamin S. Brooke², Marc Schermerhorn³, Peter Henke⁴, Rumi Faizer⁵, Andres Schanzer⁶, Philip Goodney⁷, Thomas Bower¹, Randall R. DeMartino¹, and for the Vascular Quality Initiative

¹Division of Vascular and Endovascular Surgery, Mayo Clinic, Rochester, MN

²Section of Vascular Surgery, The University of Utah School of Medicine, Salt Lake City, UT

³Division of Vascular and Endovascular Surgery, Beth Israel Deaconess Medical Center, Boston, MA

⁴Section of Vascular Surgery, University of Michigan, Ann Arbor, MI

⁵Division of Vascular Surgery, University of Minnesota, Minneapolis, MN

⁶Division of Vascular Surgery, University of Massachusetts Medical Center, Worcester, MA

⁷Section of Vascular Surgery, Dartmouth-Hitchcock Medical Center, Hanover, NH

Abstract

Background—Blood transfusions are associated with adverse events. We examined perioperative transfusion practices and associated complications following open vascular procedures nationwide in the Vascular Quality Initiative (VQI).

Methods—Adults undergoing open abdominal aortic aneurysm repair (OAR) and lower extremity arterial bypass (Bypass) within VQI (2003–2016) were identified. All emergent cases, patients with preoperative hemoglobin <7 g/dL, preoperative hospitalization >1 day, or a return to operating room during the index hospitalization were excluded. Units of red blood cells transfused were the primary outcome. Secondary outcomes were postoperative myocardial infarction (MI) and death. Patient, center, and procedural factors were evaluated. Multivariable mixed effects negative binomial regression and multivariable logistic regression were performed.

Results—We identified 24,131 procedures (OAR 3885, 16.1%; Bypass 20,246, 83.9%) among 22,532 patients (10.1% had >1 procedure). Overall, 37.5% of OAR and 19.5% of Bypass were transfused. Transfusion rates varied across estimated blood loss quartiles and across various

Correspondence to: Randall R. DeMartino, Department of Vascular and Endovascular Surgery, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA; demartino.randall@mayo.edu.

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SUPPLEMENTARY DATA

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preoperative hemoglobin levels. The overall rate of postoperative MI and death was 4.0% and 1.8% for OAR, and 2.2% and 0.7% for Bypass, respectively. In univariate and multivariable analysis, transfusions were associated with an increased risk of postoperative MI and death. A mixed effects negative binomial model demonstrated variation in transfusions across centers ($P < 0.001$). Female gender and preoperative anemia were significantly associated with transfusions.

Conclusions—Blood transfusions are variable across centers in VQI. Transfusions are associated with a higher postoperative MI and death after OAR and Bypass. Efforts to reduce transfusion may focus on center variability, gender, and preoperative anemia.

INTRODUCTION

Anemia is a common finding in vascular surgery patients before and after surgery. It is a risk factor for acute coronary syndromes and a strong predictor of major adverse cardiovascular events.^{1–5} In patients undergoing noncardiac^{6–9} and cardiac procedures,^{10–12} perioperative anemia has been associated with worse clinical outcomes and increased incidence of perioperative myocardial infarction (MI). In patients undergoing infrainguinal bypass, anemia (hematocrit $< 28\%$) has been associated with an increased rate of perioperative cardiac events.¹³

Transfusion of red blood cells offers an immediate correction for anemia, increasing tissue oxygen delivery. However, transfusions have been associated with adverse events, including an increase in perioperative MIs.^{14–16} Based on multiple randomized clinical trials and systematic reviews, national organizations advocate a restrictive transfusion strategy using a trigger hemoglobin level of 7 or below for noncardiac surgeries and recommend avoiding transfusing to hemoglobin levels above 10 mg/dL. Despite these data recommending a restrictive transfusion strategy,^{17–25} some reports have suggested that certain subgroups of patients, like cardiac surgery patients, may experience fewer cardiac complications if a more liberal trigger level of 9 g/dL is used.¹¹ However, there is a paucity of data that has evaluated the association of blood transfusions on perioperative outcomes following vascular surgery, and the limited studies have provided mixed results.^{13,26–28}

Given the conflicting data on transfusion practices in vascular surgery patients, we sought to utilize the Vascular Quality Initiative (VQI) dataset to investigate transfusion practices and predictors for blood transfusions among patients undergoing elective open abdominal aortic aneurysm repair (OAR) and arterial bypass (Bypass). The VQI is a national quality improvement registry that allows a comprehensive assessment of perioperative risk factors for transfusions within a broad sample of academic and community hospitals. Additionally, we sought to understand the associated risk of perioperative mortality and MI with red blood cell transfusions in this patient group.

METHODS

Patient Selection

Utilizing the VQI database, we identified all patients aged 18 and older who underwent an elective OAR, suprainguinal bypass, or infrainguinal bypass at participating hospitals from January 2003 to April 2016. Bypasses are reported as either infrainguinal bypass (with the

most proximal inflow from the common femoral artery [CFA] or distal sources of inflow) or suprainguinal bypass (with an inflow more proximal than the CFA, such as the aorta, axillary, common iliac, or the external iliac artery). Both infrainguinal bypass and suprainguinal bypass were combined for analysis as the Bypass group. We excluded all urgent and emergent cases ($n = 11,229$; 2269 OAR, 8960 bypass) including rupture open AAA repairs, and cases with a return to the operating room for any reason. We also excluded patients with preoperative hemoglobin < 7 g/dL (these patients had an immediate indication to proceed with transfusion prior to surgery) and patients who were hospitalized > 1 day prior to their operation (these patients may have been transfused prior to their surgery). VQI tracks total in-hospital transfusions so it is impossible to differentiate patients who underwent blood transfusion prior to surgery from those who underwent blood transfusion during or after surgery. We excluded Bypass cases without general anesthesia, as well as OAR and suprainguinal bypass cases that underwent a concomitant infrainguinal bypass. Finally, we excluded patients with unknown data on transfusion or any inclusion/exclusion criteria. The goal of this approach is to be able to describe the current practice of transfusions for elective and uncomplicated patients undergoing vascular procedures across institutions. Due to the deidentified nature of the VQI, this study was exempt from review by the Mayo Clinic Institutional Review Board and the need for consent was waved.

