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Analysis of Association of Pre-Operative Hemoglobin Levels with Post-Operative Venous Thromboembolism in Non-Cardiac Surgery Patients at a Tertiary Care Center: A Retrospective Analysis

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Abstract

Background

Preoperative anemia is common in surgical patients and has been associated with increased postoperative morbidity and mortality. Although prior studies have linked anemia to adverse surgical outcomes, its relationship with postoperative venous thromboembolism (VTE) across a broad non-cardiac surgical population remains incompletely defined. We evaluated the association between preoperative hemoglobin levels and postoperative VTE and other postoperative complications.

Methods

We conducted a retrospective cohort study of adult patients undergoing non-cardiac surgery at a tertiary academic center between 2010 and 2022 using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. Patients were categorized according to World Health Organization criteria as having normal hemoglobin, mild anemia, moderate anemia, or severe anemia. The primary outcome was postoperative VTE, defined as deep vein thrombosis or pulmonary embolism within 30 days of surgery. Multivariable logistic regression was used to evaluate associations between hemoglobin categories and postoperative outcomes after adjustment for age, sex, race, ASA class, surgical specialty, and postoperative transfusion.

Results

A total of 14,918 patients were included. The incidence of postoperative VTE increased progressively with worsening anemia severity, from 0.5% in patients with normal hemoglobin to 5.8% in those with severe anemia ($p < 0.001$). After adjustment for postoperative transfusion and other covariates, preoperative anemia remained independently associated with VTE. Compared with patients with normal hemoglobin, the odds of postoperative VTE were higher in patients with mild anemia (OR 2.80, 95% CI 1.78–4.42), moderate anemia (OR 3.59, 95% CI 1.96–6.59), and severe anemia (OR 8.96, 95% CI 3.72–21.55) (all $p < 0.001$). Postoperative transfusion was also independently associated with VTE (OR 4.34, 95% CI 2.69–7.00). Increasing anemia severity was additionally associated with higher rates of pneumonia, prolonged mechanical ventilation, dialysis, sepsis, readmission, return to the operating room, and mortality.

Conclusions

Preoperative anemia was independently associated with postoperative VTE in patients undergoing non-cardiac surgery, with a clear dose-response relationship across anemia severity categories. The association persisted after adjustment for postoperative transfusion and other important clinical factors.

These findings suggest that preoperative hemoglobin may serve as an important marker of thromboembolic and postoperative risk and support careful evaluation of anemia during preoperative assessment

Introduction

Preoperative anemia is a common finding among surgical patients, affecting approximately 30–40% of individuals undergoing major non-cardiac procedures. It has consistently been associated with increased perioperative morbidity, mortality, prolonged hospitalization, and greater healthcare resource utilization across diverse surgical populations [1–5].

Low hemoglobin has been consistently associated with adverse postoperative outcomes across a variety of surgical populations. In cardiac surgery, it is associated with in-hospital mortality, stroke, and acute kidney injury, even after adjustment for important confounders [1, 6]. Similar increases in postoperative morbidity and mortality have been observed in non-cardiac surgery [2, 7, 8], as well as in spine, major head and neck, and orthopedic surgery, including total joint arthroplasty [3, 9, 10]. Together, these findings suggest that low hemoglobin is a marker of increased perioperative risk, greater resource utilization, and worse short-term outcomes. Meta-analytic data further support its association with increased mortality across diverse surgical populations [11].

Thromboembolic complications are an important adverse outcome associated with anemia. Venous thromboembolism is a major cause of postoperative morbidity and mortality, often occurring after hospital discharge [12], and the risk may remain elevated for weeks to months after cancer surgery [13]. Preoperative anemia has been associated with postoperative deep vein thrombosis [3, 4, 14, 15], while perioperative red blood cell transfusion has been linked to new or progressive venous thromboembolism [16]. Together, these findings suggest that patients with low hemoglobin may be at increased thrombotic risk through both the underlying anemia and its management.

