From the Society for Clinical Vascular Surgery

Preoperative anemia is associated with mortality after carotid endarterectomy in symptomatic patients

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ABSTRACT

Objective: Preoperative anemia and blood transfusions are associated with worse outcomes after surgery. However, the impact of preoperative anemia and transfusions on outcomes after carotid endarterectomy (CEA) is unknown.

Methods: CEA patients from 2011 to 2015 in the American College of Surgeons National Surgical Quality Improvement Program Targeted Vascular module were compared by the presence of preoperative anemia (hematocrit <36%) after stratification by symptom status. Multivariable analysis accounted for differences in baseline characteristics. We included an interaction term in our multivariable model to assess whether the effect of anemia differed significantly between patients who received a perioperative transfusion and those who did not, with 30-day mortality as our primary outcome.

Results: Of 16,068 patients, 6734 (42%) were symptomatic, of whom 1500 (22%) had anemia. Of the 9334 asymptomatic patients, 1935 (21%) had anemia. Both symptomatic and asymptomatic anemic patients were more likely to be transfused perioperatively compared with nonanemic patients, with 7.0% vs 0.4%, and 5.8% vs 0.7% (both $P < .001$). Among symptomatic patients, those with anemia compared with those without had a higher rate of 30-day mortality (2.5% vs 0.7%; $P < .001$). After adjustment, anemic symptomatic patients had a higher 30-day mortality risk (odds ratio [OR], 3.1; 95% confidence interval [CI], 1.9-5.0; $P < .001$) compared with nonanemic symptomatic patients. In addition, in symptomatic patients, we found a significant interaction between anemia and perioperative transfusion on the outcome of 30-day mortality ($P = .004$), with a higher risk in perioperatively transfused symptomatic patients with anemia (OR, 7.8; 95% CI, 3.4-18.0; $P < .001$) than in symptomatic patients with anemia who did not receive a perioperative transfusion (OR, 2.3; 95% CI, 1.4-3.9; $P = .002$). In asymptomatic patients, anemic and nonanemic patients had comparable 30-day mortality rates (0.9% vs 0.6%; $P = .2$). After adjustment, anemia was not associated with 30-day mortality in asymptomatic patients (OR, 1.0; 95% CI, 0.5-2.0; $P = .9$), nor did we identify an interaction between anemia and perioperative transfusion in asymptomatic patients ($P = .1$). Patients who received a preoperative transfusion had a higher 30-day mortality rate than anemic patients not receiving preoperative transfusion in both symptomatic (n = 31, 9.7% vs 2.5%; $P = .04$) and asymptomatic patients (n = 21, 9.5% vs 0.9%; $P = .02$).

Conclusions: Preoperative anemia is a risk factor for 30-day mortality after CEA in symptomatic patients but not in asymptomatic patients. These results should be factored into the selection of symptomatic patients for CEA and dissuade treatment of asymptomatic patients scheduled for CEA who need a preoperative transfusion. (J Vasc Surg 2017;■:1-8.)

More than one in three patients undergoing surgery have anemia,[1] and the prevalence of anemia is projected to increase because of the exponential growth of the elderly population, of whom nearly half suffer from anemia.[2-4] This is cause for concern as anemia is associated with increased morbidity and mortality after surgery.[1,5] Because the goal of carotid endarterectomy (CEA) is the prevention of future stroke and death, anemia has the potential to diminish this intended benefit by increasing the risk of postoperative death and stroke. However, the impact of preoperative anemia on outcomes after CEA in symptomatic and asymptomatic patients is unknown.

In addition to anemia, the use of blood transfusions for the treatment of anemia has also been shown to increase morbidity and mortality for patients undergoing

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cardiac and noncardiac surgery.[6,7] These findings led to the introduction of restrictive blood transfusion protocols using a lower hemoglobin threshold for transfusion in clinical practice.[8] However, several recent studies found no difference between restrictive and liberal blood transfusion protocols in early or late survival after orthopedic and cardiac surgery.[8-10] As such, we hypothesized that it is not the combination of anemia with transfusions that results in worse outcomes after surgery but that anemia itself is an independent risk factor for perioperative complications. However, the impact of anemia, blood transfusions, and their interaction on outcomes after CEA has not been evaluated.[11-13]