Outcomes

The primary outcome of the study was the use of packed red blood cell (pRBC) transfusion practices among participating VQI hospitals. This was calculated based on the number of transfused units of pRBCs given during the hospitalization for patients undergoing elective OAR and Bypass. VQI records the total number of pRBC transfused from admission to discharge. Transfusions were analyzed by the center. We analyzed transfusions across VQI by operation (OAR or Bypass), preoperative hemoglobin levels (< 7 to < 10 , $10-12$, > 12 g/dL), and estimated blood loss (EBL) quartiles (< 100 , $100-250$, $> 250-600$, and > 600 mL) to adjust for various levels of initial hemoglobin, acute blood loss anemia, and magnitude of operation. Our secondary outcomes included postoperative in-hospital mortality and postoperative MI. Postoperative MI is defined as either an electrocardiogram or clinical MI consistent with MI, or an isolated troponin elevation without electrocardiogram ischemic changes or clinical symptoms.

Statistical Analysis

Our primary outcome of pRBC transfusion was compared across patient demographics and operative factors. In addition, we assessed the association of number of transfused pRBC with our secondary outcomes of mortality and MI. Associations with the outcomes of any transfusion, mortality, and MI were assessed initially using chi-squared tests for categorical variables, Fisher's exact tests for low frequency events, and Student's t -tests for continuous variables. For the outcome of pRBC transfusion, multivariable mixed effects negative binomial regression models were used to evaluate the factors associated with the number of pRBC units transfused, where center was included as a random effect. Negative binomial regression was chosen because pRBC transfusion is a nonparametric event where most patients receive 0–2 U of pRBCs with a severely right-skewed distribution. For the outcomes of mortality and MI, we used fixed effects multivariable logistic regression models.

Variables of clinical significance and those with a value of $P < 0.1$ by univariate analysis were included in multivariable regressions.

In our multivariable analyses, we adjusted for other potentially confounding operative factors including EBL, procedure time, proximal clamp position (OAR patients only), and inflow origin (aortic versus nonaortic for Bypass patients only). We also adjusted for center-level procedural volume. To adjust for patient-related factors, we included age, gender, presence of coronary artery disease (CAD) with or without revascularization, prior coronary artery bypass grafting or percutaneous coronary intervention (CABG/PCI), chronic obstructive pulmonary disease (COPD), smoking, congestive heart failure (CHF), chronic kidney disease, ambulatory status, region, preoperative stress test, diabetes mellitus (DM), year of surgery, and preoperative medication use as covariates. Patients with multiple separate operations were evaluated independently. P values of < 0.05 were considered significant. Analyses were performed using SAS version 9.4 (Cary, NC) and R version 3.1.1.

RESULTS

We identified 24,131 procedures in VQI from 22,532 patients who met our inclusion criteria. This comprised 3,885 (16.1%) OAR and 20,246 (83.9%) Bypass operations. Of the Bypass operations, most (15,020, 74.2%) were infrainguinal bypasses. The remaining were suprainguinal bypasses (5,226, 25.8%). Of all patients, 10.1% underwent more than 1 procedure during the study interval. Overall, 67.7% of patients were male, 27.8% had a documented history of CAD, 27.9% had a documented history of COPD, 85.4% had documented hypertension, and 35.3% had DM. Patient characteristics are listed in Table I.

During the study period, there were 214 centers that reported procedure data to the VQI. Centers reporting to the VQI averaged 30.4 ± 26.3 elective OAR and Bypass procedures annually (range 1–147). The average annual number of elective OAR cases across centers was 5.0 ± 7.7 (range 0–74) and the annual mean number of Bypass per center was 25.4 ± 23.4 (range 0–138).

Factors Associated with Transfusions

Overall, 1,457 (37.5%) of OAR and 3,941 (19.5%) of bypasses received a transfusion. Of the Bypass cases, 1,354 (25.9%) suprainguinal and 2,587 (17.2%) infrainguinal bypass cases received a transfusion. OAR cases had a higher number of pRBCs (1.1 ± 2.2 U) transfused compared with 0.5 ± 1.30 U for bypass cases ($P < 0.001$). There was variability in the use of transfusions both across EBL and preoperative anemia strata for each procedure (Table II). For example, for patients undergoing Bypass with preoperative hemoglobin < 10 and lowest EBL quartile, there was a range of 0–8 U of pRBC transfused. For patients with hemoglobin levels > 12 and an EBL of > 600 mL, 0–44 U of pRBCs were transfused. Similar variability in transfusion across preoperative hemoglobin levels and EBL was seen in OAR procedures (Table II). Although all OARs included in this analysis were infrarenal repairs, placing the clamp more proximal on the aorta was associated with increased likelihood of transfusion (31% for infrarenal cross-clamp position, 43% above one or both renal arteries, and 57% for supraceliac clamp, $P < 0.001$).

