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Impact of Preoperative Anemia on Hospitalization, Death, and Overall Survival in Patients With Peripheral Artery Disease Undergoing Endovascular Therapy: A Retrospective Cohort Study in the United States and Canada

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Impact of Preoperative Anemia on Hospitalization, Death, and Overall Survival in Patients With Peripheral Artery Disease Undergoing Endovascular Therapy: A Retrospective Cohort Study in the United States and Canada

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Abstract

Purpose: Preoperative anemia is associated with adverse outcomes after cardiac and noncardiac surgeries, but outcomes after an endovascular peripheral vascular intervention (PVI) are not well established. We aimed to assess the association of preoperative anemia with 30 day death, hospital length of stay (LOS), and overall (long term) survival in patients undergoing an endovascular PVI for peripheral artery disease. **Materials and Methods:** In this retrospective, cohort study in the United States and Canada, we queried the national Vascular Quality Initiative database for all endovascular PVIs performed between 2010 and 2019, and outcomes were correlated with patients' hemoglobin (Hb) levels. Anemia was classified as mild (Hb=10–13 g/dL for men and 10–12 g/dL for women), moderate (Hb=8–9.9 g/dL), and severe (Hb<8 g/dL). **Results:** A total of 79 707 adult patients who met study criteria underwent endovascular PVI. The mean age was 68 years, and 59% of patients were male. Anemia was documented in 38 543 patients (48%) and was mild in 27 435 (71%), moderate in 9783 (25%), and severe in 1325 (4%). The median follow-up duration was 4 years (range, 1.25–5.78 years). On univariate analysis, 30 day mortality, total LOS, and overall survival were significantly associated with the level of preoperative anemia. These associations persisted in the multivariate models. Kaplan-Meier survival analysis demonstrated an association of death with degree of anemia ($p<0.001$). **Conclusion:** The presence and degree of preoperative anemia were independently associated with increased 30 day mortality and LOS and decreased overall survival for patients with peripheral artery disease who had undergone endovascular PVI.

Clinical Impact

The findings from this study have many implications for how to approach vascular surgery in patients with variable hemoglobin levels. Our findings will strengthen our ability to conduct accurate preoperative risk stratification for patients undergoing peripheral vascular interventions. This may also mitigate healthcare expenditures if findings are applied in a way that can lower patient length of postoperative stay while also maintaining quality of care and patient safety. Our results will also serve as guidance for clinical trials, and future prospective trials should evaluate the effect of preoperative optimization of hemoglobin as a potentially modifiable risk factor for outcomes.

Keywords

peripheral vascular interventions, endovascular, peripheral artery disease, preoperative anemia, mortality

Introduction

Peripheral artery disease (PAD) is increasingly recognized as an important cause of cardiovascular morbidity and mortality and is estimated to affect 7% of adults in the United States and more than 230 million people worldwide.[1,2] Recent advances in endovascular therapies have broadened the options for treating PAD while offering a lower-risk alternative to open surgery, especially in patients with

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multiple comorbidities.[3] Endovascular techniques, such as percutaneous transluminal angioplasty, stenting, and atherectomy, have become first-line therapies for most patients with PAD.[4–8]

Preoperative anemia is a common occurrence, affecting 10% to 40% of patients facing surgery.[9–11] Anemia is particularly frequent in patients with PAD, with an estimated prevalence ranging from 47% to 75%.[12,13] This finding could be due to the presence of a chronic disease (ie, anemia of chronic diseases) or the multiple comorbidities usually present in this patient population.[14] Preoperative anemia has been shown to increase hospital length of stay (LOS), cardiac events, hospital costs, and 30 day mortality after various cardiac and noncardiac surgical procedures.[15–17] Although preoperative hemoglobin (Hb) levels are almost always measured before a procedure, few studies have explored the impact of preoperative anemia on outcomes after a peripheral vascular intervention (PVI). Such studies have been limited by small sample sizes,[18–21] inclusion of only specific subgroups (eg, older adults or patients with chronic limb-threatening ischemia[19,22]), and assessment of only cardiac morbidity or mortality, leaving other important outcomes unexplored.[18–21] Furthermore, some studies have failed to stratify the Hb level or the outcomes of interest.[18,23] To address these limitations, a large data set from the Vascular Quality Initiative (VQI) registry was analyzed to evaluate the association of preoperative anemia on postoperative outcomes in patients with PAD who have undergone a percutaneous PVI. We hypothesize that patients with more severe anemia would have worse postoperative outcomes.