Although low preoperative hemoglobin has been associated with postoperative morbidity, transfusion, and thromboembolic events, its relationship with postoperative thromboembolic complications remains incompletely understood across broad surgical populations. Prior studies have largely focused on specific surgical groups or transfusion exposure, and whether these associations persist with modern thromboprophylaxis strategies remain uncertain. Current consensus statements and clinical guidelines emphasize the importance of preoperative anemia and hemoglobin level in perioperative risk assessment and stratification [17, 18].

We evaluated the association between preoperative hemoglobin levels and postoperative outcomes across diverse non-cardiac surgeries at a tertiary care center. We hypothesized that lower preoperative hemoglobin would be associated with increased thromboembolic risk. Clarifying this relationship may improve preoperative risk stratification and identify patients who could benefit from targeted optimization. Given the retrospective design and incomplete treatment data, these findings should be interpreted as associations rather than causal relationships.

Methods

Study Design

We conducted a single-center retrospective cohort study of non-cardiac surgical patients at Cooper University Hospital between 2010 and 2022. All patients were included in the Acute Care Surgery National Surgical Quality Improvement Program (NSQIP) database during the study period.

The Cooper University Healthcare Institutional Review Board approved the study (IRB# 25–129).

NSQIP Database

The NSQIP is the largest surgical database in the United States, prospectively collecting data from more than 200 hospitals. Initially launched in 2001 with 18 hospitals, the program expanded nationally in 2004. Participation is voluntary. Data are abstracted by trained surgical clinical reviewers from medical charts, including operative and anesthesia reports, and are monitored for up to 30 days postoperatively. The data are not derived from claims or billing records. Rigorous training, routine audits, and monthly calls with the American College of Surgeons (ACS) NSQIP oversight team ensure data integrity and consistency.[15]

Inclusion and Exclusion Criteria

We included all adult patients who underwent elective or emergency surgery at Cooper University Hospital, had documented hemoglobin levels measured within seven days before surgery and were entered in the NSQIP database. Patients lacking preoperative hemoglobin measurements were excluded from the analysis.

Variables Collected

The following demographic and clinical variables were extracted: Demographics: age, gender; Surgical variables: elective vs. emergency surgery, ASA classification; Postoperative outcomes: pneumonia, pulmonary embolism (PE), mechanical ventilation > 48 hours, acute kidney injury (AKI), dialysis, cerebrovascular accident (CVA), cardiac arrest, myocardial infarction (MI), deep vein thrombosis (DVT), sepsis, delirium, hospital length of stay > 2 days, 30-day mortality, 30-day readmission, and unplanned return to the operating room within 30 days

Exposure and Outcomes

Preoperative hemoglobin level was the primary exposure of interest. Patients were categorized according to World Health Organization (WHO) criteria. According to WHO criteria, anemia was defined

as hemoglobin < 13 g/dL in men and < 12 g/dL in women. Mild anemia was defined as hemoglobin 11.0-12.9 g/dL in men and 11.0-11.9 g/dL in women, moderate anemia as 8.0-10.9 g/dL, and severe anemia as < 8.0 g/dL. The primary outcome was postoperative venous thromboembolism (VTE), defined as the occurrence of either deep vein thrombosis (DVT) or pulmonary embolism (PE) within 30 days of surgery. Secondary outcomes included postoperative pneumonia, mechanical ventilation for more than 48 hours, acute renal failure requiring dialysis, cardiac arrest requiring cardiopulmonary resuscitation, sepsis, hospital readmission within 30 days, and unplanned return to the operating room within 30 days.

Statistical Analysis

Categorical variables were compared across hemoglobin categories using chi-square tests, with the normal hemoglobin group used as the reference. Continuous variables, including age, were analyzed using one-way analysis of variance (ANOVA). Patients with missing preoperative hemoglobin measurements were excluded from the study. For all other variables included in the regression models, a complete-case analysis was performed. The proportion of missing data for covariates was low, and no imputation procedures were applied.

Separate multivariable logistic regression models were constructed to evaluate the association between preoperative hemoglobin categories and postoperative outcomes. Models were adjusted for clinically relevant covariates selected a priori based on their known associations with perioperative outcomes and preoperative hemoglobin levels. These included age, sex, race, ASA class, surgical specialty, and postoperative transfusion in the primary analysis.

