The Association Between Perioperative Hemoglobin and Acute Kidney Injury in Patients Having Noncardiac Surgery

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BACKGROUND: Acute kidney injury (AKI) is a common complication of noncardiac surgery and is associated with excess morbidity and mortality. Perioperative hemoglobin concentrations are strongly associated with surgical mortality, but little is known about their relationship with AKI. We studied hemoglobin concentration before and 24 hours after surgery and its association with AKI.
METHODS: We performed a single-center observational cohort study using clinical and administrative data from the Cleveland Clinic, Cleveland, OH. In patients with normal preoperative renal function, we examined the association between the outcome of AKI and the exposures of preoperative hemoglobin concentration and decrements in hemoglobin concentration in the first 24 hours after surgery using logistic regression and controlling for important confounding variables.
RESULTS: We included 27,381 patients who had 33,330 noncardiac surgeries. AKI developed in 2478 (7.4%) surgeries. Preoperative hemoglobin concentrations were <12.0 g/dL in 9566 (29%) patients. Hemoglobin concentrations decreased by >4.0 g/dL in 10,808 (32%) patients. Compared with patients with a preoperative hemoglobin >12.0 g/dL, the adjusted odds ratio (OR) for AKI was 2.01 (95% confidence interval [CI], 1.8–2.3) for those with a preoperative hemoglobin between 10.1 and 12.0 g/dL and was 3.7 (95% CI, 2.6–5.4) for those with a preoperative hemoglobin <8.0 g/dL. Compared with patients who did not have a decrease in postoperative hemoglobin, a decrement of 1.1 to 2.0 g/dL was associated with an adjusted OR of 1.51 (95% CI, 1.15–1.98), and a decrement of >4.0 g/dL with an OR of 4.7 (95% CI, 3.6–6.2) for AKI.
CONCLUSIONS: Low preoperative and early postoperative decrements in hemoglobin concentrations are strongly associated with postoperative AKI in a graded manner. Given the frequency of low perioperative hemoglobin and decreases in hemoglobin concentration, research is needed to determine whether there are safe treatment strategies to mitigate the risk of AKI. (Anesth Analg 2013;117:924–31)

Acute kidney injury (AKI), a sudden reduction in kidney function, occurs in approximately 7% of hospitalized patients and 7.5% of patients who have noncardiac surgery.[1,2] Small changes in serum creatinine, the most common marker of kidney function, are increasingly recognized as strong, independent risk factors for short- and long-term mortality[3,4] and markedly increased health care costs after surgery.[2,5] Severe AKI that requires dialysis is associated with mortality and hospital costs similar to those of cardiac arrest patients.[5–7]

There is no high-quality evidence demonstrating that interventions prevent or reduce the severity of postoperative AKI.[8] Identifying risk factors that are common, have a strong association with AKI, and may be modifiable is therefore an important initial step in identifying potential therapeutic targets. Preoperative anemia and perioperative transfusions are associated with AKI in cardiac surgery.[9] In noncardiac surgery, preoperative anemia is also an important risk factor for mortality.[10] Whether preoperative anemia is associated with early postoperative AKI has not been studied in noncardiac surgery. Furthermore, transfusions may be associated with AKI either because the transfusions themselves are harmful or because the reasons for transfusion cause AKI. Given both perioperative decrements in hemoglobin concentration and low preoperative hemoglobin concentrations may both trigger transfusion, we examined the independent contributions of each of these risk factors to the development of AKI.

More than 200 million patients undergo noncardiac surgery each year; thus, mitigating the risk of AKI is an important health issue.[11] If perioperative hemoglobin were strongly associated with AKI, it might be a modifiable pathway for ameliorating AKI and therefore reducing perioperative morbidity and mortality. We studied patients who had noncardiac surgery to determine whether preoperative hemoglobin concentrations and early postoperative reductions in hemoglobin concentration are associated with AKI.

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METHODS

Study Design

We performed an observational study using data from the Cleveland Clinic Perioperative Health Documentation System (PHDS), an electronic medical record–based registry of noncardiac surgery patients who had surgery between January 6, 2005 and September 21, 2010 at the Cleveland Clinic, Cleveland, OH, with additional linkage to hospital-based administrative data and death records. Use of this de-identified registry for research was approved by the Cleveland Clinic IRB. The requirement for written informed consent was waived by the IRB.