Univariate analysis demonstrated that female gender, increasing age, having a history of CAD, hypertension, history of CABG/PCI, CHF, and a preoperative hemoglobin <10 g/dL were all statistically significantly associated with increased rates of transfusion for both OAR and Bypass (Appendix A). Insulin-dependent diabetes was associated with increased transfusions for OAR, while any DM was associated with transfusion for Bypass. Any COPD was associated with increased transfusions for Bypass, while only medically treated COPD was associated with transfusion for OAR.

Multivariable models demonstrated female gender, increasing age, hypertension (OAR only), prior CABG/PCI, longer procedure times, preoperative anemia, and EBL >600 mL compared with 250 was all associated with increased transfusions (Table III). Antiplatelet use was not associated with transfusion for OAR cases, but was associated with increased risk of transfusion for Bypass cases. More proximal clamp position was associated with higher rate of transfusion for OAR. Aortic (versus nonaortic) graft origin was not associated with increased transfusion for Bypass cases.

Factors Associated with Myocardial Infarction and Postoperative Death

Postoperative MI occurred in 157 (4.0%) OAR repairs and in 451 (2.2%) Bypasses. Of the Bypasses, 145 (2.8%) suprainguinal bypasses and 306 (2.0%) infrainguinal bypasses developed an MI. Upon univariate analysis, any transfusion was associated with an increased risk of postoperative MI (2.6% with no transfusion versus 6.5% with any transfusion, $P < 0.001$) for OAR and Bypass (1.0% with no transfusion versus 7.4% with any transfusion, $P < 0.001$). Additionally, increasing age, female gender (Bypass only), cardiac disease, prior CABG/PCI, CHF, abnormal stress test, ambulatory status, and procedure time were associated with increased risk of MI for both OAR and Bypass (Appendix B). After adjustment for age, surgery year, and other demographics, a multivariable logistic regression analysis demonstrated that transfusions were associated with increased odds of MI (odds ratio [OR] 1.2/unit, 95% confidence interval [CI] 1.1–1.2, $P < 0.001$ for OAR; OR 1.3, 95% CI 1.2–1.4, $P < 0.001$ for Bypass; Table IV).

In-hospital postoperative death occurred in 70 (1.8%) OAR and in 133 (0.7%) Bypass. In the bypass group, 51 (1.0%) suprainguinal bypass and 82 (0.5%) infrainguinal bypass patients died. Upon univariate analysis, transfusions were associated with an increased risk of death for both OAR (0.7% with no transfusion versus 3.7% with any transfusion, $P < 0.001$) and Bypass (0.3% with no transfusion versus 2.1% with any transfusion, $P < 0.001$). Additionally, increasing age, CAD, CHF, nonambulatory status, increasing procedure time, preoperative anemia, and increasing EBL were associated with postoperative mortality for both OAR and Bypass (Appendix C). After adjustment for age, gender, surgery year, and other demographics, multivariable logistic regression models demonstrated that transfusions were associated with increased mortality (OR 1.3/unit, 95% CI 1.2–1.4, $P < 0.001$ for OAR; OR 1.3, 95% CI 1.3–1.4 for Bypass, $P < 0.001$). For Bypass cases, age, history of CAD, CHF, EBL >600 mL compared with 250 mL, and procedure times 3.5–5 hr and over 5 hr compared with <2.5 hr were also associated with higher odds of mortality (Table V) while a history of prior CABG/PCI was protective.

DISCUSSION

Although the transfusion of red blood cells offers an immediate therapy for anemia, they are not a benign therapy. Transfusions have been associated with many adverse events, including an increase in perioperative MIs.^{14–16} In this study, we describe variability in the use of perioperative transfusions for elective OAR and Bypass cases in the VQI when controlling for anemia and EBL. Women, older patients, preoperative anemia, and those with CAD are associated with a higher likelihood of receiving transfusions, in addition to case complexity surrogates such as operative time and EBL. The use of transfusions is significantly associated with the risk of MI and death postoperatively. Although many of these factors are difficult to control, knowledge of their associated risk may help providers to identify high-risk patient groups for transfusions and be able to target transfusion reduction strategies.

In the context of transfusions, there are little data focused specifically on vascular surgery patients and how transfusions impact perioperative outcomes. The few available studies demonstrate mixed results.^{13,26–28} Bush et al. randomized patients preoperatively who were undergoing elective aortic and infrainguinal surgery to receive either liberal (<10 g/dL) or restrictive strategy (<7 g/dL) of transfusion. They demonstrated no difference in the rate of myocardial ischemia or death between transfusion strategy groups. However, in a retrospective observational study, Bursi et al. reviewed patients admitted for major elective vascular surgery and demonstrated that patients who received transfusions had significantly worse outcomes: with a higher risk of 30-day death (hazard ratio [HR] 11.72, 95% CI 3.92–35.10, $P < 0.0001$), MI (HR 3.32, 95% CI 1.75–6.27, $P = 0.0003$), and the composite end point of MI or death (HR 4.02, 95% CI 2.23–7.27, $P = 0.0001$).