The primary outcome was postoperative venous thromboembolism (VTE), and secondary outcomes included pneumonia, prolonged mechanical ventilation (> 48 hours), dialysis, cardiac arrest requiring cardiopulmonary resuscitation, sepsis, 30-day readmission, and unplanned return to the operating room within 30 days.

Odds ratios (ORs) with 95% confidence intervals (CIs) and corresponding p-values were reported. All statistical analyses were performed using SPSS version 26 (IBM Corporation, Armonk, NY), and a two-sided p-value < 0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 14,918 patients met the inclusion criteria and were categorized into normal hemoglobin, mild anemia, moderate anemia, and severe anemia groups. Patients with worsening anemia were older, more likely to be female (mild anemia), more likely to be Black, and had progressively higher ASA classifications, reflecting greater baseline illness severity (all p < 0.001) (Table 1).

Table 1
Baseline Characteristics by Pre-operative Hemoglobin Category:

Variable	Normal	Mild	Moderate	Severe	p-value
Age (mean SD)	56.6 (14.8)	58.8 (16.7)	61.9 (15.6)	59.9 (16.5)	< 0.001
Female (%)	60.4	70.6	56.7	54.2	< 0.001
White (%)	81.4	69.0	71.3	63.7	< 0.001
Black (%)	16.2	28.2	26.9	33.6	< 0.001
ASA Life-threatening (%)	2.0	5.2	12.3	26.4	< 0.001

Postoperative Outcomes (Table 2)

Table 2
Unadjusted Postoperative Outcomes by Hemoglobin Category:

Outcome	Normal	Mild	Moderate	Severe	p-value
VTE	0.5	1.5	2.3	5.8	< 0.001
PE	0.4	0.4	1.3	0.0	0.003
Pneumonia	1.0	2.1	2.8	5.8	< 0.001
Vent > 48h	0.6	1.9	3.6	3.3	< 0.001
Dialysis	0.2	0.7	1.9	3.3	< 0.001
Renal Insufficiency	0.4	0.7	1.9	0.0	< 0.001
MI	0.3	0.4	1.0	0.8	0.005
CVA	0.2	0.5	0.9	3.3	0.874
CPR	0.3	0.5	1.3	2.5	< 0.001
Sepsis	2.7	6.3	10.2	19.0	< 0.001
Readmission	5.8	9.6	16.6	12.4	< 0.001
Return to OR	3.5	5.8	10.2	7.4	< 0.001
Mortality	0.5	1.3	4.0	5.0	< 0.001

Postoperative venous thromboembolism (VTE)

The incidence of postoperative VTE increased progressively with worsening anemia severity, ranging from 0.5% in patients with normal hemoglobin to 5.8% in those with severe anemia ($p < 0.001$). In multivariable analysis, preoperative anemia remained independently associated with VTE after adjustment for age, sex, race, ASA class, surgical specialty, and postoperative transfusion. Compared with patients with normal hemoglobin, adjusted odds ratios for VTE were 2.80 (95% CI 1.78–4.42) for

mild anemia, 3.59 (95% CI 1.96–6.59) for moderate anemia, and 8.96 (95% CI 3.72–21.55) for severe anemia (all p < 0.001). Postoperative transfusion was also independently associated with VTE (OR 4.34, 95% CI 2.69–7.00). A graded association was similarly observed in models that did not include postoperative transfusion (Tables 3 and 4).

Table 3
Multivariable Analysis: Primary Outcome (VTE)

Hemoglobin Category	Adjusted OR	95% CI	p-value
Mild anemia	3.33	2.14–5.18	< 0.001
Moderate anemia	5.26	2.95–9.38	< 0.001
Severe anemia	15.71	6.83–36.10	< 0.001

Models adjusted for age, sex, race, ASA classification, emergency surgery, and surgical category.