Patients

Patients who had at least 1 preoperative and 1 postoperative creatinine measure within 7 days of surgery as well as a preoperative hemoglobin and at least 1 postoperative hemoglobin within 1 day of surgery were included. To reduce concerns of confounding related to preoperative chronic kidney disease (a potent risk factor for AKI), patients who had an estimated glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 according to the 4-variable Modification of Diet in Renal Disease equation were excluded from study.[12] Patients undergoing removal of urinary obstruction, nephrectomy, or renal transplantation were also excluded. Of note, the Cleveland Clinic does not perform obstetrical surgery (i.e., cesarean delivery).

Outcomes and Exposures

We defined AKI according to changes in serum creatinine between preoperative and postoperative values. The preoperative creatinine was defined as the concentration measured closest to the time before surgery. The postoperative value used was the highest concentration measured within 7 days of surgery. Consistent with the Acute Kidney Injury Network definition of AKI, patients were considered to have AKI if the highest postoperative concentration was either >1.5-fold or >0.3 mg/dL more than the preoperative concentration.[4] We further stratified the severity of AKI as mild (1.5- to 2-fold or >0.3 mg/dL increase in creatinine), moderate (>2- to 3-fold increase in creatinine) or severe (>3-fold increase in creatinine).

Perioperative Hemoglobin

Both the preoperative hemoglobin level and the change between preoperative hemoglobin and lowest hemoglobin in the 24 hours after surgery were examined for an association with AKI. The preoperative hemoglobin was the value recorded closest to the time preceding the operation.

Other Exposures

Patient's age and sex were determined from the registry. The Risk Stratification Index (RSI) for 30-day mortality, a validated score using administrative data codes, was calculated for all patients.[13] Intraoperative estimated blood loss and transfusion of red blood cells (autologous and allogeneic) were recorded in the clinical database. Surgeries were classified according to the Agency for Healthcare Research and Quality descriptors and whether they were emergency or elective procedures using the Clinical Classification Software.

Statistical Analysis

Patient characteristics were calculated as mean (SD), median (25th–75th percentile), or frequency (%) as appropriate. To assess the association between perioperative hemoglobin and AKI, we developed a multivariable logistic regression model in which presence or absence of AKI was the outcome (i.e., dependent variable). The main exposures (i.e., independent variables), preoperative hemoglobin concentration, and change in hemoglobin concentration were categorized into groups felt to be clinically important. Preoperative hemoglobin concentration was categorized as >12.0 g/dL, 12.0 to 10.1 g/dL, 10.0 to 8.1 g/dL, and ≤8.0 g/dL. Change in hemoglobin concentration was categorized as no decrement (referent group), 0 to 1 g/dL decrement, 1.1 to 2.0 g/dL decrement, 2.1 to 3.0 g/dL decrement, 3.1 to 4.0 g/dL decrement, and >4.0 g/dL decrement.

We adjusted all models for age, sex, the RSI for 30-day mortality, the volume of red blood cells transfused intraoperatively, and the type of surgery performed. We accommodated the correlation of multiple surgeries within individual patients by calculating estimated standard errors adjusted for intragroup correlations using clustered sandwich estimators.[14,15] We reported adjusted odds ratios (ORs) and associated 95% confidence intervals (CIs) and *P*-values. *P*-values <0.05 without adjustment for multiple testing were considered significant.

We performed sensitivity analyses by constructing logistic regression models similar to the primary analysis, but (1) using alternative definitions of AKI (limited to AKI within 3 days of surgery, moderate AKI, and severe AKI), (2) by subgroups of surgeries (elective only, most recent surgery only, abdominal surgery only, orthopedic surgery only, and vascular surgery only), and (3) using alternatives to the RSI to control confounding (Charlson comorbidity index and individual comorbidities).

We examined the association between 30-day all-cause mortality and AKI with a logistic regression model adjusted for patient age, sex, RSI score, procedure type, emergency surgery status, estimated blood loss, transfusion volume, change in hemoglobin concentration and preoperative hemoglobin concentration. All analyses were completed using Stata version 11 MP (StataCorp LP, College Station, TX).

RESULTS

Among the 106,122 noncardiac surgeries in the PHDS database, 22,383 were excluded for an estimated GFR <60 mL/min/1.73 m^2, 13,169 were excluded for missing preoperative creatinine or hemoglobin concentrations, 28,144 were excluded for missing follow-up laboratory values, 4715 were excluded because surgery was for removal of urinary obstruction, nephrectomy, or renal transplant procedures, and 4481 were excluded for other missing covariate data (demographics, estimated blood loss, transfusion data, and emergency surgery designation) (Fig. 1). Among the eligible 33,330 surgeries performed in 27,381 patients, AKI occurred in 2478 (7.4%) surgeries.