In a similar study by Obi et al., researchers demonstrated that transfusions were associated with an increased rate of MI/death. They reviewed a multicenter statewide quality improvement registry of a 22-hospital consortium in Michigan from 2012 to 2013. They reviewed patients undergoing peripheral artery bypass, endovascular aortic repairs, and open aortic aneurysm repair. In their cohort, 24.8% of patients received a perioperative transfusion. Similar to our results, those with preoperative anemia, CAD, DM, CHF, previous CABG, cerebrovascular disease, and those on hemodialysis were more likely to receive a transfusion. Our results also demonstrate similar findings in VQI for patients with CAD, COPD, diabetes, preoperative anemia, and history of myocardial disease. We also demonstrated that those who undergo elective OAR and Bypass procedures requiring transfusion have similarly higher rates of MI or postoperative death. Interestingly, we demonstrated that women were more likely to be transfused and our data additionally demonstrate that women who received a transfusion had an associated higher rate of MI and mortality. Two important differences exist between our studies. First, they reviewed a statewide registry while we reviewed a national registry. Second, they did include urgent repairs in their analysis while we did not. In both studies, emergent cases were excluded.²⁹

In an effort to reduce transfusions, identification of high risk patients is necessary. In our analysis, several factors are closely associated with the need for transfusions. Many risk factors may not be modifiable, such as age and sex. Additionally, operative time and EBL may not be easily modifiable factors. Yet, this emphasizes that technique and efficiency in

the operating room are associated with significant impact on patient outcomes. Potentially, the most modifiable risk factor is preoperative anemia. We identified that preoperative hemoglobin levels <12 mg/dL were significantly associated with transfusions. Efforts to resolve underlying anemia may reduce the need for transfusion perioperatively.

Although a transfusion trigger threshold is critical for the postoperative period, preoperative optimization and prevention of the need for a transfusion is equally elusive. Unfortunately, preoperative iron supplementation has had mixed results with regards to decreasing the need for a postoperative transfusion. There are 3 prospective randomized controlled trials concerning preoperative iron supplementation. In review of the gynecology literature, there are some indications that preoperative intravenous iron supplementation does decrease perioperative transfusions in patients with preoperative menorrhagia. However, in the colorectal literature the benefit of preoperative supplementation is mixed. Dr. Lidder did show a decrease in postoperative transfusions when preoperative anemic patients were given oral ferrous sulfate. However, Edwards et al. found no difference in postoperative transfusion requirements when preoperative intravenous iron supplementation was given. Preoperative evaluation by a dedicated center may help with decreasing variation in perioperative cardiac medications and risk factor modification.^{30–32}

Based on multiple randomized controlled clinical trials, guidelines recommend that for nonbleeding patients, a hemoglobin level of 7 or below should trigger transfusion for noncardiac surgeries, and one should avoid transfusing above a level of 10 mg/dL.^{17–25} Others have found that a restrictive strategy is unfavorable and that transfusions of cardiac surgery patients to a level of 9 g/dL yield fewer cardiac events.¹¹ Despite these recommendations, controversy remains about the use and extent of transfusions for patients who are stable or without symptoms, for more complex patients with multiple comorbidities, and for vascular surgery patients who develop anemia due to acute blood loss. In our analysis, it appears that CAD was associated with a higher risk of transfusions. This may indicate that those with CAD are transfused at more liberal triggers to potentially reduce the risk of cardiac ischemia. In addition, there was variability in the use of transfusion across centers. Optimal thresholds for transfusion in the vascular surgery population are illdefined and likely lead to this variation. Further work is needed to define these thresholds so optimization strategies for transfusions can be successful. Fortunately, there is a multicenter randomized controlled trial that is underway that will address this question in a more definitive way. Dr. Kouglas and fellow researchers at Baylor College of Medicine are currently conducting the “TOP Trial: Transfusion Triggers after Operations in High Cardiac Risk Patients.” They will assign patients to a liberal (hemoglobin <10 gm/dL) or a restrictive group (hemoglobin <7 gm/dL) transfusion trigger threshold and look at the 90 mortality and other ischemic events in this high-risk population.

Our study has several limitations. Although we expect most blood loss requiring transfusion to occur in the operating room, VQI does not gather other causes for bleeding during the perioperative period, such as gastrointestinal bleeding. Thus, some patients will need transfusions out of perioperative window for other causes that we were unable to account for. To minimize this confounding, we have limited our study to only elective procedures and we excluded returns to the operating room to limit other reasons for transfusion.

Additionally, we were only able to determine the total number of transfusions during an admission in VQI. We assumed that most transfusions were administered in the perioperative period from operative blood loss and other episodes occur at random within surgical types. Furthermore, the specific indication for transfusion (hypovolemia, cardiac ischemia, symptomatic anemia, need for pressors, tachycardia, or acidosis) and the nadir hemoglobin is not tracked in VQI. Likewise, no temporal data are available as to when the transfusion was given during the hospitalizations (i.e., intraoperative, immediately postoperatively, or multiple days later). We have stratified patients according to the EBL and preoperative hemoglobin to minimize the confounding of nadir hemoglobin. Finally, the timing from transfusion to MI is unknown. Further efforts to describe the context of transfusion and MI after vascular surgery are necessary. Perhaps the most significant limitation of this study and all the published literature to date on this topic is that we are not closer to determining the optimum transfusion threshold for patients undergoing major vascular surgery. This remains a significant unmet need that warrants further investigations with prospective study.

CONCLUSION

Our data suggest there is significant variation with regards to transfusion of pRBCs following major vascular surgery procedures in hospitals within VQI. We have identified specific patient groups that are at high risk for transfusion after OAR and bypass. Additionally, the use of transfusions is significantly associated with postoperative MI and death after OAR and Bypass. These data are important to understand drivers of transfusions during and after vascular surgery. This work can help to inform practice efforts to reduce transfusion use. Ideally, future randomized controlled trials can be performed to better understand the impact of using different transfusion strategies after vascular surgery on postoperative outcomes. Immediate efforts to reduce transfusion may focus on center variability, sex, and preoperative anemia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table I

