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## Preoperative antiplatelet and statin treatment was not associated with reduced myocardial infarction after high-risk vascular operations in the Vascular Quality Initiative

Randall R. De Martino, MD, MS<sup>a</sup>, Adam W. Beck, MD<sup>b</sup>, Andrew W. Hoel, MD<sup>c</sup>, John W. Hallett, MD<sup>d</sup>, Shipra Arya, MD<sup>e</sup>, Gilbert R. Upchurch Jr, MD<sup>f</sup>, Jack L. Cronenwett, MD<sup>g</sup>, and Philip P. Goodney, MD, MS<sup>g</sup> for the Vascular Quality Initiative

<sup>a</sup>Division of Vascular and Endovascular Surgery, Mayo Clinic, Rochester

<sup>b</sup>Division of Vascular Surgery & Endovascular Therapy, University of Florida College of Medicine, Gainesville

<sup>c</sup>Division of Vascular Surgery, Northwestern University Feinberg School of Medicine, Chicago

<sup>d</sup>Roper Vascular Care, Roper St. Francis Heart & Vascular Center, Charleston

<sup>e</sup>Division of Vascular Surgery and Endovascular Therapy, Emory University, Atlanta

<sup>f</sup>Division of Vascular and Endovascular Surgery, University of Virginia, Charlottesville

<sup>g</sup>Division of Vascular Surgery, Dartmouth-Hitchcock Medical Center, Lebanon

### Abstract

**Objective**—Medical management with antiplatelet (AP) and statin therapy is recommended for nearly all patients undergoing vascular surgery to reduce cardiovascular events. We assessed the association between preoperative use of AP and statin medications and postoperative in-hospital myocardial infarction (MI) in patients undergoing high-risk open surgery.

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Correspondence: Randall R. De Martino, MD, MS, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (demartino.randall@mayo.edu).

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#### AUTHOR CONTRIBUTIONS

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**Methods**—We studied patients who underwent elective suprainguinal (n = 3039) and infrainguinal (n = 8323) bypass and open infrarenal abdominal aortic aneurysm repair (n = 3007) in the Vascular Quality Initiative (VQI, 2005–2014). We assessed the association between AP or statin use and in-hospital postoperative MI and MI/death. Multivariable logistic analyses were performed to identify the patient, procedure, and preoperative medication factors associated with postoperative MI and MI/death across procedures and patient cardiac risk strata. Secondary end points included bleeding, transfusion, and thrombotic complications.

**Results**—Most patients were taking both AP and statin preoperatively (56% both agents vs 19% AP only, 13% statin only, and 12% neither agent). Use of both agents was more common for patients in the highest cardiac risk stratum (low, 54%; intermediate, 59%; high, 61%;  $P < .01$ ). Increased cardiac risk was associated with higher MI rates (1.8% vs 3.8% vs 6.5% for low, intermediate, and high risk;  $P < .01$ ). By univariate analysis, MI rate was paradoxically higher for patients taking both agents (3.7%, vs statin only 2.8%, AP only 2.6%, or neither AP nor statin 2.4%;  $P = .003$ ). After multivariable adjustment, rates of MI in patients taking preoperative AP only (odds ratio [OR], 0.9; 95% confidence interval [CI], 0.7–1.2) and statin only (OR, 0.8; 95% CI, 0.6–1.2) were not different from those in patients taking either or neither medication (neither agent compared with taking both agents: OR, 1.0; 95% CI, 0.7–1.4;  $P > .05$  for all). Similarly, rates of MI/death were not associated with medication status after multivariable adjustment. Estimated blood loss  $>1$  liter (OR, 2.4; 95% CI, 1.6–3.7;  $P < .01$ ) and transfusions of 1 or 2 units (OR, 2.5; 95% CI, 2.0–3.3;  $P < .01$ ) and 3 units (OR, 4.0; 95% CI, 3.1–5.3;  $P < .01$ ) were highly associated with MI, with similar findings related to composite MI/death in multivariable analysis. Rates of blood loss were slightly higher with AP use for all procedures; however, increased transfusions occurred only for infrainguinal bypass with AP use. Rates of reoperation for bleeding, graft thrombosis, or graft revision did not differ by preoperative AP use.