Patients who did and did not develop AKI differed significantly; specifically, they were older, more frequently male, had a higher risk of 30-day mortality, more cardiovascular disease, and more often had emergency surgery (Table 1).

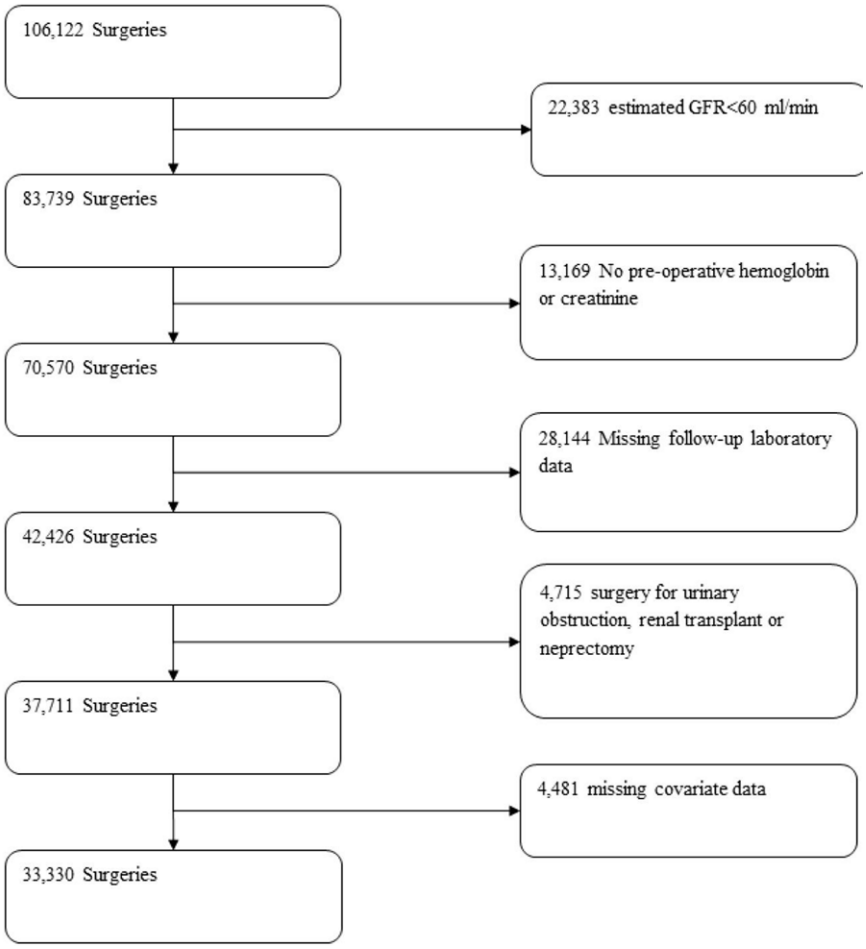

Figure 1. Flow of patients in study. GFR = glomerular filtration rate.

In 9566 (29%) surgeries, patients had a preoperative hemoglobin concentration <12.0 g/dL. Patients with lower preoperative hemoglobin concentrations were older, had higher RSI scores, more often had emergency procedures, and were transfused larger volumes of red blood cells (Table 2). Lower preoperative hemoglobin concentrations were associated with a graded risk of postoperative AKI. Each category of lower preoperative hemoglobin below the