Table 4
Preoperative Anemia and Postoperative VTE Before and After Adjustment for Postoperative Transfusion

Variable	Model 1: Without Transfusion OR (95% CI)	Model 2: With Transfusion OR (95% CI)
Normal hemoglobin	Reference	Reference
Mild anemia	3.33 (2.14–5.18)	2.80 (1.78–4.42)
Moderate anemia	5.26 (2.95–9.38)	3.59 (1.96–6.59)
Severe anemia	15.71 (6.83–36.10)	8.96 (3.72–21.55)
Postoperative transfusion	Not included	4.34 (2.69–7.00)

Model 1 adjusted for age, sex, race, emergency surgery, and surgical specialty.

Model 2 adjusted for age, sex, race, emergency surgery, surgical specialty, and postoperative transfusion.

Note

The temporal relationship between postoperative transfusion and VTE could not be determined because timing data were unavailable.

Mortality

Mortality differed significantly across groups (p < 0.001), with the highest rate in the severe anemia group (5.00%), followed by moderate anemia (4.00%), and the lowest in the normal group (0.50%). (Table 2). This association persisted after multivariable analysis.

Postoperative pneumonia and ventilation

Rates of postoperative pneumonia and prolonged mechanical ventilation increased progressively with anemia severity (both $p < 0.001$). After adjustment, mild, moderate, and severe anemia remained independently associated with postoperative pneumonia, with similar graded associations observed for prolonged mechanical ventilation (Table 5).

Table 5
Multivariable Analysis: Secondary Outcomes

Outcome	Mild Anemia	Moderate Anemia	Severe Anemia
Pneumonia	2.16 (1.53–3.06; p < 0.001)	2.29 (1.35–3.87; p = 0.002)	5.54 (2.36–13.04; p < 0.001)
Mortality	1.93 (1.10–2.5; p = 0.002)	3.2 (2.1–4.4; p < 0.001)	4.3 (2.7–6.8; p < 0.001)
Prolonged Ventilation (> 48 h)	2.16 (1.52–3.05; p < 0.001)	2.28 (1.35–3.85; p = 0.002)	5.56 (2.37–13.08; p < 0.001)
Dialysis	1.98 (0.96–4.08; p = 0.063)	3.21 (1.30–7.94; p = 0.012)	9.47 (2.75–32.55; p < 0.001)
Cardiopulmonary Resuscitation (CPR)	1.61 (0.83–3.12; p = 0.157)	2.10 (0.86–5.11; p = 0.104)	3.99 (0.92–17.39; p = 0.065)
Sepsis	2.59 (2.10–3.20; p < 0.001)	4.26 (3.20–5.68; p < 0.001)	9.10 (5.45–15.19; p < 0.001)
Readmission	1.50 (1.27–1.77; p < 0.001)	2.38 (1.88–3.00; p < 0.001)	1.58 (0.88–2.81; p = 0.123)
Return to Operating Room	1.52 (1.23–1.88; p < 0.001)	2.62 (1.97–3.49; p < 0.001)	1.58 (0.75–3.31; p = 0.230)

Values represent adjusted odds ratios with 95% confidence intervals and corresponding p-values.

Models adjusted for age, sex, race, ASA classification, emergency surgery, and surgical specialty.

Renal outcomes

Postoperative renal insufficiency and dialysis occurred more frequently in patients with worsening anemia ($p < 0.001$). In adjusted analyses, moderate and severe anemia were independently associated with postoperative dialysis, whereas mild anemia was not statistically significant (Table 5).

Cardiac and circulatory outcomes

The incidence of cardiopulmonary resuscitation and myocardial infarction differed significantly across hemoglobin groups ($p < 0.001$ and $p = 0.005$, respectively). However, after multivariable adjustment, no hemoglobin category remained independently associated with cardiopulmonary resuscitation.

Postoperative sepsis

The incidence of postoperative sepsis increased progressively across anemia categories, from 2.7% in patients with normal hemoglobin to 19.0% in those with severe anemia ($p < 0.001$). Mild, moderate, and severe anemia remained independently associated with postoperative sepsis after adjustment (Table 5).

Readmission and return to operating room (ROR)

Hospital readmission and unplanned return to the operating room increased with worsening anemia severity (both $p < 0.001$). In adjusted analyses, mild and moderate anemia remained independently associated with both outcomes, whereas severe anemia was not statistically significant (Table 5).