**Conclusions**—Preoperative AP and statin medications as used in VQI were not associated with the rate of in-hospital MI/death after major open vascular operations. Rather, predicted cardiac risk and operative blood loss were significantly associated with in-hospital MI or MI/death. AP and statin medications appear to be more useful in reducing late mortality than early postoperative MI/death in VQI. However, they were not harmful, so their long-term benefit argues for continued use.

Patients undergoing major vascular surgery have high rates of concomitant cardiovascular disease burden,<sup>1,2</sup> and management of these patients includes treatment with antiplatelet (AP) medications (aspirin or P2Y<sub>12a</sub> antagonists such as clopidogrel) and cholesterol control with 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (statins). In addition, blood pressure control and smoking cessation remain important additional treatments.<sup>3</sup> These measures have been shown to reduce long-term risks of myocardial infarction (MI) and stroke.<sup>4</sup> Prior work has shown that increasing the use of these medications is associated with a significant reduction in overall 5-year mortality after vascular surgery.<sup>5</sup>

Despite the known long-term benefits of aspirin for secondary prevention of cardiovascular disease, the benefit of continued AP medication in the perioperative setting for noncardiac, noncarotid vascular surgery is unclear.<sup>6</sup> AP medications are thought necessary for carotid interventions and often for surgical bypass; however, aspirin has been shown to have higher rates of bleeding when it is used perioperatively without reducing MI rates in other settings.<sup>6</sup> Although statin therapy has been shown to be effective in the preoperative setting for

vascular surgery to reduce MI,<sup>7</sup> the effect of statins in patients taking other cardioprotective medications, such as AP agents, remains unclear in real-world practice.

The purpose of this study was to describe the perioperative use of AP and statin medications in patients undergoing open infrarenal abdominal aortic aneurysm repair (OAR) and arterial bypass procedures in the Vascular Quality Initiative (VQI). In addition, we also sought to evaluate the association of these cardioprotective medications with postoperative MI and bleeding risks.

## METHODS

### Database

This is a retrospective analysis of data collected prospectively by the VQI, a nationwide quality improvement initiative developed originally in 2002 in New England<sup>8</sup> to improve outcomes of vascular procedures.<sup>9</sup> Registry data are compared with hospital claims in annual audits, and missing cases are retrieved to track all procedures.<sup>8</sup>

### Construction of analytic cohort

All patients undergoing first-time procedures within the VQI data set from 2005 to 2014 for infrainguinal and suprainguinal arterial bypass and OAR were identified. This yielded our initial cohort of 19,388 patients. These patients were selected because multiple guidelines support the use of AP (aspirin or clopidogrel) and statin medications as long-term medications for patients with symptomatic peripheral arterial disease to reduce cardiovascular events.<sup>2,3,10–12</sup> Although aneurysmal disease carries no specified societal recommendations regarding medication treatment with AP and statin medications, most of these patients have indications for known coronary risk factors that support their use,<sup>13</sup> including a history of coronary artery disease, hypertension, positive stress test result, prior coronary revascularization, prior arterial bypass or peripheral intervention, and prior carotid revascularization (all variables collected in VQI). Overall, 89% of abdominal aortic aneurysm patients in our cohort had at least one of these cardiovascular risk factors to recommend AP and statin use.

All cases were elective; urgent or emergent cases were excluded (1466 emergent and 3398 urgent, 114 missing urgency data). These exclusion criteria were designed to provide a cohort of patients with the potential to be prescribed AP and statin medications before elective surgery. Finally, patients were removed from analysis for missing preoperative medication data (n = 41; 0.28%). This resulted in 14,369 patients with preoperative data available.

### Definitions of exposures and outcomes

Our primary exposure was the use of AP or statin medication preoperatively. Statin use was defined as taking any type of statin medication at any dose. Patients were considered to be taking AP medication if they were taking aspirin (any dose) or any P2Y<sub>12a</sub> antagonist (commonly clopidogrel). Preoperative medication use was defined as taking the medication within 36 hours of surgery, but changes before this are not recorded. Patients classified as

being intolerant to AP and statin were considered as not taking these medications (only 62 eligible patients [0.4%] were classified as being intolerant to any AP and 223 patients [1.6%] intolerant to statins). No serologic tests were done on drug efficacy, lipid levels, or other biochemical markers.