Patient characteristics for OAR and AB procedures

Risk factor	Procedure type			P value
	All (n = 24,131)	OAR (n = 3,885)	Bypass (n = 20,246)	
Gender				
Male, %	67.7	73.3	66.6	<0.001
Age				
Mean (standard deviation)	66.2 (10.5)	69.2 (8.3)	65.7 (10.7)	<0.001
CAD				
%	27.8	25.6	28.2	<0.001
COPD				
%	27.9	31.8	27.1	<0.001
Smoking status				
Ever smoked (prior or current), %	89.0	90.9	88.6	<0.001
Hypertension				
%	85.4	84.1	85.6	0.02
Diabetes				
Diet, %	4.0	3.9	4.0	<0.001
Noninsulin meds, %	15.9	9.7	17.1	
Insulin, %	15.5	2.7	17.9	
CHF				
%	11.1	6.8	11.9	<0.001
Total procedure time category				
Not available, n	1,955	17	1,938	
<2.5 hr, %	21.2	12.5	23.0	<0.001
2.5 to <3.5 hr, %	28.0	29.6	27.7	
3.5 to <5 hr, %	29.9	34.4	28.9	
>5 hr, %	21.0	23.5	20.4	
Proximal clamp position (OAR)				
Infrarenal, %		55.3	—	
Above one renal, %		14.8	—	
Above both renals, %		23.5	—	
Supraceliac, %		6.4	—	
Preoperative hemoglobin				
Not available, n	1,069	87	982	
<10, %	6.1	2.9	6.7	<0.001
10 to <12	18.8	12.9	20.0	
12+	75.1	84.2	73.3	

AB, arterial bypass.

Table II

Transfusions across EBL quartiles for OAR and AB stratified by preoperative hemoglobin levels

Preoperative hemoglobin	EBL quartile			
	<100 mL	100–250 mL	>250–600 mL	>600 mL
OAR				
<10				
<i>N</i> transfused/ <i>N</i> total, % transfused	1/2 (50.0%)	2/4 (50.0%)	6/13 (46.2%)	66/92 (71.7%)
Median (IQR)	5 (0–10)	1.5 (0–3)	0 (0–2)	2 (0–4)
Range	0–10	0–3	0–4	0–14
10 to <12				
<i>N</i> transfused/ <i>N</i> total, % transfused	2/3 (66.7%)	2/12 (16.7%)	47/100 (47.0%)	251/370 (67.8%)
Median (IQR)	1 (0–6)	0 (0–0)	0 (0–2)	2 (0–3)
Range	0–6	0–2	0–8	0–20
12+				
<i>N</i> transfused/ <i>N</i> total, % transfused	2/7 (28.6%)	4/52 (7.7%)	90/505 (17.8%)	966/2615 (36.9%)
Median (IQR)	0 (0–1)	0 (0–0)	0 (0–0)	0 (0–2)
Range	0–2	0–2	0–5	0–33
AB				
<10				
<i>N</i> transfused/ <i>N</i> total, % transfused	118/359 (32.9%)	186/377 (49.3%)	238/361 (65.9%)	149/179 (83.2%)
Median (IQR)	0 (0–1)	0 (0–2)	1 (0–2)	2 (1–5)
Range	0–8	0–17	0–8	0–20
10 to <12				
<i>N</i> transfused/ <i>N</i> total, % transfused	154/1,148 (13.4%)	264/1,126 (23.4%)	505/1,079 (46.8%)	355/463 (76.7%)
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–2)	2 (1–4)
Range	0–9	0–20	0–12	0–20
12+				
<i>N</i> transfused/ <i>N</i> total, % transfused	133/4,419 (3.0%)	267/4,245 (6.3%)	655/3,581 (18.3%)	845/1,713 (49.3%)
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–2)
Range	0–11	0–13	0–13	0–44

AB, arterial bypass; IQR, interquartile range.

Table III
Multivariable negative binomial mixed effects models of number of transfusions in OAAA and AB

Risk factor	OAR			Bypass			P value	Upper 95% CI for IRR	Lower 95% CI for IRR	Upper 95% CI for IRR	P value
	IRR	Lower 95% CI for IRR	Upper 95% CI for IRR	IRR	Lower 95% CI for IRR	Upper 95% CI for IRR					
Gender											
Male	1.0			1.0							
Female	1.4	1.2	1.6	<0.001	1.5	1.4		1.6			<0.001
Age category (quartiles)											
<60	1.0			1.0							
60–66	1.4	1.1	1.7	0.006	1.2	1.1		1.3			<0.001
67–73	1.7	1.4	2.1	<0.001	1.3	1.2		1.5			<0.001
74+	2.0	1.6	2.5	<0.001	1.6	1.4		1.7			<0.001
Preoperative ASA or P2Y12 antagonist											
None	1.0			1.0							
ASA only	0.9	0.8	1.1	0.44	1.1	1.0		1.2			0.04
Both	1.2	0.9	1.6	0.21	1.6	1.5		1.8			<0.001
P2Y12 antagonists only	0.7	0.4	1.1	0.10	1.4	1.2		1.7			<0.001
Total procedure time category (hr)											
<2.5	1.0			1.0							
2.5 to <3.5	1.2	0.9	1.5	0.14	1.3	1.2		1.5			<0.001
3.5 to <5	1.9	1.5	2.4	<0.001	1.6	1.4		1.8			<0.001
>5	3.3	2.6	4.2	<0.001	2.2	2.0		2.6			<0.001
Unknown	1.3	0.5	3.7	0.58	1.7	1.3		2.2			<0.001
Preoperative hemoglobin											
12+	1.0			1.0							
10 to <12	1.9	1.6	2.2	<0.001	2.1	2.0		2.3			<0.001
<10	2.5	1.8	3.3	<0.001	4.0	3.6		4.5			<0.001
Unknown	0.1	0.05	0.3	<0.001	1.5	1.0		2.2			0.04
EBL quartiles (Q1 and Q2 combined) (mL)											
250	1.0			1.0							
>250 to 600	1.4	0.8	2.5	0.23	2.2	2.0		2.4			<0.001