Delirium

There was no significant association between preoperative hemoglobin levels and postoperative delirium ($p = 0.128$).

Postoperative cerebrovascular accident (CVA)

There was no significant difference in postoperative CVA across hemoglobin groups ($p = 0.874$).

Additional predictors

Increasing age and male sex were independently associated with multiple postoperative outcomes. Higher ASA class, particularly life-threatening or moribund status, was associated with increased odds of readmission and return to the operating room.

Discussion

In this large retrospective cohort of nearly 15,000 patients undergoing non-cardiac surgery, preoperative anemia was independently associated with postoperative venous thromboembolism (VTE), with risk increasing across anemia severity categories. This association persisted after adjustment for demographic characteristics, surgical factors, and postoperative transfusion, suggesting that preoperative hemoglobin provides prognostic information beyond transfusion exposure. Increasing anemia severity was also associated with higher rates of pulmonary complications, renal failure requiring dialysis, sepsis, readmission, return to the operating room, and mortality, reinforcing the broader prognostic significance of preoperative anemia. Key strengths of this study include the large sample size, inclusion of a broad range of non-cardiac surgical procedures, and assessment of VTE as a primary outcome. The observed dose-response relationship across anemia severity categories further supports the robustness of the association.

Our findings extend a substantial body of literature linking preoperative anemia to adverse surgical outcomes. Previous studies have demonstrated increased postoperative morbidity and mortality among anemic patients undergoing both cardiac and non-cardiac surgery [2, 7, 8, 11, 15], while procedure-specific investigations in orthopedic, trauma, colorectal, and oncologic populations have reported associations between anemia and postoperative thromboembolic complications [3, 4, 19–22]. However, most prior studies evaluated VTE within selected surgical populations or as part of composite

outcomes. In contrast, our study evaluated VTE as the primary outcome in a large and diverse non-cardiac surgical cohort and demonstrated a clear dose-response relationship between anemia severity and postoperative VTE.

A unique aspect of our study is the evaluation of postoperative transfusion as a potential confounder. Patients with anemia are more likely to receive perioperative blood transfusions, and transfusion itself has been associated with adverse postoperative outcomes and thromboembolic complications [16, 25, 26]. After adjustment for postoperative transfusion, the association between preoperative anemia and VTE remained significant across all anemia categories. However, because both transfusion and VTE occurred during the postoperative period and the timing of these events was unavailable, these findings should not be interpreted as evidence that transfusion mediates or causes postoperative VTE.

Several biological mechanisms may explain these observations. Preoperative anemia frequently reflects chronic inflammation, malignancy, chronic kidney disease, and other systemic illnesses, many of which are associated with increased thrombotic risk [5, 19–21]. In addition, alterations in red blood cell biology may contribute directly to thrombogenesis through enhanced platelet activation, thrombin generation, endothelial interactions, and changes in blood rheology [21, 23]. Reduced mobility, prolonged hospitalization, and increased physiologic stress may further increase thrombotic risk in patients with more severe anemia [20, 21]. Severe anemia may also reflect broader physiologic vulnerability, which has been associated with worse postoperative outcomes [24]. Nevertheless, whether anemia directly contributes to thrombosis or primarily serves as a marker of underlying patient vulnerability cannot be determined from this observational study.

The graded relationship observed across anemia severity categories strengthens the clinical relevance of these findings. Progressively lower hemoglobin levels were associated with progressively greater odds of postoperative VTE and several additional postoperative complications. Similar dose-response relationships have been reported in orthopedic and elderly surgical populations [4, 11], suggesting that preoperative hemoglobin functions as a marker of perioperative risk across diverse surgical settings.

These findings have important implications for perioperative practice. Hemoglobin is routinely measured, inexpensive, widely available, and potentially modifiable. Current patient blood management and perioperative guidelines emphasize the early identification and evaluation of preoperative anemia [17, 18, 27, 28]. Our findings suggest that preoperative hemoglobin may provide additional value for perioperative risk stratification, particularly with respect to thromboembolic risk. However, because detailed information regarding anemia etiology, transfusion practices, and thromboprophylaxis was not available, these findings should be interpreted as demonstrating association rather than causation. Further prospective studies are needed to determine whether correction of anemia or individualized thromboprophylaxis strategies can reduce postoperative thromboembolic risk.

