

Anemia Increases Mortality After Open or Endovascular Treatment in Patients with Critical Limb Ischemia: A Retrospective Analysis

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WHAT THIS STUDY ADDS

Anemia is a clinically important and frequent finding in surgical patients. Higher rates of morbidity and mortality have been reported among anemic patients undergoing cardiac surgery. The effects of the pre-operative hemoglobin value in a population undergoing vascular surgery are less clear. This study evaluates the relationship between pre-operative anemia and mortality in patients undergoing surgery for critical limb ischemia. The results indicate that pre-operative anemia is a risk factor for both immediate and long-term survival among patients with critical limb ischemia undergoing revascularization (specially when hemoglobin <10 g/dL). Treatment of anemia before surgery for critical limb ischemia is therefore suggested.

Objectives: Pre-operative anemia has been associated with increased post-operative morbidity and mortality in elective cardiac surgery, but its association with post-operative mortality after open or endovascular surgery for critical limb ischemia (CLI) is not well established. The aim of this study was to evaluate the relationship between pre-operative anemia and mortality in surgery for CLI.

Materials and methods: A retrospective study of 403 consecutive patients (mean age = 73; 73% male) undergoing open ($n = 191$, 47%) or endovascular ($n = 212$, 53%) surgery for CLI between 2005 and 2013 was performed. Neither redo revascularization procedures (ipsilateral or contralateral) nor acute limb ischemia patients were included as new cases.

Results: The best cut off (receiver operating characteristic curve) that related pre-operative hemoglobin to mortality was 10 g/dL. The immediate (in hospital or < 30 days) mortality rate was 8% (32 patients), with no significant differences between open and endovascular surgery. Patients with a pre-operative hemoglobin <10 g/dL had a higher immediate mortality rate (17.7% vs. 5.1%), with a risk (OR), adjusted by age and prior myocardial infarction, of 3.9, 95% CI 1.8–8.4 ($p = 0.001$). The mean follow up of the cohort was 30 months (97% complete). Similarly, a pre-operative hemoglobin <10 g/dL was significantly associated with a lower 1 year (55 vs. 83%) and 5 year survival rate (21 vs. 53%) with an associated risk (HR) of 2.5, 95% CI 1.8–3.4 ($p < 0.001$) adjusted by age, previous myocardial infarction, chronic renal failure, stroke, diabetes mellitus, and ischemic ulcers.

Conclusions: Pre-operative anemia is a risk factor for immediate and late mortality among patients with CLI, regardless of other risk factors and the type of revascularization technique. Prospective studies are needed to evaluate the potential effect of its treatment on survival outcomes.

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INTRODUCTION

Anemia is a clinically important and frequent finding in surgical patients.¹ In patients undergoing cardiac surgery the impact of the pre-operative hemoglobin value has been

well documented. Higher rates of morbidity, early^{2–6} and late mortality² have been reported among anemic patients, especially in elderly patients. Although much less reported, anemia has also been shown to increase the risk of cardiac events and mortality in non-cardiac surgical patients,^{7–10} including those submitted to vascular interventions.^{11–15} However, the available evidence regarding vascular patients is scarce and limited by small samples studies, failure to adjust for major confounders and inclusion of a mix of different vascular procedures (i.e. carotid surgery, aortic aneurysm repair, and peripheral bypass). Therefore, the effects on outcome of pre-operative hemoglobin values in populations undergoing vascular surgery remain unclear.

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Table 1. Baseline characteristics and type of surgery according to pre-operative hemoglobin.