Table 1. Characteristics of Included Patients

	No AKI *N* = 30,852	AKI *N* = 2478)	Standardized difference
Age, mean (SD), y	55.6 (15.6)	59.7 (14.6)	27.0
Female, *n* (%)	15,924 (51.6)	912 (36.8)	−30.1
ASA class, *n* (%)			
I	607 (2.0)	16 (0.6)	12.3
II	12,673 (41.1)	575 (23.2)	39.0
III	15,426 (50.0)	1,343 (54.2)	−8.0
IV	2,074 (6.7)	529 (21.4)	−43.3
V	53 (0.2)	14 (0.6)	−6.3
30-Day mortality RSI, mean score (SD)	−0.3 (1.15)	0.83 (1.42)	66.1
Diabetes mellitus, *n* (%)	474 (1.5)	60 (2.4)	−6.5
History of MI, *n* (%)	1231 (4.0)	129 (5.2)	−5.7
History of CHF, *n* (%)	916 (3.0)	185 (7.5)	−20.3
History of PVD, *n* (%)	1135 (3.7)	219 (8.8)	−21.2
History of stroke, *n* (%)	1519 (4.9)	94 (3.8)	5.4
Preoperative hemoglobin, mean (SD), g/dL	13.1 (2.0)	12.3 (2.3)	−36.0
Estimated GFR, median (25th–75th percentile), mL/min/1.73 m^2	87 (75–103)	85 (72–103)	−5.0
Emergency procedure, *n* (%)	1802 (5.8)	365 (14.7)	29.7
Estimated blood loss, median (25th–75th percentile), mL	200 (100–400)	390 (150–900)	45.0
Amount transfused, median (25th–75th percentile), mL	0 (0–0)	0 (0–320)	44.8
Case duration, median (25th–75th percentile), h	4.0 (2.8–5.3)	4.5 (3.0–6.6)	25.4

AKI = acute kidney injury; RSI = Risk Stratification Index; MI = myocardial infarction; CHF = congestive heart failure; PVD = peripheral vascular disease; GFR = glomerular filtration rate.

Table 2. Patient Characteristics for Each Preoperative Hemoglobin Range

	Preoperative hemoglobin (g/dL)			
	>12.0	10.1 to 12.0	8.1 to 10.0	<8.1
	N = 23,764	*N* = 6173	*N* = 2997	*N* = 396
Age, mean (SD), y	55.7 (15.0)	56.4 (16.8)	56.4 (16.8)	53.5 (16.4)
Female, *n* (%)	11,072 (46.6)	3935 (63.7)	1632 (54.4)	197 (49.7)
RSI, median score (25th to 75th percentile)	−0.09 (−0.72 to 0.28)	0.26 (−0.21 to 1.12)	0.85 (0.19 to 1.79)	1.14 (0.48 to 2.05)
Emergency procedure, *n* (%)	849 (3.6)	621 (10.1)	540 (18.0)	157 (39.6)
EBL, median (25th to 75th percentile), mL	200 (100 to 450)	200 (100 to 500)	200 (50 to 400)	200 (75 to 850)
Volume of transfusions, median (25th to 75th percentile), mL	0 (0 to 0)	0 (0 to 0)	0 (0 to 360)	320 (0 to 885)

RSI = Risk Stratification Index; EBL = estimated blood loss.

reference category was associated with a clinically and statistically significant increased risk starting with an OR of 2.0 (95% CI, 1.8–2.3) for hemoglobin concentrations between 10.1 and 12.0 g/dL and increasing to an OR of 3.7 (95% CI, 2.6–5.4) for hemoglobin concentrations <8.0 g/dL (Fig. 2).

In 17,128 (51%) surgeries, patients had a decrement in hemoglobin of >3.0 g/dL, and in 10,808 (32%) surgeries, a decrement of >4.0 g/dL. Patients with larger decrements in postoperative hemoglobin had lower RSI scores (i.e., lower risk of 30-day mortality) and were less frequently undergoing emergency surgery, and in all but the most extreme category of decrement in hemoglobin were younger (Table 3). However, larger decrements in hemoglobin also occurred in patients with lower estimated GFRs, greater estimated blood losses, and longer case durations. There was no apparent increase in transfusion volumes in those with larger decrements in hemoglobin concentration. Larger decrements in hemoglobin concentration were associated with a graded increase in the risk of AKI. Decrements as small as 1.1 to 2.0 g/dL were significantly associated with AKI with an adjusted OR of 1.5 (95% CI, 1.2–2.0) and decrements >4.0 g/dL associated with an OR of 4.7 (95% CI, 3.6–6.2) (Fig. 3). In contrast, compared with no transfusion, transfusion with 250 mL packed red blood cells carried an OR of 1.05 (95% CI, 1.03–1.07), while a transfusion of 1000 mL packed red blood cells carried an OR of 1.20 (95% CI, 1.11–1.30).