Risk factor	OAR					Bypass				
	IRR	Lower 95% CI for IRR	Upper 95% CI for IRR	P value	IRR	Lower 95% CI for IRR	Upper 95% CI for IRR	P value	IRR	P value
>600	2.7	1.6	4.8	<0.001	6.1	5.5	6.7	<0.001		
Proximal clamp position										
Infrarenal	1.0				–					
Above both renals	1.2	1.1	1.4	0.006	–					
Above one renal	1.3	1.1	1.5	0.004	–					
Supraceliac	1.9	1.5	2.4	<0.001	–					
CAD										
None	1.0				1.0					
MI but no symptoms	1.0	0.8	1.2	0.91	1.0	0.9	1.1	0.91		
Stable angina	1.3	0.9	1.7	0.13	1.0	0.9	1.2	0.62		
Unstable angina or MI < 6 months	0.8	0.4	1.6	0.58	1.3	1.0	1.7	0.04		
COPD										
No	1.0				1.0					
Not treated	1.1	0.9	1.3	0.55	1.0	0.9	1.2	0.48		
On home oxygen	1.0	0.7	1.5	0.85	1.2	1.0	1.4	0.12		
On meds	1.2	1.1	1.4	0.008	1.1	1.0	1.2	0.18		
Smoking status										
No	1.0				1.0					
Ever smoked (prior or current)	0.7	0.6	0.9	0.002	0.9	0.8	1.0	0.008		
Diabetes										
No	1.0				1.0					
Diet	1.1	0.8	1.4	0.53	1.0	0.8	1.2	0.83		
Insulin	1.0	0.7	1.4	1.0	1.0	0.9	1.1	0.74		
Noninsulin meds	1.0	0.9	1.3	0.74	1.0	0.9	1.1	0.83		
Hypertension										
None	1.0				1.0					
Yes	1.4	1.2	1.7	<0.001	1.1	1.0	1.2	0.27		
Prior CABG or prior PCI										
No	1.0				1.0					
Any	1.2	1.0	1.4	0.04	1.1	1.0	1.2	0.03		

Risk factor	OAR				Bypass			
	IRR	Lower 95% CI for IRR	Upper 95% CI for IRR	P value	IRR	Lower 95% CI for IRR	Upper 95% CI for IRR	P value
CHF								
None	1.0				1.0			
Asymptomatic, history of CHF	1.0	0.8	1.3	0.88	1.2	1.1	1.3	0.004
Mild	1.0	0.7	1.5	0.81	1.3	1.1	1.6	0.001
Moderate/severe	1.4	0.7	2.8	0.28	1.0	0.8	1.3	0.84
Any stress								
Normal	1.0				1.0			
Abnormal	1.2	1.0	1.4	0.10	1.0	0.9	1.1	0.70
Not done	1.0	0.9	1.1	0.80	1.0	0.9	1.0	0.40
Ambulatory status								
Ambulatory	1.0				1.0			
Ambulatory with assistance, wheelchair, bedridden	1.3	1.0	1.7	0.07	1.1	1.1	1.2	0.001
Unknown	0.4	0.1	1.4	0.15	0.7	0.4	1.1	0.12
Preoperative any beta-blockers								
None	1.0				1.0			
Any	0.9	0.8	1.0	0.18	1.1	1.0	1.1	0.15
Preoperative statin								
None	1.0				1.0			
Yes	1.0	0.9	1.1	0.78	1.0	0.9	1.1	0.64
Preoperative ACE inhibitor/ARB								
No	1.0				1.0			
Unknown	2.8	0.8	9.5	0.11	1.1	1.0	1.3	0.17
Yes	1.0	0.8	1.1	0.67	1.1	1.0	1.2	0.07
Inflow origin								
Other	–				1.0			
Aortic	–				0.9	0.8	1.0	0.10
Surgery year								
2003–2010	1.0				1.0			
2011	1.6	1.2	2.2	0.003	0.9	0.7	1.1	0.39
2012	1.5	1.1	2.0	0.02	0.9	0.7	1.2	0.55

Risk factor	OAR					Bypass				
	IRR	Lower 95% CI for IRR	Upper 95% CI for IRR	P value	IRR	Lower 95% CI for IRR	Upper 95% CI for IRR	P value		
2013	1.4	0.9	2.1	0.12	0.8	0.6	1.0	0.04		
2014	1.2	0.8	1.8	0.31	0.8	0.6	1.0	0.08		
2015	1.1	0.7	1.6	0.75	0.7	0.5	0.9	0.01		
2016	1.0	0.6	1.5	0.86	0.8	0.6	1.0	0.06		

AB, arterial bypass; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; ASA, aspirin; IRR, incident rate ratio.