Our primary outcome was postoperative, in-hospital MI. Postoperative MI is defined as either an electrocardiographic (ECG) or clinical MI consistent with MI or an isolated troponin elevation without ECG ischemic changes or clinical symptoms. Although troponin-only elevation may have fewer clinical implications, both definitions were included in the primary end point to catch all myocardial ischemic events. Further, even troponin-only elevation events are important as they have been associated with reduced survival.<sup>14</sup> Thus, given the importance of troponin elevation MI, they were included in our primary outcome as a measure of postoperative cardiac ischemia. In preliminary analysis, trends in rates for clinical and ECG MI were similar to those that included troponin elevations across cardiac risk strata and medication status (Supplementary Table I, online only). Secondary end points included in-hospital postoperative death and transfusion rates (total units transfused during hospitalization), estimated blood loss (EBL), and reoperation for bleeding based on AP status. For arterial bypasses, we also evaluated reoperation for graft thrombosis and discharge graft patency based on AP status. Definitions of medical comorbidities in the VQI cohort have been previously published.<sup>15</sup> Cardiac risk was defined as low, intermediate, and high risk by the scoring system developed by Bertges et al<sup>16</sup> using the Vascular Study Group of New England registry (low cardiac risk, -1 to 4 points; intermediate cardiac risk, 5 or 6 points; high cardiac risk, 7 points). Factors (and their point values) include age ≥ 80 years (4), age 70 to 79 years (3), age 60 to 69 years (2), coronary artery disease (2), congestive heart failure (2), chronic obstructive pulmonary disease (2), creatinine level >1.8 mg/dL (2), smoking history (1), insulin-dependent diabetes mellitus (1), long-term use of beta blockers (1), and prior coronary artery bypass or stent/angioplasty (-1). This scoring system has been shown to be more accurate for cardiac risk prediction than the Revised Cardiac Risk Index.<sup>16</sup>

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 Institutional Review Board at Mayo Clinic has approved the use of de-identified data from VQI for research purposes. Patient consent was not obtained. The VQI is a federally listed Patient Safety Organization authorized under the Patient Safety and Quality Improvement Act of 2005 to allow collection of patient data without consent for quality improvement purposes.

### Statistical analysis

Demographic information of patients was compared across medical regimen groups (neither AP nor statin, AP only, statin only, both medications) to assess for differences in cardiac risk factors that may account for the different medical treatment strategies and are possible confounders. Then, we examined the association of medication use status for our primary outcome of postoperative MI and MI/death (with Bonferroni corrections for six comparisons among the four exposure groups; these comparisons were deemed significant if  $P < .05/6 = .$

0083). Explanatory variables for analysis included patient and procedural characteristics as well as medication status to assess for possible confounding between medication use and our outcomes of MI and MI/ death. Univariate comparisons were performed with the *t*-test or  $\chi^2$  test for continuous and categorical data, respectively. EBL and transfusions were evaluated with the Wilcoxon rank sum test because of their nonparametric distribution. We chose potentially confounding variables to be included in a multivariable logistic model by assessing the relationship between the exposures of patient characteristics, operative details, and medical regimens, with the outcome MI or MI/death based on their univariate association with the primary outcomes of MI and MI/ death. Variables of clinical significance and those with a *P* value of  $< .4$  by univariate analysis were included in our final logistic models for MI and MI/death. Continuous variables with a nonlinear relationship with MI were categorized for analysis. Age was categorized by quartiles. Probability values of  $< .05$  were considered significant. Analyses were done with SAS version 9.3 (SAS Institute, Cary, NC) and Stata Release 13 (Stata Corp, College Station, Tex).

## RESULTS

### Patient characteristics

From 2005 to 2014, 14,369 patients underwent first-time operative procedures in the VQI for OAR repair ( $n = 3007$ ), suprainguinal bypass ( $n = 3039$ ), and infrainguinal bypass ( $n = 8323$ ). Overall, a majority of patients were taking both AP and statin medication (56% taking both vs 12% taking neither medication, 19% taking AP only, and 13% taking statin only). Patients taking both medications had higher rates of diabetes, current tobacco use, coronary artery disease, congestive heart failure, and positive stress test results and were more likely to be male (Table I). Medication status was not associated with a meaningful difference in age or statistical difference in race or the presence of chronic obstructive pulmonary disease (Table I). When stratified by cardiac risk, patients taking neither medication or AP only were more likely to be at low cardiac risk ( $P < .01$ ; Fig).

Alternatively, patients taking both AP and statin agents were more likely to be at high cardiac risk (61% at high risk vs 54% at low risk taking both medications;  $P < .01$ ; Fig).