	Total (<i>n</i> = 403)	Hb < 10 mg/dL (<i>n</i> = 90)	Hb ≥ 10 mg/dL (<i>n</i> = 313)	<i>p</i>
Sex				0.686
Male	295 (73%)	64 (71%)	231 (74%)	
Female	108 (27%)	26 (29%)	82 (26%)	
Age (mean ± SD)	73 ± 10	75 ± 10	72 ± 10	0.053
Smoking				0.112
Never smokers	167 (41%)	29 (32%)	138 (44%)	
Former smokers	154 (38%)	41 (46%)	113 (36%)	
Current smokers	82 (20%)	20 (22%)	62 (20%)	
Hypertension	323 (80%)	79 (88%)	244 (72%)	0.050
Diabetes mellitus	259 (64%)	61 (68%)	198 (63%)	0.456
Hypercholesterolemia	245 (61%)	62 (67%)	183 (59%)	0.086
Renal disease (GFR <60 mL/min)	97 (24%)	33 (37%)	64 (21%)	0.002
Coronary heart disease	110 (27%)	33 (37%)	77 (25%)	0.031
Previous myocardial infarction	56 (14%)	13 (26%)	43 (14%)	0.863
Previous stroke	48 (12%)	12 (13%)	36 (12%)	0.712
Critical limb ischemia				0.064
Rest pain	151 (37%)	26 (29%)	125 (40%)	
Ischemic ulcer	252 (63%)	64 (71%)	188 (60%)	
Type of revascularization				0.231
Open surgery	212 (53%)	48 (53%)	143 (46%)	
Endovascular surgery	191 (47%)	42 (47%)	170 (54%)	
Ankle-brachial index (AB)	0.35 ± 11	0.34 ± 11	0.36 ± 11	0.546

The Mann–Whitney *U* test was used for comparing age and ABI, and the chi-square test was used for other variables.

Finding risk factors associated with increased peri- and post-operative events is very important in decision making and pre-operative planning. The aim of this study was to evaluate the relationship between pre-operative anemia and mortality in patients undergoing surgery (open or endovascular) for critical limb ischemia (CLI).

MATERIALS AND METHODS

Study design and population

Patients consecutively submitted to open or endovascular surgery for critical limb ischemia in the Vascular Surgery Department of the Hospital del Mar (Barcelona, Spain) between January 2005 and December 2013 were retrospectively reviewed from an institutional computerized registry. The sample included 403 patients (mean age 73 years; 73% male) with resting foot pain (*n* = 151; 37.5%) or ischemic ulcers (*n* = 252; 62.5%).

Data collected at baseline included age, sex, cardiovascular risk factors, and ankle–brachial index (ABI). Patients were classified as smokers (current or ex < 1 year), former smokers (quit 1 ≥ year), or never smokers. Hypertension and diabetes were considered if previously diagnosed by a physician or under treatment. Dyslipidemia was defined by medical history or when low-density lipoprotein (LDL) cholesterol > 200 mg/dL. Chronic renal failure was considered when the glomerular filtration rate (GFR) was

<60 mL/min. The pre-operative hemoglobin was defined as the last measurement obtained before surgery. Pre-operative anemia was defined according to the World Health Organization criteria for this disease (hemoglobin <13 g/dL in men and <12 g/dL in women).¹⁶ Coronary heart disease, including history of angina, myocardial infarction, and previous cerebrovascular disease, including ischemic stroke and transient ischemic attack, were reviewed using hospital or primary care records. Trained technicians measured the ABI with a continuous Doppler device (8 MHz probe). Mean ABI was 0.35 among 323 patients, while the remaining 80 (20%) had non-evaluable pressure recordings suggesting arterial calcification. Characteristics of patients analyzed at baseline are shown in Table 1.

One hundred and ninety-one patients (47%) underwent open surgery while 212 (53%) underwent endovascular treatment. In both cases several different techniques were used (Table 2). The most frequent revascularization procedures were iliac (13%) and femoral (35%) primary stenting and infrainguinal bypass (31%). Patients submitted to hybrid procedures were considered within the open surgery group.

Patients received single antiplatelet therapy after open surgery and double antiplatelet therapy for 4 months after endovascular treatment (single therapy thereafter).

Table 2. Revascularization procedures performed in the study group (*n* = 403).

	Iliac	Common femoral	Femoropopliteal	Below the knee	Total
Open surgery	27 (14%)	39 (20%)	57 (30%)	68 (36%)	191
Endovascular	53 (25%)	0	140 (66%)	19 (9%)	212

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