Materials and Methods

VQI Database

The VQI is a prospectively validated registry that collects demographic, clinical, procedural, and outcome variables and follow-up data in 14 major vascular modules and includes more than 800 000 vascular procedures performed in the United States and Canada.[24] Each participating center enters consecutive procedures, which are ensured by an annual audit against hospital claims data submitted by each center.[25] Further details about the Society for Vascular Surgery Patient Safety Organization and the VQI are available online.[24,25]

Patients

We analyzed the national VQI module for patients who underwent a PVI between January 1, 2010, and December 30, 2019. Patients with unknown Hb levels and those who underwent concomitant open procedures were excluded from the study. Patients who had the intervention for an aneurysmal disease or unknown indications were also excluded. Anemia was classified as mild (Hb=10–13 g/dL for men and 10–12 g/dL for women), moderate (Hb=8–9.9 g/dL), and severe (Hb$<$8 g/dL) using the World Health Organization definition of anemia.[26]

The present study was reviewed and approved by our institutional review board and conducted in accordance with the Health Insurance Portability and Accountability Act and the prevailing ethical principles governing research.

Variables

Sociodemographic variables collected included sex, age, tobacco use, and race/ethnicity (African American, White, and other). Past medical history included coronary artery disease (CAD), congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), diabetes, hypertension, end-stage renal disease (ESRD), prior carotid intervention, and prior lower-extremity intervention (bypass, endarterectomy, PVI, or amputation). Preoperative variables included American Society of Anesthesiologist (ASA) class, PVI indication, PAD severity, preoperative use of antiplatelets, anticoagulants, antihypertensive medications, and preoperative Hb (most recent Hb measurement prior to intervention). Postoperative variables included target artery dissection or thrombosis, pulmonary complications (pneumonia and need for ventilation), renal complications (new need for dialysis or acute kidney injury defined as an increase in creatinine $>$0.5 mg/dL from baseline), cardiac complications (myocardial infarction, CHF, and dysrhythmia), and access-site hematoma.

End Points

The primary endpoint was 30 day mortality. Secondary endpoints were hospital LOS and overall survival. Overall survival reflects the longest time of survival data available for the patient, with survival days calculated by the VQI registry as the last date of contact (or date of death) for the patient minus the date of the procedure.

Sensitivity Analysis

We compared the demographics, comorbidities, and preoperative variables between the included and excluded patients for our sensitivity analysis. Due to the large sample size in both groups, we used the standardized mean difference to compare the variables. The standardized mean difference compares the difference in means in units of the pooled standard deviation, which is not influenced by sample size.[27] A standardized difference of $>$0.1 denotes a clinically meaningful statistical difference.

Statistical Analysis

Patients were stratified into 4 groups based on Hb level (normal, mild, moderate, and severely anemic). Continuous variables were presented as means and standard deviation or medians and interquartile range, while categorical variables were described with frequency and percentages. Analysis of variance, Kruskal-Wallis, or chi-square tests were used as appropriate to compare the baseline demographics, comorbidities, preoperative variables, and postoperative outcomes stratified by anemia level. Multivariate logistic regression, generalized linear regression, and proportional Cox models were used to evaluate the effect of anemia on the postoperative outcomes of interest. The Kaplan-Meier curve was used to analyze the survival time according to anemia severity. Variables with missing rate of >5% were excluded from the analysis. An unknown category was created for other categorical variables with missing values to account for missingness. Any variable with a p value <0.1 or that was thought to be related to the outcome of interest was included in the multivariate analyses. A p value <0.05 was considered statistically significant. All analyses were performed using R 4.02.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

During the study period, 204 953 PVIs were entered into the VQI registry. After applying the exclusion criteria, 79 707 patients who underwent endovascular PVIs were included in the analysis.

Preoperative Variables

The mean patient age was 68 years (standard deviation=11), and 59% were male (n=46 891). Anemia was documented in 38 543 patients (48%) and was mild in 27 435 (71%), moderate in 9783 (25%), and severe in 1325 (4%). A total of 41 164 patients (52%) had a normal Hb level.