### Postoperative in-hospital MI

Overall, there were 463 postoperative in-hospital MIs (3.2%), and this varied by procedure (4.7% OAR, 3.3% suprainguinal bypass, 2.7% infrainguinal bypass;  $P < .01$ ). In addition, MI rates increased with increasing cardiac risk (low risk, 1.8%; intermediate risk, 3.8%; high risk, 6.5%;  $P < .01$ ). In evaluating the association of medication use with MI rates and adjusting for multiple comparisons, there was a higher MI rate among patients taking both medications preoperatively compared with those taking neither medication (3.7% both vs 2.4% neither medication;  $P = .008$ ) or taking AP-only regimens (3.7% both vs 2.6% AP only;  $P = .008$ ). MI rates for those taking statin only were not different from the rates of those taking both medications (3.7% both vs 2.8% statin only;  $P = .06$ ; Table II, A). Stratified by cardiac risk, there was a nonsignificant trend of increased MI rates for patients taking both medications (Table II, A). The rate of MI or death was not different by medication status (Table II, B). Similarly, the rates of MI by medication use were not

significantly different when each procedure was evaluated individually and stratified by cardiac risk (Supplementary Table II, online only).

Because of differences in medical management by cardiac risk, multivariable adjustment was performed on postoperative MI rates to adjust for confounders. The odds of MI were increased with age, positive stress test result, increasing severity of diabetes, coronary artery disease, and Vascular Study Group of New England cardiac risk (Table III). Notably, transfusions and increasing EBL were highly associated with MI. After adjustment for these patient factors, preoperative medication status had no significant association with postoperative MI in patients taking AP only (odds ratio [OR], 0.9; 95% confidence interval [CI], 0.7–1.2;  $P = .31$ ), statin only (OR, 0.8; 95% CI, 0.6–1.2;  $P = .28$ ), or neither agent (OR, 1.0; 95% CI, 0.7–1.4;  $P = .94$  compared with taking both agents; Table III). Similarly, the odds of MI or death was not different by medication status in patients taking AP only (OR, 1.0; 95% CI, 0.8–1.2;  $P = .75$ ), statin only (OR, 1.0; 95% CI, 0.8–1.3;  $P = .93$ ), or neither agent (OR, 1.0; 95% CI, 0.8–1.5;  $P = .67$  compared with taking both agents; Supplementary Table III, online only). Neither beta blocker nor angiotensin-converting enzyme inhibitor use preoperatively was associated with MI.

### **Bleeding complications, return to operating room, and graft patency**

To assess for potential bleeding risks associated with AP use, we examined both EBL and total transfusions by AP use (aspirin or P2Y<sub>12a</sub> antagonist) at the time of operation. Overall, there was no significant difference in EBL by AP status, but stratified by procedure, there was a small but statistically significant increase in EBL with AP use in unadjusted analysis (Table IV, *A*). Overall, transfusion rates were slightly higher with AP use, and this was due to a higher transfusion rate for patients undergoing infrainguinal bypasses on AP agents (Table IV, *B*). Reoperation was uncommon (8.4% of all cases, 7.2% for OAR, 7.3% for suprainguinal bypass, and 9.3% for infrainguinal bypass). However, of all patients taken back to the operating room, rate of bleeding, graft thrombosis, or graft revision was similar among patients regardless of AP use (Table V). Finally, discharge from the hospital with a patent graft was not affected by preoperative AP use (Table V).

## **DISCUSSION**

Patients undergoing major vascular surgery have a significant burden of cardiovascular risk factors putting them at risk for cardiovascular events. Many authors have published data regarding the long-term benefit of AP and statin medications in preventing these events.<sup>5,17,18</sup> However, the immediate perioperative cardiovascular benefit of these medications appears to be less important than patient-related factors, such as their estimated cardiac risk strata, and procedural factors, such as blood loss. Our data suggest that most patients undergoing major vascular surgery are receiving both AP and statin therapy at the time of surgery. In our analysis, lack of AP or statin therapy was not associated with increased MI/death rates, suggesting that the majority of patients are appropriately prescribed these medications preoperatively on the basis of their perceived cardiac risk. However, these findings do not offset the importance of long-term treatment of patients with peripheral vascular disease to reduce their risk of cardiovascular morbidity and mortality.<sup>5</sup>



