Perioperative management with antiplatelet and statin medication is associated with reduced mortality following vascular surgery

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Objective: **Many patients undergoing vascular surgical procedures are not on appropriate medical therapy. This study sought to examine the variation and impact of antiplatelet (AP) and statin therapy on early and late mortality in patients undergoing vascular surgery in our region.**

Methods: **We studied all patients (n = 14,489) undergoing elective carotid endarterectomy (n = 6978), carotid stenting (n = 524), and suprainguinal (n = 763) and infrainguinal bypass (n = 3053), as well as patients with known coronary risk factors undergoing open (n = 1044) and endovascular (n = 2127) abdominal aortic aneurysm repair from 2005 to 2012 in the Vascular Study Group of New England. Optimal medical management was defined as treatment with both AP and statin agents, preoperatively and at discharge. We analyzed temporal, procedural, and center variation of medication use. Multivariable analyses were used to determine the adjusted impact of AP and statin therapy on 30-day mortality and 5-year survival.**

Results: **Optimal medical management improved over the study interval (55% in 2005 to 68% in 2012; *P* trend < .01) with carotid interventions having the highest rates of optimal medications use (carotid artery stenting, 78%; carotid endarterectomy, 74%) and abdominal aortic aneurysm repair in patients with known cardiac risk factors having the lowest (open, 57%; endovascular aneurysm repair, 56%). Optimal medication use varied by center as well (range, 40%-86%). Preoperative AP and statin use was associated with reduced 30-day mortality (odds ratio, 0.76; 95% confidence interval [CI], 0.5-1.05; *P* = .09). AP and statin prescription at discharge was additive in survival benefit with improved 5-year survival (hazard ratio, 0.5; 95% CI, 0.4-0.7; *P* < .01) that was consistent across procedure types. Patients prescribed AP and statin at discharge had 5-year survival of 79% (95% CI, 77%-81%) compared with only 61% (95% CI, 52%-68%; *P* < .001) for patients on neither medication.**

Conclusions: **AP and statin therapy preoperatively and at discharge was associated with reduced 30-day mortality and an absolute 18% improved 5-year survival after vascular surgery. However, one-third of patients are suboptimally managed in real world practice. This demonstrates an opportunity for quality improvement that can substantially improve survival after vascular surgery. (J Vasc Surg 2014;59:1615-21.)**

Peripheral arterial disease (PAD) and abdominal aortic aneurysms (AAAs) are prevalent conditions encountered by vascular surgeons with a high rate of associated cardiovascular disease.[1,2] Only 8% of patients undergoing major vascular surgical procedures have nondiseased coronary arteries.[3] This results in a high incidence of clinical coronary and cerebrovascular disease among those with PAD and AAA.[1,4] Patients with AAA have a two-fold higher risk of heart attack and 1.8-fold higher risk of stroke compared with population-based controls,[5] and approximately 75% of those with PAD will ultimately die from cardiovascular causes.[1,6]

Despite their high prevalence of cardiac disease, many patients undergoing vascular surgery are not prescribed appropriate cardiovascular medications, including antiplatelet (AP) medications (aspirin or clopidogrel) and HMG-CoA reductase inhibitors (statins). Of all PAD patients, 40% to 60% are not on AP agents, and 40% to 70% are not on statins.[7,8] This is correlated with increased risk of mortality, even in those with no known associated coronary artery disease (CAD).[8]

The variation in optimal medication management among patients undergoing vascular surgery in real world practice has not been described. Further, the benefit of optimal medication utilization is not known in this patient subset. The purpose of this study was to define the variation in perioperative medication usage among patients

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undergoing vascular surgery in New England. We also analyzed the effect of optimal medication utilization on postoperative survival.