Table 1 shows the baseline demographics, past medical history, and preoperative variables among the different groups. Age and sex were associated with anemia severity. Comorbidities such as CAD, CHF, diabetes, elevated body mass index, and hypertension were associated with the degree of anemia and were more likely to be present in patients with anemia. African American patients, those with ASA class 4 and 5, and those with ESRD had a positive linear trend with anemia severity. White patients and current smokers had a reverse linear trend with anemia severity. Patients with moderate and severe anemia were less likely to be on preoperative antiplatelet medications, statins, and antihypertensive medications than patients with normal Hb.

Most patients had an elective intervention, and patients with urgent or emergent procedure timing tended to have more severe anemia. Claudication was the most common preoperative presenting symptom in this cohort. Patients who presented with acute limb ischemia or tissue loss had a positive linear trend with anemia severity.

Primary Outcome

Thirty-day mortality. The crude 30 day mortality for the study cohort was 2% (n=1538). Table 2 shows results of univariate and multivariate analyses for the main outcomes. On univariate analysis, patients with more severe anemia had a higher odd of dying at 30 days. This association persisted after accounting for all potential confounders on the multivariate analysis. As compared to patients with a normal Hb level, patients with mild anemia had 1.7 times the odds of dying at 30 days (95% confidence interval [CI] 1.5–1.9; p<0.001). The odds ratio (OR) increased to 2.6 (95% CI 2.2–3.0; p<0.001) and to 2.8 (95% CI 2.1–3.6; p<0.001) for the moderate and severe anemia groups, respectively.

Female sex (OR 1.2; p<0.001), ASA class 4 and 5 (OR 2.9; p=0.002), history of CHF (OR 1.8; p<0.001), ESRD (OR 2.1; p<0.004), COPD (OR 1.3; p<0.001), CAD (OR 1.3; p<0.001), and presenting urgently or emergently (OR 2.2; p<0.001) were associated with increased 30 day mortality (Supplementary Table 1). Patients preoperatively maintained on statins, angiotensin-converting enzyme inhibitors, and clopidogrel had a lower 30 day mortality rate.

Secondary Outcomes

Overall survival. The median follow-up duration was 4 years (range 1.25–5.78 years). The hazard of dying during the follow-up period increased with higher anemia severity on the univariate analysis (Table 2). Similarly, this persisted after accounting for potential confounders, where patients with mild anemia had 1.4 times the hazard of dying as compared to patients with a normal Hb level (95% CI 1.4–1.5; p<0.001). The hazard ratio increased to 1.8 (95% CI 1.6–2.0; p<0.001) for the moderate and severe anemia groups. Kaplan-Meier survival curves showed an association of decreased survival with the degree of anemia severity for patients with anemia relative to patients with a normal Hb level (p<0.001; Figure 1).

Factors that were associated with decreased long-term survival included ASA class 4 and 5; history of CAD, CHF, COPD, diabetes, or ESRD; and presenting urgently or emergently. Patients taking aspirin, statin, or clopidogrel were noted to have improved overall survival (Supplementary Table 2).

Table 1. Baseline Characteristics, Comorbidities, and Preoperative Variables Stratified by Anemia Severity.