The implications of perioperative AP agents on MI and bleeding risks are interesting, and this link has been suggested in previous publications. The Perioperative Ischemic Evaluation 2 (POISE-2) trial randomized >10,000 patients to aspirin therapy or placebo before noncardiac surgery.<sup>6</sup> Although aspirin treatment did not reduce death or nonfatal MI rates (7% vs 7.1%), major bleeding occurred more frequently in patients taking aspirin (4.6% vs 3.8%;  $P = .04$ ). This finding was consistent among the subset of 600 patients undergoing noncarotid vascular surgery. This challenges the concept that AP agents are important for preventing perioperative MI rates. It may be that acute thrombotic coronary events are not the primary cause of perioperative MI, or bleeding may cause more myocardial supply and demand mismatch, negating the potential benefits of aspirin therapy. In our analysis, we did not see lower MI rates in patients treated with AP agents. In our multivariable model to adjust for patient factors, AP use was not associated with lower MI rates. However, our data are not in the setting of a randomized trial and carry wide CIs (95% CI, 0.7–1.3; Table III).

Balancing the risks of bleeding and thrombotic events with AP use is important in the perioperative setting. Interestingly, our data suggest that transfusions and blood loss were strongly associated with the risk of a postoperative in-hospital MI. Transfusion has previously been shown to be associated with cardiovascular events in vascular surgical patients.<sup>19,20</sup> Valentijn et al<sup>19</sup> demonstrated that transfusion after vascular surgery was associated with increased odds of cardiovascular events (OR, 6.4; 95% CI, 4.3–9.4). However, the relationship between MI and transfusion may be confounded by the indication for the transfusion (anemia vs myocardial ischemia). VQI does not collect the indications for transfusion, so our data cannot address this limitation. However, the VQI now tracks the lowest hemoglobin level, enabling future study of this type of clinical question. Our data did suggest a small but significant increase in unadjusted bleeding complications for those taking AP agents. However, these differences were small and may not be clinically important, suggesting that these agents appear safe to use perioperatively. A more detailed analysis of these outcomes is necessary to verify these findings because they may be confounded by the perioperative use of other anticoagulants (such as heparin), use of dual AP agents, institutional guidelines for transfusion thresholds, and other factors we cannot account for in the VQI database. The findings must also be placed in the context of the type of procedure. Finally, our analysis did not see increased rates of reoperation for graft revision or graft thrombosis with lack of AP use.

Our data suggest that nearly 70% of patients are taking a statin medication at the time of surgery. The Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography (DECREASE) III study randomized nearly 500 patients to fluvastatin vs placebo before carotid, lower extremity, or abdominal aortic procedures who were not already taking a statin. Fluvastatin treatment was associated with a reduction in myocardial ischemia (10.8% vs 19%) and reduction in death or nonfatal MI (4.8% vs 10.1%).<sup>7</sup> Yet, a similar benefit to statins was not seen in the DECREASE IV study that randomized patients to fluvastatin undergoing noncardiovascular surgery.<sup>21</sup> This may suggest differences in populations of patients and in cardiac risk or divergent findings. In a meta-analysis of statin use for only vascular surgery patients, statin use appeared to lower perioperative cardiac events. However, this analysis was mostly from observational studies.<sup>22</sup> Two thirds of the patients in our analysis were taking a statin at the time of surgery and would not be eligible

for inclusion in the DECREASE III trial. Unlike with AP agents, there are few risks to perioperative statin use, and we would expect either a beneficial effect of statin on MI or a null effect. If a protective effect of MI is present, we may be underpowered to identify this (type II error).

Our study has important limitations. Notably, our findings are observational, and we presume that patients were selected for AP and statin medication on the basis of their perceived cardiac risks. Further, the recording of medication use is likely more accurate than cardiac history, so our multivariable models may not be able to completely correct for the confounding effect of higher risk patients more likely receiving medical management with AP agents and statins. This bias would tend to minimize potential beneficial impact of medical management in the multivariable model. Second, patients did not undergo routine ECG and laboratory testing, so asymptomatic myocardial ischemia was likely underdiagnosed. However, this bias would likely occur across all medication usage patterns and should not affect our overall conclusions. In addition, we included troponin-only ischemia, which has not been used in all studies; however, it has been associated with poor long-term survival. Supplementary Table I (online only) demonstrated that the trends for clinical MI were not different from our analysis including troponin-only events and should not change our findings. Third, although our study is sufficiently powered to detect a 50% reduction in MI rate with AP and statin use compared with neither medication (3% overall to 1%, power 97% with  $\alpha$  5%), not all patients were of similar cardiac risk. We are underpowered to detect a 50% reduction in MI rates for high cardiac risk patients (power 60% with  $\alpha$  5%). Our results that AP and statin medications did not reduce MI may be due to the inclusion of these low-risk patients. Finally, our MI rate is lower than in recent randomized trials as noted before, and this may reflect improved care, less routine ECG assessment, or different groups of patients.<sup>6,7,21</sup> Because of these limitations, we cannot make any inferences about the causal relationship of AP agents and statins to MI in the perioperative period. However, this offers evidence to inform future study design to understand the implications of these medications in the perioperative period for this group of patients.