Sensitivity analyses in which the outcome definition was altered, the type of surgery was restricted, or the method of adjustment was altered were broadly similar to the main analysis (Tables 4–6). For example, models in which AKI was defined as a moderate (>2-fold increase in serum creatinine) or severe (>3-fold increase in serum creatinine) also demonstrated a graded increase in the risk of AKI for each lower category of preoperative hemoglobin and each larger category of decrement in postoperative hemoglobin (Table 4). AKI defined by the highest creatinine within 3 days of surgery rather than within 7 days of surgery occurred in 2043 surgeries (6.1%) and did not change the relationships between preoperative hemoglobin and the postoperative decrement in hemoglobin materially (Table 4).

AKI was independently associated with 30-day mortality with an adjusted OR of 2.6 (95% CI, 2.0–3.3). Increasing severity of AKI was associated with mortality in a graded manner. The adjusted OR for mild AKI and death was 1.8 (95% CI, 1.3–2.4), moderate AKI was 3.5 (95% CI, 2.3–5.4), and severe AKI was 6.9 (95% CI, 4.5–10.5).

DISCUSSION

In this large, single-center study, we demonstrated that preoperative hemoglobin concentrations and postoperative decrements in hemoglobin are both independently associated with AKI. Given the graded relationship between the degree of preoperative anemia and odds of AKI and

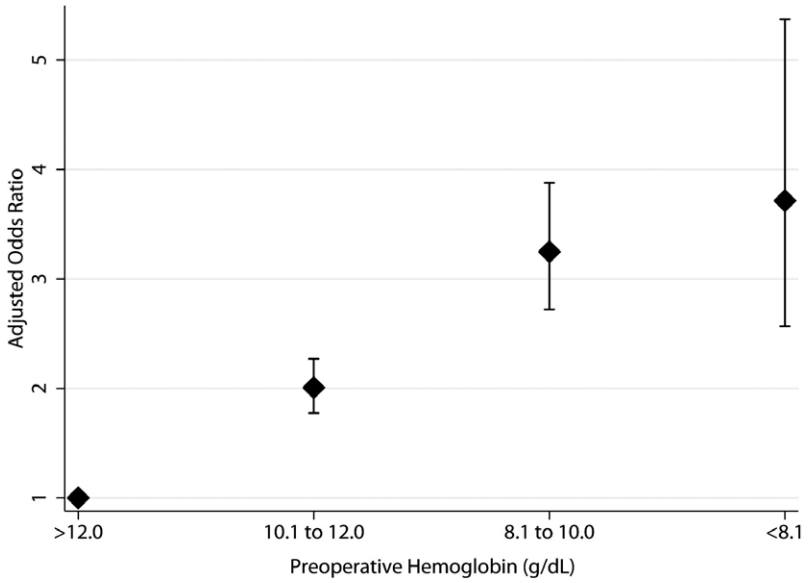

Figure 2. Adjusted odds ratio for each category of preoperative hemoglobin in patients undergoing noncardiac surgery. Estimates were adjusted for age, sex, Risk Stratification Index for 30-day mortality, type of surgery, estimated blood loss, red blood cell transfusion volume, and postoperative decrement in hemoglobin.

Table 3. Patient Characteristics for Each Degree of Decrement in Hemoglobin

	Decrement in hemoglobin in 24 h postoperatively (g/dL)					
	None	0.1 to 1.0	1.1 to 2.0	2.1 to 3.0	3.1 to 4.0	>4.0
	N = 1144	*N* = 2809	*N* = 5372	*N* = 6877	*N* = 6320	*N* = 10,808
Age, mean (SD), y	56.1 (16.8)	55.4 (16.7)	54.2 (16.2)	54.6 (16.0)	55.9 (15.4)	57.6 (14.3)
Female, *n* (%)	569 (49.7)	1451 (51.7)	2827 (52.6)	3796 (55.2)	3404 (53.9)	4789 (44.3)
RSI, median score (25th to 75th percentile)	0.81 (0.05 to 1.79)	0.40 (−0.01 to 1.26)	0.05 (−0.19 to 0.83)	0.0 (−0.40 to 0.50)	0.00 (−0.63 to 0.35)	−0.18 (−1.07 to 0.34)
Emergency procedure, *n* (%)	264 (23.1)	345 (12.3)	492 (9.2)	434 (6.3)	288 (4.6)	344 (3.2)
Preoperative hemoglobin, mean (SD), g/dL	9.4 (2.0)	10.9 (2.0)	12.1 (2.0)	13.0 (1.8)	13.4 (1.6)	14.2 (1.4)
EBL, median (25th to 75th percentile), mL	100 (50 to 400)	100 (50 to 200)	100 (50 to 200)	150 (75 to 300)	200 (100 to 400)	400 (200 to 800)
Volume of transfusions, median (25th to 75th percentile), mL	0 (0 to 630)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)

RSI = Risk Stratification Index; EBL = estimated blood loss.

magnitude of decrement in postoperative hemoglobin, these findings are consistent with an ischemic cause of postoperative AKI.[16,17] The importance of these findings is highlighted by the large proportion of patients undergoing noncardiac surgery who had low preoperative hemoglobin concentrations or substantial postoperative decrements in hemoglobin.