Variables	Normal hemoglobin (n=41 164)	Mild anemia (n=27 435)	Moderate anemia (n=9783)	Severe anemia (n=1325)	p Value
Baseline characteristics					
Age, years	66±11	70±11	70±12	68±12	<0.001
Male	23 730 (57.6%)	17 309 (63.1%)	5134 (52.5%)	718 (54.2%)	
Female	17 434 (42.4%)	10 126 (36.9%)	4649 (47.5%)	607 (45.8%)	
Body mass index, kg/m^2	28.1±6.1	27.7±6.3	27.6±6.8	27.6±7.2	<0.001
Race					<0.001
African American	4429 (10.8%)	4842 (17.6%)	2256 (23.1%)	366 (27.6%)	
White	35 151 (85.4%)	20 910 (76.2%)	6842 (69.9%)	858 (64.8%)	
Other	1584 (3.9%)	1683 (6.1%)	685 (7.0%)	101 (7.6%)	
Smoking					<0.001
Prior	16 349 (39.7%)	13 107 (47.8%)	4458 (45.6%)	598 (45.1%)	
Current	18 575 (45.1%)	7277 (26.5%)	2269 (23.2%)	308 (23.2%)	
Comorbidities					
Coronary artery disease	11 374 (27.6%)	8976 (32.7%)	3398 (34.7%)	428 (32.3%)	<0.001
Congestive heart failure	4839 (11.8%)	6583 (24.0%)	3179 (32.5%)	423 (31.9%)	<0.001
COPD	10 450 (25.4%)	6920 (25.2%)	2593 (26.5%)	344 (26.0%)	0.081
Diabetes	17 115 (41.6%)	16 685 (60.8%)	6659 (68.1%)	881 (66.5%)	<0.001
End-stage renal disease	962 (2.3%)	3415 (12.4%)	2302 (23.5%)	367 (27.7%)	<0.001
Hypertension	35 318 (85.8%)	25 117 (91.6%)	9046 (92.5%)	1203 (90.8%)	<0.001
Preoperative creatinine, mg/dL	1.0±5.0	1.2±0.6	1.3±0.8	1.4±1.1	<0.001
Prior PCI	8205 (23.3%)	6085 (25.8%)	2076 (24.1%)	240 (19.8%)	<0.001
Prior CEA	3046 (8.7%)	2323 (9.9%)	703 (8.1%)	90 (7.4%)	<0.001
Prior amputation	2827 (6.9%)	4975 (18.2%)	2740 (28.1%)	402 (30.4%)	<0.001
Prior CABG	6407 (18.2%)	6007 (25.5%)	2112 (24.4%)	269 (22.2%)	<0.001
Prior aneurysm	928 (2.3%)	656 (2.4%)	200 (2.0%)	29 (2.2%)	0.248
Prior lower-extremity vascular intervention	19 511 (47.4%)	14 280 (52.1%)	5027 (51.4%)	657 (49.6%)	<0.001
Preoperative statin	28 269 (68.7%)	19 363 (70.6%)	6563 (67.1%)	824 (62.2%)	<0.001
Preoperative ACEi	19 208 (54.7%)	13 184 (56.1%)	4315 (50.0%)	563 (46.6%)	<0.001
Preoperative aspirin	31 137 (75.7%)	20 358 (74.2%)	6951 (71.1%)	910 (68.7%)	<0.001
Preoperative P2Y12 inhibitors	16 768 (40.7%)	11 592 (42.3%)	3969 (40.6%)	489 (36.9%)	<0.001
Preoperative anticoagulant	599 (1.5%)	550 (2.0%)	295 (3.0%)	44 (3.3%)	<0.001
Perioperative variables					
Presenting symptoms					<0.001
Asymptomatic	1380 (3.4%)	880 (3.2%)	272 (2.8%)	44 (3.3%)	
Claudication	24 309 (59.1%)	9304 (33.9%)	1563 (16.0%)	173 (13.1%)	
Acute limb ischemia	3186 (7.7%)	2518 (9.2%)	1208 (12.3%)	189 (14.3%)	
Ischemic rest pain	5387 (13.1%)	3696 (13.5%)	1221 (12.5%)	160 (12.1%)	
Tissue loss	6902 (16.8%)	11 037 (40.2%)	5519 (56.4%)	759 (57.3%)	
Urgency					<0.001
Elective	36 198 (88.0%)	21 809 (79.5%)	6726 (68.8%)	861 (65.1%)	
Urgent/emergent	4948 (12.0%)	5607 (20.5%)	3050 (31.2%)	461 (34.9%)	
ASA class					<0.001
1	782 (1.9%)	340 (1.2%)	92 (0.9%)	24 (1.8%)	
2	10 417 (25.3%)	4770 (17.4%)	1210 (12.4%)	118 (8.9%)	
3	27 453 (66.7%)	18 762 (68.4%)	6413 (65.6%)	826 (62.3%)	
4 and 5	2512 (6.1%)	3563 (13.0%)	2068 (21.1%)	357 (26.9%)	

Data presented as mean ± standard deviation or number (%).

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ASA, American Society of Anesthesiologists; CABG, coronary artery bypass graft; CEA, carotid endarterectomy; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention.