## CONCLUSIONS

Most patients undergoing vascular surgery are treated with AP agents and statins, particularly those at high cardiac risk. Although our prior work identified a key role for these medications in long-term survival,<sup>5</sup> our work herein failed to identify an association between MI rates with AP or statin use in the short term, especially in the context of other important factors, such as cardiac risk, type of operation, bleeding, and transfusions. Reducing perioperative cardiac events is likely not as simple as routine treatment with AP agents and statins. A clearer understanding of the patient and procedural factors associated with optimal results remains necessary.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.



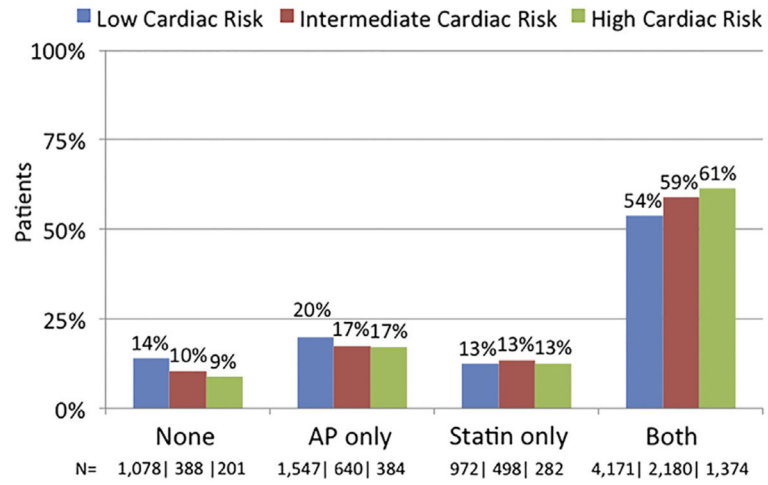
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**Fig.** Preoperative medication status within each cardiac risk stratum. *AP*, Antiplatelet agent (aspirin or P2Y<sub>12a</sub> antagonist).

Table 1

## Patient characteristics

	None, % (n = 1740)	AP only, % (N = 2708)	Statin only, % (n = 1819)	Both, % (n = 8102)	P <sup>a</sup>
Age, years, mean (SD)	65 (13)	66 (11.7)	67.5 (10.5)	66.9 (10.1)	<.01
Sex					.002
Male	12	18	13	57	
Female	12	20	13	54	
Hispanic	13	20	13	53	.58
Race					.34
White	12	19	13	60	
American Indian	9	15	21	55	
Asian	15	18	15	52	
Black	15	20	12	54	
Native Hawaiian	0	25	0	75	
>1	20	0	20	60	
Unknown	16	20	14	54	
Smoking status					<.01
Never	15	22	13	50	
Prior (>12 months ago)	10	17	13	60	
Current	13	20	12	54	
Hypertension	10	18	13	59	<.01
Diabetes mellitus					<.01
None	14	20	12	53	
Diet controlled	11	17	12	59	
Oral medication only	8	15	14	64	
Insulin dependent	9	17	13	62	
Coronary artery disease					<.01
None	14	20	14	51	
History of MI	6	15	10	68	
Stable angina	6	14	10	70	
Unstable angina or recent MI	5	17	8	72	