Limitations:

This study has several limitations. As a single-center observational study, it cannot establish causality, and its generalizability to other institutions may be limited. In addition, the analysis relies on the accuracy and completeness of NSQIP data, and misclassification or missing data may have influenced the results. The study period spanned more than a decade, during which perioperative care, transfusion practices, and thromboprophylaxis strategies may have evolved. Although this reflects real-world practice, temporal changes in care could have influenced the observed associations.

Although we adjusted for key demographic, clinical, and procedural variables, important factors were not available in the dataset, including anemia etiology, iron studies, inflammatory markers, nutritional status, and other potential confounders. We were also unable to distinguish among specific causes of anemia, such as iron deficiency, chronic disease, malignancy, or acute blood loss, which may have different prognostic implications.

Several perioperative factors that may influence postoperative outcomes were not captured. Detailed information regarding thromboprophylaxis, including type, timing, duration, and adherence, was unavailable. We also lacked data on transfusion timing, indication, and volume, limiting our ability to distinguish the effects of baseline anemia from those related to its management. In addition, information on intraoperative blood loss and the development of postoperative anemia was not available and may have independently contributed to postoperative complications and VTE risk. We were also unable to determine whether preoperative anemia was corrected before surgery or whether such correction modified outcomes.

Residual confounding also remains possible. Factors such as surgical complexity, duration of immobilization, perioperative care pathways, clinical urgency, and baseline illness severity may have influenced the observed associations despite statistical adjustment. Therefore, our findings should be interpreted as associations between preoperative hemoglobin levels and postoperative outcomes rather than evidence of a direct causal relationship.

Conclusion

In conclusion, preoperative anemia was independently associated with postoperative VTE in patients undergoing non-cardiac surgery, with a clear dose-response relationship across anemia severity categories. The association persisted after adjustment for postoperative transfusion and other important clinical factors, suggesting that preoperative hemoglobin is an important marker of thromboembolic risk. Future prospective studies should determine whether correction of anemia or incorporation of hemoglobin into perioperative risk assessment models can improve postoperative outcomes and help individualize thromboprophylaxis strategies.

Abbreviations

ACS: American College of Surgeons

AKI: Acute Kidney Injury

ASA: American Society of Anesthesiologists

CI: Confidence Interval

CPR: Cardiopulmonary Resuscitation

CVA: Cerebrovascular Accident

DVT: Deep Vein Thrombosis

IRB: Institutional Review Board

MI: Myocardial Infarction

NSQIP: National Surgical Quality Improvement Program

OR: Odds Ratio

PE: Pulmonary Embolism

ROR: Return to Operating Room

VTE: Venous Thromboembolism

WHO: World Health Organization

Declarations

Ethics Approval and Consent to Participate

This study was reviewed and approved by the **Cooper University Healthcare Institutional Review Board (IRB# 25–129)**. The study was conducted in accordance with applicable institutional guidelines and regulations and with the ethical principles of the Declaration of Helsinki.

Because this study involved retrospective analysis of existing data and posed minimal risk to participants, the requirement for informed consent was waived by the Cooper University Healthcare Institutional Review Board.

Consent for Publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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Author Contribution

RP and RJ conceived and designed the study. TJ, SK, NK, and TG contributed to the development of the Introduction and Methods sections. KH performed the statistical analyses and contributed to data interpretation. PP, RP, and RJ drafted the Discussion section and interpreted the study findings. All authors critically reviewed the manuscript and approved the final version for publication.

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Data Availability

The data that support the findings of this study were obtained from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database and institutional records from Cooper University Hospital. The data are not publicly available because they contain potentially identifiable patient information and are subject to institutional and ACS NSQIP data use restrictions. De-identified data may be made available from the corresponding author upon reasonable request and with appropriate institutional approvals.

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