Table 2. Univariate and Multivariate Analyses for Overall Survival, 30 Day Mortality, and Total Length of Hospital Stay Based on Preoperative Anemia Level.

	Overall survival (univariate)			Overall survival (multivariate)		
Predictors	HR	95% CI	p	HR	95% CI	p
Normal hemoglobin	1			1		
Mild anemia	2.24	2.17–2.32	<0.001	1.44	1.39–1.50	<0.001
Moderate anemia	3.51	3.37–3.66	<0.001	1.77	1.69–1.85	<0.001
Severe anemia	3.51	3.21–3.85	<0.001	1.79	1.63–1.97	<0.001
	30 Day death (univariate)			30 Day death (multivariate)		
Predictors	OR	95% CI	p	OR	95% CI	p
Normal hemoglobin	1			1		
Mild anemia	2.98	2.61–3.41	<0.001	1.68	1.45–1.94	<0.001
Moderate anemia	6.63	5.76–7.64	<0.001	2.57	2.20–3.01	<0.001
Severe anemia	7.92	6.12–10.1	<0.001	2.77	2.10–3.62	<0.001
	Total LOS (univariate)			Total LOS (multivariate)		
Predictors	IRR	95% CI	p	IRR	95% CI	p
Normal hemoglobin	1			1		
Mild anemia	2.01	1.96–2.07	<0.001	1.41	1.37–1.44	<0.001
Moderate anemia	4.38	4.22–4.55	<0.001	2.49	2.40–2.59	<0.001
Severe anemia	6.11	5.58–6.70	<0.001	3.48	3.20–3.79	<0.001

Abbreviations: CI, confidence interval; HR, hazard ratio; IRR, incidence risk ratio; LOS, length of stay; OR, odds ratio.

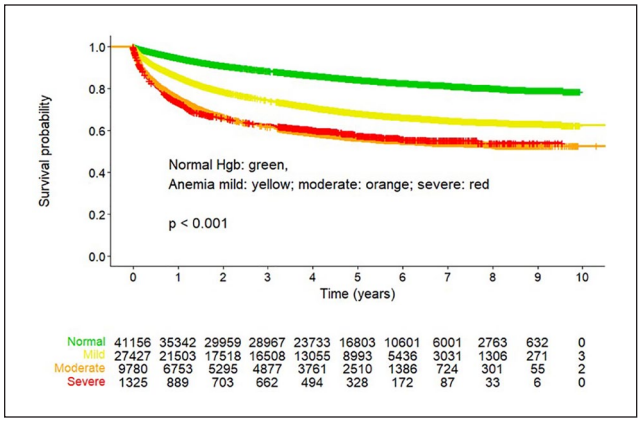

Figure 1. Kaplan-Meier curves comparing survival time stratified by anemia severity. Hgb, hemoglobin.

Total LOS. The median total LOS was 1 day (interquartile range 0–4). The risk of staying longer in the hospital increased with higher anemia severity. This association persisted on the multivariate analysis; patients with mild anemia had 1.7 times the odds of staying longer in the hospital relative to patients with a normal Hb level (95% CI 1.6–1.7; p<0.001). This increased to 3.1 (95% CI 3.0–3.2; p<0.001) and to 5.0 (95% CI 4.5–5.5; p<0.001) for the moderate and severe anemia groups, respectively.

Factors associated with an increased LOS included higher ASA classes; history of CAD, COPD, or hypertension; prior coronary artery bypass grafting or amputation; and urgent/emergent presentation (Supplementary Table 3).

Sensitivity Analysis

Patients in the excluded sample were more likely to be asymptomatic or have lower preoperative ASA class scores (Supplementary Table 4). No clinically meaningful statistical differences were observed when comparing the baseline characteristics, comorbidities, or other preoperative variables between the included and excluded patients.