METHODS

Subjects and database. This is a retrospective analysis of data collected prospectively by the Vascular Study Group of New England (VSGNE), a regional cooperative quality improvement initiative developed in 2002 to study regional outcomes in vascular surgery.[9] Of note, registry data are compared with hospital claims in annual audits, and missing cases are retrieved to yield a >99% complete capture rate for all tracked procedures.[9] Mortality data is supplemented by semiannual matching of registry data with the Social Security Death Index (SSDI). Data from 2003 and 2004 was excluded since discharge statin use was not tracked until 2005. We selected all patients from 2005 to 2012 undergoing their first time interventions in the VSGNE for carotid endarterectomy (CEA), carotid artery stenting (CAS), infrainguinal and suprainguinal arterial bypass, and AAA repair (open [oAAA] or endovascular [EVAR]). This yielded our initial cohort of 17,806 patients. These patients were selected because multiple guidelines support AP and statin use for cerebrovascular disease and symptomatic PAD.[1,6,10-12] Patients undergoing AAA repair were only included if they had known coronary risk factors that support both aspirin and statin use,[13] including a history of CAD, hypertension, positive stress test, prior coronary revascularization, a prior arterial bypass or peripheral intervention, or prior carotid revascularization. Only 366 (10%) of all eligible AAA repairs were excluded. Of note, these excluded patients with AAA had similar perioperative mortality, but slightly better overall survival than the remaining AAA patients (78% vs 71% at 5 years). All cases were elective; urgent or emergent cases were excluded (2263 emergent and 681 urgent). These exclusion criteria were designed to provide a cohort of patients with the potential to be placed on AP and statin medications before elective surgery. Finally, patients were removed from analysis for missing preoperative medication data (n = 5). This resulted in 14,489 patients with data available for 30-day analysis (Fig 1). Our 5-year survival analysis was based on the hypothesis that survival may be affected by medications prescribed at discharge. Therefore, we excluded patients from the 5-year survival analysis if they died in-hospital postoperatively (n = 111) or had missing discharge medication data (n = 629). This left 13,749 patients for 5-year survival analysis (Fig 1).

Statin use was defined as being on any type of statin medication at any dose. Patients were considered on AP medication if they were on aspirin (any dose) or any P2Y12a antagonist (commonly clopidogrel). Preoperative medication use was defined as taking the medication within 36 hours of surgery. Patients classified as being intolerant to AP and statin were considered as not taking these medications (only four patients were intolerant to any AP, and 181 were intolerant to statins). Patients were not assessed for medication adherence at any point, and no serological tests were done on drug efficacy, lipid levels, or other biochemical markers.

Long-term survival was determined from the VSGNE database and by matching patient information with the SSDI. There is no information on any patient's cause of death, only the time from the procedure until their death. Patients not in the SSDI or not having a hospital record of dying were considered alive with survival days ending at the time of data harvest (December 2012). Definitions of medical comorbidities in the VSGNE cohort have been previously published.[14]

Data collection and statistical analysis. Physicians, nurses, or clinical data abstractors entered data prospectively on clinical and demographic variables. Research analysts were blinded to patient, surgeon, and hospital identity. The Committee for the Protection of Human Subjects at Dartmouth Medical School has approved the use of deidentified data from VSGNE for research purposes.

Optimal medical management was defined as AP and statin use preoperatively and at discharge. Our primary outcomes were 30-day death and 5-year survival. Patients were stratified by their medication utilization (none, AP only, statin only, or both). To study 30-day death, preoperative variables were compared using χ^2 for categorical variables with Fisher exact correction if event rates were low. A two-sample *t*-test or Wilcoxon rank sum test was used to compare normal or non-normal continuous data respectively. Variables with a *P* value of <0.1 were included in a backwards stepwise logistic regression analysis to identify factors associated with 30-day death. For survival analysis, univariate comparisons were made with log-rank or Cox proportional hazards for categorical and continuous variable respectively starting at 30 days to exclude events within 30 days. Variables of clinical significance and those with a *P* value of <0.1 by univariate survival analysis were included in a backwards stepwise multivariable Cox proportional hazards model to identify significant predictors of long-term mortality. Variables for both logistic and Cox models were removed using the likelihood ratio test. Continuous variables with nonlinear risk were categorized for analysis. Age was categorized by quartiles. Probability values of <0.05 were considered significant. Analyses were done using Stata release 11 (Stata Corp, College Station, Tex).

RESULTS

Patient population and medication variation. From 2005 to 2012, a total of 14,489 patients underwent their first elective procedure in the VSGNE, of which, 52% were for carotid interventions, 26% arterial bypass, and 22% AAA repair (Fig 2). Patients on average were 70 years of age (standard deviation, 9.9) and male (66%). Prevalent comorbidities included hypertension (89%) and history of tobacco use (84%). Less common comorbidities included; diabetes (32%), CAD (33%), chronic obstructive pulmonary disease (COPD; 26%), and congestive heart failure (CHF; 10%; Table I).

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