Our finding that preoperative hemoglobin concentrations are strongly associated with AKI is consistent with findings in cardiac surgery.[9] Our study extends previous work to noncardiac surgery and shows that low hemoglobin concentration and substantial decrements in hemoglobin are important risk factors for AKI, a finding, to our knowledge, not previously demonstrated.[1,18,19] Given that hemoglobin concentrations <12 g/dL are common in patients undergoing noncardiac surgery, and that the association between lower hemoglobin levels and AKI is strong, risk prediction tools for postoperative AKI may be improved substantially by considering perioperative hemoglobin concentrations.

Our finding that a decrement in postoperative hemoglobin is strongly associated with postoperative AKI is new. The relationship between the number of transfusions required and AKI was described in cardiac surgery and demonstrated less than a 10% increase in risk of AKI for each unit transfused.[9] Even after adjusting estimates for transfusion, which are less numerous in noncardiac than cardiac surgery, even a relatively small decrement in hemoglobin was strongly associated with AKI.

Larger decrements in hemoglobin presumably reduce the oxygen-carrying capacity of blood which may be of particular importance to renal tubules that operate under near anaerobic conditions.[20,21] Furthermore, decrements in hemoglobin may represent bleeding (subclinical or overt) which may reduce renal perfusion pressures and result in transfusions that may carry their own risk. Larger decrements in hemoglobin may also result from more extensive surgery resulting in greater systemic inflammation that may compound the risk of AKI. The extent to which decrements in hemoglobin or the precipitating factors are responsible for the observed increase in AKI is unclear. In either case, the measured decrement in hemoglobin is an easily and objectively quantified risk factor (unlike subclinical blood loss, systemic inflammation, or renal perfusion pressure) and may serve as a valuable early indicator of postoperative morbidity. Finally, decrements in hemoglobin may precipitate studies with nephrotoxic agents (i.e., contrast) to investigate a source of bleeding. However, it seems unlikely that contrast administration could account for a >4-fold increase in the risk of AKI.

We note, though, that larger decrements in hemoglobin were observed in generally healthier individuals with higher preoperative hemoglobin concentrations. Transfusion practices are often guided by threshold values for at-risk groups.[22] Larger decrements in hemoglobin/bleeding are presumably tolerated without transfusions when patients are healthier and have relatively higher preoperative hemoglobin values. Our results suggest that hemoglobin decrements might be considered in addition to absolute hemoglobin concentrations when considering when to transfuse surgical patients. That said, transfusions

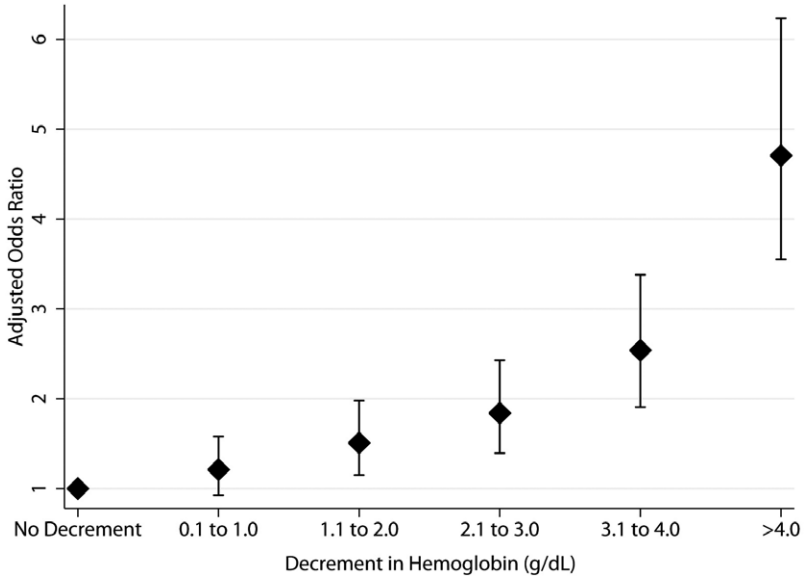

Figure 3. Adjusted odds ratio for each category of decrement in hemoglobin within 24 hours after noncardiac surgery. Estimates were adjusted for age, sex, Risk Stratification Index for 30-day mortality, type of surgery, estimated blood loss, red blood cell transfusion volume, and preoperative hemoglobin.