Discussion

Using a large multicenter database looking at patients with PAD undergoing PVIs, this study documented a crude 30 day mortality of 2%. In addition, this analysis showed that preoperative anemia is independently associated with increased 30 day mortality and LOS and decreased overall survival, with higher anemia severity correlating with worse outcomes. The prevalence of anemia in our cohort was 48%, which falls within the range of what has been reported in other vascular surgery studies focusing on PAD (42%–65%).[18,19,23]

These results concur with other studies that have evaluated the impact of preoperative anemia on postoperative outcomes in cardiac, orthopedic, gastrointestinal, and other noncardiac surgeries.[14–17,28,29] In vascular surgery, some published studies have investigated the impact of preoperative anemia on postoperative outcomes, and many of them have included patients who received different types of vascular procedures (open and endovascular abdominal aortic aneurysm repair, carotid endarterectomies, open aortic repair, and distal bypasses).[30–33]

Toor et al[19] retrospectively evaluated 101 patients with advanced PAD who underwent nonemergent percutaneous transluminal angioplasty and found that a low preprocedural Hb level was associated with increased adverse peripheral vascular outcomes (composite of death, amputation, or target-lesion revascularization) (OR 4.2; 95% CI 1.6–11.2; p=0.004). Oshin and Torella[18] studied 360 patients who underwent an open peripheral arterial surgery between 2004 and 2011 under the care of a single specialist and showed that a low preoperative Hb level was associated with major adverse cardiac events (OR 1.4; CI 1.13–1.7; p=0.002, for every 1 g/dL drop below the mean) and death (OR 1.5; CI 1.14–1.86; p=0.002, for every 1 g/dL drop below the mean). These findings were in accordance with another study by Jaffery et al[34] who looked at 346 patients undergoing PVIs and demonstrated that a preoperative Hb drop of every 1 g/dL was associated with increased 9 month all-cause mortality (OR 1.6; 95% CI 1.2–2.0; p=0.001). Bodewes et al[22] performed a retrospective review of the National Surgical Quality Improvement Program registry and looked at older adult patients with chronic limb-threatening ischemia who underwent a nonemergent infrainguinal bypass surgery. They showed an inverse association between preoperative hematocrit levels and 30 day mortality, major adverse cardiac events, and unplanned returns to the operating room, with the highest event rates occurring in the most anemic patients. These findings were mirrored by another retrospective study of 403 patients with chronic limb-threatening ischemia who had open or endovascular surgery between 2005 and 2013, showing that preoperative anemia (defined as Hb$<$10 mg/dL) is a risk factor for immediate and long-term mortality (hazard ratio 2.5; 95% CI 1.8–3.4; p$<$0.001).[20] Finally, a study by Ambulgekar et al[23] evaluated the outcomes of patients with anemia who had percutaneous PVIs and showed that preoperative anemia was associated with greater likelihood of major cardiovascular events, amputation, and any adverse outcome.

The current study is the largest analysis to date on the association of preoperative anemia with postoperative outcomes after percutaneous PVIs in PAD patients. Findings of this investigation are consistent with the aforementioned studies in showing that preoperative anemia is an independent predictor of worse postoperative outcomes. However, in this study, PAD patients were not restricted to a particular disease severity or age group; rather, they were stratified based on urgency. Only percutaneous PVIs were included to limit the potential confounding effect of intraoperative transfusions during an open surgery. In addition, short-term outcomes and long-term survival with a median follow-up of 4 years, the longest to date in the literature, were analyzed. The large size of the study cohort along with the comprehensive data collected by the VQI reinforces the granularity of the results and limits the number of known risk factors that could confound the effect of anemia on the outcomes.

The overall 30 day mortality in this study was 2% and was significantly higher in patients with more severe anemia (6% for the severely anemic, 5% for the moderately anemic, and 2% for the mildly anemic) than in patients with a normal Hb level (0.8%; p$<$0.001). Oshin and Torella[18] reported a 30 day mortality of 5% where lower Hb levels were associated with higher mortality rates. Velescu et al[20] reported in-hospital and 30 day mortality of 8% in patients with anemia. The higher 30 day mortality rates reported in these studies might be explained by the inclusion of patients undergoing open procedures, which are associated with higher mortality rates than endovascular procedures for PAD treatment.[35]

This investigation suggests that even patients with mild anemia have a significantly increased risk of longer LOS and short-term as well as long-term mortality. These findings, coupled with the fact that most percutaneous PVIs performed for PAD are elective (87% in this study), should lead to careful assessment of patients with PAD and anemia to seek possible reversible causes (eg, iron deficiency or malnutrition) and, if time permits, optimization of the patient's Hb level before a procedure. However, many patients presenting with advanced PAD (ie, chronic limb-threatening ischemia or acute limb ischemia) cannot wait for the time required to assess and correct anemia. In these instances, using preoperative anemia as a risk-stratification tool may guide vascular interventionists in their procedural selection and patient/family counseling. Future studies are needed to specifically address whether anemia correction leads to improvement in outcomes in patients undergoing PVIs and, if so, which methods of anemia correction are most beneficial.