Multivariable logistic regression analysis of MIs for OAR and Bypass

Risk factor	OAR			Bypass			P value
	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value	Odds ratio estimate	Lower 95% confidence limit for odds ratio	
Gender							
Male	1.0				1.0		
Female	1.0	0.7	1.6	0.82	1.2	1.0	1.5
Age							
<60	1.0				1.0		
60–66	1.1	0.5	2.2	0.86	1.4	1.0	2.0
67–73	1.5	0.8	3.0	0.23	1.6	1.1	2.2
74+	1.8	0.9	3.5	0.11	2.2	1.6	3.1
Preoperative ASA or P2Y12 antagonist use							
None	1.0				1.0		
ASA only	1.3	0.8	2.0	0.25	0.9	0.7	1.3
P2Y12 antagonist only	1.4	0.4	4.5	0.60	1.2	0.8	2.0
Both	2.1	1.1	4.2	0.03	1.0	0.7	1.5
Total procedure time category (hr)							
<2.5	1.0				1.0		
2.5 to <3.5	1.1	0.5	2.2	0.80	1.8	1.1	2.8
3.5 to <5	1.0	0.5	2.0	0.94	2.2	1.4	3.3
>5	1.9	1.0	3.9	0.07	2.9	1.8	4.5
Preoperative hemoglobin							
<10	1.1	0.4	2.8	0.82	0.8	0.5	1.1
10 to <12	1.0	0.6	1.7	0.96	1.0	0.8	1.3
12+/unknown	1.0				1.0		
EBL (mL)							
250	1.0				1.0		
>250–600	0.5	0.2	1.7	0.29	1.7	1.3	2.3
>600	0.5	0.2	1.6	0.26	2.1	1.5	2.9

Risk factor	OAR				Bypass			
	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value
Proximal clamp position (open AAA)								
Infrarenal	1.0							
Above one renal	0.8	0.5	1.4	0.51				
Above both renals	1.0	0.7	1.5	0.98				
Supraceliac	1.6	0.9	2.9	0.12				
CAD								
None	1.0				1.0			
History of MI but no symptoms	0.8	0.5	1.3	0.40	1.5	1.2	2.0	0.003
Stable angina	0.8	0.4	1.7	0.55	2.1	1.5	3.0	<0.001
Unstable angina or MI < 6 months	1.0	0.3	4.1	0.95	2.4	1.3	4.5	0.007
COPD								
No	1.0				1.0			
Not treated	1.3	0.8	2.1	0.31	1.3	0.9	1.8	0.11
On meds	1.6	1.0	2.5	0.04	0.7	0.5	1.0	0.07
On home oxygen	1.0	0.3	3.5	0.95	1.0	0.5	1.8	0.97
Smoking status								
Never smoked	1.0				1.0			
Ever smoked (prior or current)	1.0	0.5	1.8	0.93	0.8	0.6	1.1	0.14
Diabetes								
None	1.0				1.0			
Diet	1.9	1.0	3.7	0.06	0.8	0.4	1.4	0.43
Noninsulin meds	0.8	0.4	1.4	0.41	1.3	1.0	1.7	0.06
Insulin	0.6	0.2	1.9	0.36	1.6	1.3	2.1	<0.001
Prior CABG or prior PCI								
None	1.0				1.0			
Any	1.9	1.3	2.9	0.002	1.4	1.1	1.9	0.005
Any CHF								
None	1.0				1.0			
Asymptomatic, history of CHF	1.8	0.9	3.5	0.10	1.2	0.8	1.6	0.40

Risk factor	OAR			Bypass			P value
	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	
Mild	2.2	1.0	5.2	1.8	1.2	2.8	0.006
Moderate/severe	2.4	0.6	9.5	1.2	0.6	2.2	0.65
Preoperative stress test							
Not done	0.9	0.6	1.4	1.0	0.8	1.3	0.77
Normal	1.0			1.0			
Abnormal	1.2	0.7	2.0	1.9	1.4	2.6	<0.001
Ambulatory status							
Ambulatory/unknown	1.0			1.0			
Ambulatory with assistance, wheelchair, bedridden	1.6	0.8	3.4	1.2	1.0	1.6	0.09
Preoperative statin							
No	1.0			1.0			
Yes	0.9	0.6	1.4	0.9	0.7	1.2	0.49
Transfusion: no. of units of pRBC	1.2	1.1	1.2	1.3	1.2	1.4	<0.001
Region identification							
3	1.0			1.0			
5	0.4	0.1	2.1	0.7	0.3	1.3	0.27
6	0.2	0.02	2.6	0.3	0.1	1.3	0.13
7	0.7	0.2	3.0	0.8	0.4	1.6	0.49
8	0.9	0.2	3.8	0.7	0.4	1.4	0.32
10	0.5	0.1	2.7	1.0	0.5	2.2	0.98
11	0.5	0.1	2.1	1.2	0.6	2.2	0.66
12	1.0	0.2	4.3	1.0	0.5	1.9	0.90
13	1.1	0.3	5.0	0.7	0.3	1.5	0.30
14	2.1	0.6	7.8	1.4	0.7	2.7	0.30
18	0.6	0.2	2.8	0.5	0.2	1.1	0.08
19	2.6	0.7	9.5	1.0	0.4	2.4	0.95
21	0.9	0.2	3.0	1.2	0.7	2.2	0.47
22	2.5	0.4	15.6	2.0	0.7	5.3	0.18
23	0.6	0.2	3.2	0.8	0.4	1.8	0.57

Risk factor	OAR			Bypass			P value	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value
	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio				
24	2.2	0.5	9.3	1.5	0.965	3.4	0.28	0.7	3.4	0.28
25/999	5.5	1.5	19.8	3.7	0.009	7.1	<0.001	1.9	7.1	<0.001
Surgery year										
2003–2010	1.0			1.0						
2011	0.7	0.3	1.7	0.7	0.42	1.5	0.36	0.3	1.5	0.36
2012	1.1	0.5	2.3	0.9	0.89	1.8	0.85	0.5	1.8	0.85
2013	0.8	0.4	1.8	1.3	0.65	2.4	0.51	0.6	2.4	0.51
2014	0.7	0.3	1.4	0.9	0.28	1.7	0.69	0.4	1.7	0.69
2015	0.7	0.3	1.4	1.1	0.29	2.2	0.73	0.6	2.2	0.73
2016	0.9	0.3	2.4	1.1	0.83	2.3	0.87	0.5	2.3	0.87

AAA, abdominal aortic aneurysm; ASA, aspirin.