are themselves associated with adverse outcomes and whether they provide net perioperative benefit remains to be determined in randomized studies that evaluate a constellation of potential adverse outcomes.[23–26] An alternative strategy is aggressive prevention of bleeding. The use of agents such as tranexamic acid is currently under study in several areas of noncardiac surgery and may help mitigate decrements in hemoglobin concentration and consequently AKI.

Our study has several notable strengths. We were able to use all laboratory data on all patients to define categories of hemoglobin and change in hemoglobin, an approach not available to most administrative databases. Our data also included almost 2500 events in more than 30,000 surgeries, allowing us to make precise estimates without the risk of overfitting our statistical models.[27] Finally, we were able to characterize patients' comorbidities using the highly predictive RSI which incorporates a large number of administrative codes rather than relying on our limited ability to correctly select coded comorbidities that might be associated with perioperative hemoglobin, changes in hemoglobin, and AKI.

Our results suggest that preoperative hemoglobin in patients having elective surgery may be a rational therapeutic target. However, we cannot make causal inferences from observational data and certainly cannot predict from our analysis whether therapies such as erythropoiesis-stimulating drugs, autologous donation, or other transfusion strategies will reduce mortality.

Our results are from a single center with a high-acuity population which may limit generalizability. But although the details may vary from center to center, it seems likely that our risk-adjusted associations will prove generally applicable across centers, especially given their consistency with studies in patients having cardiac surgery.[9]

Only one-third of all surgeries were eligible for our study, with many excluded for lack of laboratory data. Patients who did not have hemoglobin or creatinine measured preoperatively or postoperatively (most of whom had ambulatory surgery) were presumably at lower risk of postoperative morbidity than those who had measurements. While it seems likely that the relative associations are largely preserved, they are probably of little practical consequence given the low

Table 4. Estimates of Association Between Preoperative Hemoglobin Concentration and Change in Hemoglobin Concentration with AKI in Sensitivity Analyses in Which the End Point Is Alternatively Defined

	Adjusted odds ratio (95% confidence interval)		
	Moderate AKI	**Severe AKI**	**AKI within 3 d of surgery**
Preoperative hemoglobin, g/dL			
>12.0	Referent	Referent	Referent
10.1–12.0	2.00 (1.59–2.52)	1.84 (1.26–2.69)	2.03 (1.78–2.32)
8.1–10.0	2.87 (2.07–3.96)	2.93 (1.76–4.87)	3.03 (2.49–3.68)
<8.1	3.52 (1.89–6.54)	2.24 (0.62–8.08)	2.80 (1.85–4.22)
Change in hemoglobin, g/dL			
No decrement	Referent	Referent	Referent
0.1–1.0	0.97 (0.60–1.55)	1.60 (0.65–3.94)	1.03 (0.77–1.40)
1.1–2.0	1.72 (1.10–2.68)	2.06 (0.82–5.18)	1.44 (1.07–1.93)
2.1–3.0	2.44 (1.55–3.84)	3.94 (1.60–9.73)	1.73 (1.27–2.35)
3.1–4.0	2.72 (1.68–4.38)	4.03 (1.57–10.31)	2.49 (1.82–3.41)
>4.0	5.22 (3.30–8.26)	7.32 (2.95–18.19)	4.79 (3.52–6.52)

AKI = acute kidney injury.

Table 5. Estimates of Association Between Preoperative Hemoglobin Concentration and Change in Hemoglobin Concentration with Acute Kidney Injury in Sensitivity Analyses in Which the Type of Surgery Is Restricted