Thus, our aim was to compare 30-day adverse event rates, in particular mortality, stroke, and myocardial infarction (MI), after CEA between patients with and without preoperative anemia. Subsequently, we assessed effect modification between anemia and perioperative transfusion on 30-day adverse events.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis of the prospectively collected data of the Targeted Vascular module of the National Surgical Quality Improvement Program registry
- **Take Home Message:** Preoperative anemia, present in >20% of 16,068 patients undergoing carotid endarterectomy, led to higher rates of 30-day mortality (2.5% vs 0.7%) in symptomatic patients and a higher risk after adjustment (odds ratio, 3.1). Preoperative anemia was not associated with elevated mortality in asymptomatic patients.
- **Recommendation:** This study suggests that preoperative anemia carries a higher mortality risk in symptomatic patients who undergo carotid endarterectomy.

METHODS

Registry. We used the Targeted Vascular module of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) registry for this analysis. The goal of the ACS NSQIP is to improve the quality of surgical care by prospectively recording 30-day postoperative outcomes in a national clinical registry. The Targeted Vascular module is a subset of ACS NSQIP that captures patients undergoing certain vascular procedures to include additional procedure-related clinical variables and disease-specific outcomes, chosen by vascular surgeons. Trained clinical reviewers categorize procedures using *Current Procedural Terminology* codes and collect data on predefined variables from medical charts, operative case logs, and, if necessary, letters or phone calls to patients to ensure complete 30-day follow-up. The reliability of ACS NSQIP data collection has been validated previously.[14,15] More information on the ACS NSQIP registry is available at www.facs.org/quality-programs/acs-nsqip.

The Beth Israel Deaconess Medical Center Institutional Review Board approved this project and waived the need for informed consent for the use of the deidentified data in the ACS NSQIP.

Patient cohort. We included all patients (N = 18,045) who underwent CEA from 2011 to 2015. We excluded patients undergoing CEA with concomitant cardiac surgery (n = 22 [0.1%]), emergency cases (n = 459 [2.5%]), those missing preoperative hematocrit (HCT) values (n = 654 [3.6%]), patients with unknown preoperative symptom status (n = 346 [1.9%]), and patients with a reported occlusion of the ipsilateral internal carotid artery (n = 196 [1.1%]). We additionally excluded from our main analysis all patients who received a preoperative blood transfusion (ie, in the 72 hours before surgery; n = 52 [0.3%]), in part because of the unreliability of the preoperative HCT value as HCT was measured on or after the day of the preoperative transfusion in the majority of these patients (n = 43 [83%]). This resulted in a study sample of 16,068 patients.

Variables. Our main exposure variable was the presence of preoperative anemia, which we defined as an HCT level of <36% of blood volume.[16,17] The last HCT measurement before the index procedure is recorded as the preoperative HCT level in the ACS NSQIP, which was obtained within 1 month before surgery in 95% of all patients, with a median of 3 days before surgery for anemic patients (interquartile range [IQR], 0-8 days) and 5 days before surgery for nonanemic patients (IQR, 1-9 days). The ACS NSQIP Targeted Vascular module defined symptomatic patients as having an ipsilateral neurologic event preceding the intervention (ie, stroke, transient ischemic attack, or amaurosis fugax). We defined impaired kidney function as an estimated glomerular filtration rate <60 mL/min/1.73 m^2 based on preoperative creatinine values, calculated by the Cockcroft-Gault equation.[18] The ACS NSQIP defined perioperative transfusions as at least one unit of packed red blood cells given during surgery or within 72 hours postoperatively, which included blood transfused to patients collected by a cell saver.

Our primary end point was 30-day mortality. Secondary end points were 30-day ipsilateral stroke, hereafter referred to as 30-day stroke, and 30-day MI. Outcomes were collected for 30 days after the index procedure for all patients, as defined by the NSQIP.

The definition of stroke included any ipsilateral motor, sensory, or cognitive dysfunction that persisted for ≥24 hours or radiologic evidence of cerebral infarction. MI was recorded when electrocardiographic changes were indicative of an acute MI (ie, new >1-mm ST