	None, % (n = 1740)	AP only, % (N = 2708)	Statin only, % (n = 1819)	Both, % (n = 8102)	P <sup>a</sup>
Prior coronary revascularization	5	14	11	70	<.01
Congestive heart failure					<.01
None	13	19	13	56	
Asymptomatic	9	17	13	60	
Mild	9	18	11	62	
Moderate	7	18	12	62	
Severe	8	13	4	75	
COPD					.24
None	12	19	12	56	
Not treated	13	19	12	57	
On medication	11	18	14	57	
On oxygen	12	20	15	53	
Dialysis					.09
No	12	19	13	56	
Transplant	8	23	8	60	
On dialysis	10	23	10	56	
Creatinine > 1.8 mg/dL	9.5	18	16	57	.02
Stress test					<.01
Not done	13	20	12	54	
Normal	12	18	14	56	
Abnormal	7	14	11	67	
Beta blockers					<.01
None	18	23	14	45	
Perioperative (30 days)	10	22	10	58	
Chronic	8	16	13	64	
Operative day only	21	17	17	45	
Preoperative ACE inhibitors	1	16	13	64	<.01

ACE, Angiotensin-converting enzyme; AP, antiplatelet agent (aspirin or P2Y<sub>12</sub> antagonist); COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; SD, standard deviation.

<sup>a</sup> P-value represents analysis of variance for age comparison and  $\chi^2$  remaining comparison of demographics across medication groups.

Table II

<b>A. Myocardial infarction (MI) rates</b>					
	None, %	AP only, %	Statin only, %	Both, %	<i>P</i> <sup>a</sup>
Overall	2.4	2.6	2.8	3.7	.003 <sup>b</sup>
Cardiac risk					
Low	1.4	1.5	1.9	2.1	.3
Medium	3.1	2.5	3.0	4.6	.054
High	5.0	6.0	5.3	7.1	.48
<b>B. Myocardial infarction (MI) or death rates</b>					
	None, %	AP only, %	Statin only, %	Both, %	<i>P</i> <sup>a</sup>
Overall	3	4	4	5	.06
Cardiac risk					
Low	1.9	1.8	2.2	2.4	.41
Medium	4.6	4.2	4.4	5.3	.62
High	7.0	8.1	9.2	8.9	.78

AP: Antiplatelet agent (aspirin or P2Y12a antagonist).

<sup>a</sup>  $\chi^2$  comparison.

<sup>b</sup> *P*-value listed for overall comparison across groups. After correction for multiple comparisons, MI rate for patients taking both medications was significantly higher than for patients taking neither medication (*P* = .008) and AP only (*P* = .008) but not compared with those taking statin only (*P* = .06).



Table III

Multivariable factors associated with postoperative myocardial infarction (MI)

Variable	OR	95% CI	Overall	
			<i>P</i> <sup>a</sup>	<i>P</i> <sup>b</sup>
Cardiac risk			.08	
Low	1.0 Reference			
Intermediate	1.3	0.9–1.9		.06
High	1.8	1.2–2.9		<.01
Medication status			.59	
Both AP and statin	1.0 Reference			
AP only	0.9	0.7–1.2		.31
Statin only	0.8	0.6–1.2		.28
Neither agent	1.0	0.7–1.4		.94
Age quartiles			.06	
<60	1.0 Reference			
60–67	1.4	1.0–2.0		.07
68–74	1.5	1.0–2.2		.04
>75	1.8	1.2–2.6		<.01
Male	1.1	0.9–1.3		.48
Hispanic	0.5	0.2–0.9		.04
Race			<.01	
White	1.0 Reference			
American Indian	1.5	0.4–6.6		.6
Asian	33	1.5–7.3		<.01
Black	0.5	0.3–0.8		<.01
Other <sup>c</sup>	1.0	0.5–2.0		.94
Smoking			.05	
Never	1.0 Reference			
Current	0.8	0.6–1.2		.32
Prior (>12 months ago)	1.1	0.8–1.5		.42
Hypertension	1.2	0.8–1.7		.31
Diabetes mellitus			.003	
None	1.0 Reference			
Diet	1.2	0.8–1.8		.48
Oral medication	1.5	1.1–1.9		<.01
Insulin	1.6	1.2–2.1		<.01
Coronary artery disease			.04	
None	1.0 Reference			
Prior MI	1.1	0.8–1.5		.60
Stable angina	1.6	1.1–2.2		<.01
Unstable angina or MI	1.5	0.8–2.6		.21
CABG or PCI within 5 years	1.2	0.9–1.5		.12