Table V

Multivariable logistic regression models of mortality for OAR and AB

Risk factor	OAR				Bypass			
	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value
Gender								
Male	1.0				1.0			
Female	1.0	0.6	1.9	0.94	1.4	0.9	2.1	0.10
Age								
<60	1.0				1.0			
60–66	2.5	0.5	12.3	0.27	2.4	1.0	5.6	0.04
67–73	2.8	0.6	13.3	0.19	3.8	1.7	8.4	0.001
74+	4.5	1.0	21.0	0.05	4.8	2.2	10.4	<0.001
Preoperative ASA or P2Y12 antagonist use								
None	1.0				1.0			
ASA only	0.8	0.4	1.5	0.46	0.7	0.4	1.2	0.25
P2Y12 antagonist only	0.8	0.1	6.7	0.83	1.7	0.9	3.4	0.13
Both	1.8	0.7	4.5	0.24	0.6	0.3	1.1	0.11
Total procedure time category (hr)								
<2.5	1.0				1.0			
2.5 to <3.5	2.1	0.7	6.8	0.20	1.8	0.8	4.2	0.15
3.5 to <5	1.4	0.4	4.6	0.54	2.3	1.0	5.1	0.04
>5	2.0	0.6	6.4	0.24	2.5	1.1	5.7	0.03
Preoperative hemoglobin (g/dL)								
<10	1.6	0.5	4.6	0.42	0.7	0.4	1.4	0.28
10 to <12	1.2	0.6	2.3	0.67	1.1	0.7	1.7	0.67
12+/ unknown	1.0				1.0			
EBL quartiles (Q1 and Q2 combined) (mL)								
250	1.0				1.0			
>250–600	0.8	0.1	7.3	0.86	1.5	0.9	2.5	0.11
>600	0.7	0.1	5.8	0.77	1.9	1.1	3.3	0.03

Risk factor	OAR						Bypass					
	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	P value
Proximal clamp position												
Infrarenal	1.0											
Above one renal	1.4	0.7	3.0	0.31								
Above both renals	0.9	0.5	1.9	0.82								
Supraceliac	1.2	0.5	3.0	0.68								
CAD												
None	1.0				1.0							
History of MI but no symptoms	1.4	0.7	2.9	0.33	1.8					1.1	3.0	0.02
Stable angina, unstable angina or MI < 6 months	1.6	0.6	4.6	0.35	1.8					0.9	3.6	0.08
COPD												
No	1.0				1.0							
Not treated	1.6	0.7	3.3	0.25	1.2					0.6	2.3	0.60
On meds	2.2	1.2	4.2	0.02	1.2					0.7	2.0	0.61
On home oxygen	1.6	0.4	6.3	0.49	2.0					0.9	4.6	0.09
Smoking status (any)												
Never smoked	1.0				1.0							
Ever smoked (prior or current)	1.3	0.5	3.6	0.62	0.5					0.3	0.8	0.012
Diabetes												
None	1.0				1.0							
Diet	1.6	0.5	5.1	0.44	2.0					0.9	4.2	0.09
Noninsulin meds	1.3	0.6	2.9	0.51	1.4					0.8	2.3	0.24
Insulin	1.2	0.3	4.6	0.76	0.9					0.6	1.6	0.86
Prior CABG or prior PCI												
None	1.0				1.0							
Any	1.0	0.5	2.0	0.90	0.6					0.4	1.0	0.03
Any CHF												
None	1.0				1.0							
Asymptomatic, history of CHF	0.9	0.3	2.9	0.85	3.1					1.9	5.2	<0.001
Mild	2.9	0.9	9.0	0.07	3.3					1.6	6.8	0.001

Risk factor	OAR			Bypass			P value
	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	Odds ratio estimate	Lower 95% confidence limit for odds ratio	Upper 95% confidence limit for odds ratio	
Moderate/severe	6.2	1.3	29.4	4.6	1.8	11.4	0.001
Any stress							
Not done	1.3	0.7	2.3	1.0	0.6	1.5	0.86
Normal	1.0			1.0			
Abnormal	1.2	0.5	2.7	1.0	0.5	2.0	0.94
Ambulatory status							
Ambulatory/unknown	1.0			1.0			
Ambulatory with assistance, wheelchair, bedridden	2.0	1.2	6.8	1.5	1.0	2.4	0.048
Preoperative statin (yes/no)							
No	1.0			1.0			
Yes	1.1	0.6	2.2	1.1	0.7	1.7	0.74
Transfusion: No. of units of pRBC	1.3	1.2	1.4	1.3	1.3	1.4	<0.001
Surgery year (collapsed)							
2003–2010	1.0			1.0			
2011	0.4	0.3	6.2	0.9	0.1	5.6	0.91
2012	1.8	0.5	6.7	1.7	0.3	9.5	0.55
2013	1.3	0.3	4.7	2.2	0.4	12.2	0.36
2014	0.9	0.2	3.2	1.3	0.2	7.2	0.78
2015	1.0	0.3	3.7	1.6	0.3	8.7	0.61
2016	1.1	0.2	6.1	1.6	0.3	10.5	0.61
Average number of cases at center within a year							
<10	2.6	1.1	6.0	0.9	0.3	2.7	0.82
10 to <25	0.5	0.2	1.5	0.8	0.4	1.5	0.52
25 to <40	0.8	0.4	1.8	0.9	0.5	1.5	0.69
40+	1.0			1.0			
Unable to calculate	2.8	0.5	14.4	0.6	0.1	4.7	0.65

AB, arterial bypass; ASA, aspirin.