	Adjusted odds ratio (95% confidence interval)				
	Last operation only	Elective procedures only	General surgery only	Orthopedic surgery only	Vascular surgery only
Preoperative Hemoglobin, g/dL					
>12.0	Referent	Referent	Referent	Referent	Referent
10.1–12.0	2.03 (1.74–2.38)	2.41 (2.14–2.72)	1.99 (1.63–2.42)	1.81 (1.39–2.35)	1.63 (1.12–2.38)
8.1–10.0	3.15 (2.50–3.97)	4.62 (3.88–5.51)	3.92 (2.96–5.19)	3.09 (2.08–4.58)	2.41 (1.44–4.02)
<8.1	4.12 (2.54–6.70)	5.45 (3.74–7.93)	4.50 (2.45–8.28)	4.24 (1.73–10.4)	1.50 (0.53–4.22)
Change in hemoglobin, g/dL					
No decrement	Referent	Referent	Referent	Referent	Referent
0.1–1.0	1.09 (0.78–1.54)	1.22 (0.94–1.60)	1.62 (1.01–2.61)	1.32 (0.67–2.60)	1.03 (0.52–2.04)
1.1–2.0	1.34 (0.95–1.90)	1.51 (1.15–1.98)	2.41 (1.50–3.85)	1.30 (0.62–2.70)	0.89 (0.44–1.80)
2.1–3.0	1.59 (1.11–2.27)	1.82 (1.37–2.41)	2.49 (1.53–4.05)	2.12 (1.04–4.37)	1.58 (0.78–3.23)
3.1–4.0	2.10 (1.46–3.02)	2.49 (1.86–3.33)	4.00 (2.43–6.57)	2.65 (1.27–5.53)	1.81 (0.85–3.82)
>4.0	3.92 (2.74–5.62)	4.60 (3.45–6.12)	7.74 (4.75–12.6)	4.11 (1.98–8.56)	3.23 (1.54–6.78)

absolute rate of AKI in patients undergoing ambulatory surgery.

A final limitation is that our study population was restricted to patients with well-preserved preoperative kidney function. However, chronic kidney disease appears to be a risk multiplier for AKI. It is therefore likely that the associations between perioperative hemoglobin and AKI are preserved or even greater in patients with chronic kidney disease.

In summary, even slight reductions in preoperative hemoglobin concentrations and small decrements in hemoglobin are strongly associated with AKI in patients undergoing noncardiac surgery. Whether intervening to improve or maintain perioperative hemoglobin concentration reduces postoperative mortality remains unknown. Furthermore, liberal transfusion strategies and/or the use of erythropoiesis-stimulating drugs would improve perioperative hemoglobin but may be associated with net harm.[28,29] Alternatively, strategies to mitigate intraoperative and early postoperative blood loss such as reversal of coagulant deficiencies or changes in preoperative anticoagulant/antiplatelet use may be useful to reduce the early decrement in hemoglobin. Further research targeting perioperative hemoglobin management is clearly needed given the volume of noncardiac surgery globally, the frequency of preoperative anemia, the large decrements in hemoglobin that commonly accompany major surgery, and the frequency of AKI and its serious implications for patient outcomes and health care costs.

Table 6. Estimates of Association Between Preoperative Hemoglobin Concentration and Change in Hemoglobin Concentration with Acute Kidney Injury in Sensitivity Analyses in Which the Method of Adjustment Is Altered

	Adjusted odds ratio (95% confidence interval)	
	Individual comorbidity adjusted	Charlson comorbidity score adjusted
Preoperative hemoglobin, g/dL		
>12.0	Referent	Referent
10.1–12.0	2.41 (2.14–2.72)	2.48 (2.20–2.80)
8.1–10.0	4.62 (3.88–5.51)	4.78 (4.03–5.68)
<8.1	5.45 (3.74–7.93)	5.52 (3.80–8.03)
Change in hemoglobin, g/dL		
No decrement	Referent	Referent
0.1–1.0	1.22 (0.94–1.60)	1.25 (0.95–1.63)
1.1–2.0	1.51 (1.15–1.98)	1.51 (1.15–1.99)
2.1–3.0	1.82 (1.37–2.41)	1.82 (1.38–2.41)
3.1–4.0	2.49 (1.86–3.33)	2.48 (1.87–3.31)
>4.0	4.60 (3.45–6.12)	4.56 (3.44–6.04)

DISCLOSURES

Name: Michael Walsh, MD, MSc.
Contribution: This author helped design and conduct the study, analyze the data, and write the manuscript.
Attestation: Michael Walsh 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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Contribution: This author helped design and conduct the study, analyze the data, and write the manuscript.
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Attestation: Hooman Honar reviewed the analysis of the data and approved the final manuscript.
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Contribution: This author helped design and conduct the study, analyze the data, and write the manuscript.
Attestation: Daniel I. Sessler has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
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