Variable	OR	Overall		
		95% CI	<i>pa</i>	<i>pb</i>
Congestive heart failure	1.2	0.9–1.6		.2
Chronic obstructive pulmonary disease			.76	
None	1.0 Reference			
History, but not treated	0.9	0.6–1.3		.56
On medication	1.0	0.7–1.3		.77
On oxygen	0.7	0.4–1.3		.31
On dialysis	0.8	0.2–3.0		.80
Preoperative stress test			<.01	
Normal	1.0 Reference	1.3–2.4		
(+ ) Ischemia	1.7	0.9–2.0		<.01
(+ ) MI	1.3	0.6–2.3		.22
(+ ) Both	1.2	0.6–0.9		.55
Not done	0.7			<.01
Procedure			.19	
Infringuinal bypass	1.0 Reference			
Suprainguinal bypass	1.3	0.9–1.7		.12
OAR	1	0.7–1.4		.92
Blood transfusion			<.01	
None	1.0 Reference			
1 or 2	2.5	2.0–3.3		<.01
3	4.0	3.1–5.3		<.01
Unknown/missing	5.5	3.7–8.4		<.01
EBL			<.01	
<150 mL	1.0 Reference			
150–350 mL	1.3	0.9–1.9		.15
351–1000 mL	1.6	1.1–2.3		.02
>1000 mL	2.4	1.6–3.7		<.01
Unknown/missing	1.3	0.8–2.1		.38
Transfer from home or rehabilitation facility vs hospital	1.5	0.9–2.5		.15
Preoperative living at home (vs nursing home)	1.0	0.6–1.8		.98
Prior bypass	0.9	0.7–1.2		.42
Prior CEA or CAS	1.1	0.8–1.5		.72
Prior PTA/stent	0.9	0.7–1.1		.28
Prior major amputation	1.5	0.9–2.5		.13
Beta blocker use			.75	
None	1.0 Reference			
Preoperative within 30 days only	1.2	0.9–1.9		.22
Chronic use (>30 days)	1.1	0.9–1.5		.35
Intolerant	1.2	0.5–3.0		.74
Operative day only	1.4	0.6–2.9		.43

*AP*, Antiplatelet; *CABG*, coronary artery bypass; *CAS*, carotid artery stent; *CEA*, carotid endarterectomy; *CI*, confidence interval; *EBL*, estimated blood loss; *OAR*, open abdominal aortic aneurysm repair; *OR*, odds ratio; *PCI*, percutaneous coronary intervention; *PTA*, percutaneous transluminal angioplasty.

<sup>a</sup>Overall *P* value for given categorical variable.

<sup>b</sup>*P* value for indicator variable within each group compared with reference.

<sup>c</sup>Native Hawaiian/Pacific Islander or >1 race.

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**Table IV****A, Estimated blood loss (EBL) by procedure and antiplatelet (AP) status preoperatively**

	No AP	AP	<i>p</i> <sup>a</sup>
Overall EBL, mL	300 (150–800)	300 (150–750)	.287
OAR, mL	1180 (750–1850)	1200 (750–2000)	.02
Suprainguinal bypass, mL	350 (150–600)	350 (200–700)	.015
Infrainguinal bypass, mL	200 (100–300)	200 (100–350)	<.01

**B, Total hospital transfusions by procedure and antiplatelet (AP) status preoperatively**

	No AP	AP	<i>p</i> <sup>a</sup>
Overall transfusions	0 (0–1)	0 (0–2)	.01
OAR, units	0 (0–2)	0 (0–2)	.422
Suprainguinal bypass, units	0 (0–1)	0 (0–2)	.065
Infrainguinal bypass, units	0 (0–0)	0 (0–1)	<.01

OAR, Open abdominal aortic aneurysm repair.

All values are presented as medians with interquartile ranges.

<sup>a</sup>Rank sum comparison.

**Table V**

Causes for return to operating room for complications and discharge graft patency by antiplatelet (*AP*) use (N = 1208 returns)

Complication	No AP, %	AP, %	<i>P</i> <sup>a</sup>
Return for bleeding			
Total	14	17	.33
OAR	22	33	.12
Infringuinal bypass	13	15	.66
Suprainguinal bypass	86	80	.89
Return for graft thrombosis			
Total	27	24	.30
Infringuinal bypass	27	24	.35
Suprainguinal bypass	28	25	.66
Return for graft revision			
Overall	22	18	.27
Infringuinal bypass	24	19	.10
Suprainguinal bypass	12	17	.37
Discharge with patent graft			
Overall	95	95	.12
Infringuinal bypass	94	95	.57
Suprainguinal bypass	96	96	.09

OAR, Open abdominal aortic aneurysm repair.

<sup>a</sup>  $\chi^2$  comparison.