Anemia causes tissue hypoxia due to impaired oxygen delivery.[36] As a physiologic compensatory mechanism to improve oxygen extraction, anemia causes systemic arterial vasodilation and a subsequent decrease in systemic vascular resistance.[36] This drop in resistance stimulates the sympathetic nervous system, which leads to an increase in the heart rate and cardiac output.[37] Impaired oxygen delivery along with this sympathetic activation can compromise coronary blood flow leading to myocardial ischemia.[38,39] Another outcome of these changes is left ventricular hypertrophy and accompanying dysfunction,[40] both of which

increase cardiovascular mortality.[39,41] These changes are especially important in patients with atherosclerotic occlusive disease, an older population with an overall CAD and CHF prevalence of 30% and 20%, respectively. Up to 71% of patients with PAD have subclinical CAD.[42,43] The presence of CAD and cardiac dysfunction further limits the compensatory capacity of the heart and compounds the negative effects of anemia.

Anemia can be the result of iron deficiency, malnutrition, bone marrow depression, and systemic inflammation due to PAD, and it is a common comorbid condition in patients with diabetes and renal dysfunction; all these conditions can alter life expectancy as well.[39,41] In this study, the analyses were adjusted for all the available preoperative variables to limit confounding in the multivariate analyses. However, further studies are needed to determine whether anemia is the causative factor for increased mortality or a reflection of the frailty and comorbidities often present in the PAD population.

Preoperative, intraoperative, and postoperative blood transfusions for correcting anemia should be limited, as they have been associated with postoperative complications, for example, transfusion-associated lung injury, cardiac events, infections, and increased mortality.[44–46] The United States Food and Drug Administration has recommended the use of iron, folic acid, vitamin B12, and erythropoietin a month or 2 before elective procedures to promote erythropoiesis instead of blood transfusions.[47] However, erythropoiesis-stimulating agents can increase the risk of thrombotic cardiovascular complications, especially in patients with ESRD, which limits their use in patients undergoing a surgery for PAD. Newer agents, such as third-generation intravenous iron compounds, carboxymaltose, and hypoxia-inducible factor prolyl-hydroxylase inhibitors, are currently under investigation and may hold promise for future application.[48–50]

Limitations

This study has several limitations. First, its retrospective methodology allows determination of association, not causation. Second, more than half of the initial cohort was excluded, owing mostly to missing Hb levels. The VQI stopped collecting the preoperative Hb variable beginning in 2017. Based on the results of this study, it may be worthwhile to consider adding back the preoperative Hb variable to the VQI. Third, this analysis was limited by the absence of information about other potential confounding variables such as the cause of preoperative anemia and its chronicity as well as the requirement for preoperative, intraoperative, and postoperative blood transfusion requirements, which may have influenced the outcomes. However, this study evaluated patients with low risk of intraoperative and postoperative blood loss because of the less invasive nature of PVIs. In addition, some studies have shown anemia's harmful effect despite accounting for transfusion requirements.[23,51] Nonetheless, future studies should address this shortcoming.

Conclusion

This analysis demonstrated that anemia is common in patients with PAD who require PVI and that the presence and degree of preoperative anemia are independent predictors of 30 day mortality, LOS, and overall survival. The presence and degree of anemia should be components of preoperative risk stratification for patients with PAD undergoing PVIs. Anemia should be a listed variable in all reports detailing outcomes of PVI. Future prospective trials should evaluate the effect of preoperative optimization of Hb as a potentially modifiable risk factor for outcomes.

Authors' Note

Previous Presentation: This study was presented as an oral presentation at the 45th Midwestern Vascular Surgical Society Meeting, Chicago, IL, September 9–11, 2021.

Declaration of Conflicting Interests

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Supplemental Material

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