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Perioperative beta blockers and statins for noncardiac surgery patients with coronary stents

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ABSTRACT

Importance: Recent publications report that perioperative initiation of statin therapy is associated with improved outcomes particularly among patients with increased cardiac risk. However, findings on associations with beta blocker (BB) initiation are mixed.
Objective: This study examines associations between perioperative statin and BB use in a national sample of patients with cardiac stents.
Design: Retrospective cohort study.
Setting: VA Medical Centers nationwide.
Participants: We identified Veterans Affairs (VA) patients undergoing non-cardiac surgery in the within two years after stent placement between October 2002 and September 2011 with BB and/or statin prescriptions within one year prior to surgery. Using VA inpatient data we identified major adverse cardiac or cerebrovascular events (MACCE) within 30 days of surgery. General usage patterns and percent of days covered by medication were calculated as additional markers of medication use. Adjusted logistic regression was used to examine associations between medication use and 30-day postoperative outcomes.
Results: 23,537 patients underwent surgery within 2 years following stent placement, of whom 20,566 (88.6%) had prescriptions for beta blockers and statins within 365 days prior to surgery. Of those, 13,501 (65.6%) used both BB and statins prior to surgery, while 2626 (12.8%) used only BB, 2346 (11.4%) used only statins, and 2093 (10.2%) used neither. In fully adjusted models, the only significant association was between perioperative statin use and decreased mortality (OR 0.65, 95% CI 0.48–0.87).
Conclusions: Our results suggest that maintaining statin therapy perioperatively is associated with reduced 30 day mortality in stented patients undergoing non-cardiac surgery who have previously been prescribed both beta blockers and statins.

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1. Introduction

In recent years, much study has been devoted to the perioperative use of beta blockers (BB) and statins to reduce mortality and cardiac events. Results of BB studies have been mixed, with initial small trials showing improved outcomes with BB use but others such as the POISE trial and a large retrospective study by Lindenauer et al. suggesting that the cardio-protective effects of BB use may come with an increased stroke risk, and possibly increased overall mortality.[1–3] Perioperative statin use has generally been associated with improved outcomes, particularly decreased mortality.[3–6] Studies of both drug classes suggest that the benefits of perioperative use increase with increased underlying cardiac risk.[2,3,7] Many studies, particularly RCTs have been devoted to effects of initiating BB or Statin therapy perioperatively, while most observational studies have not distinguished between initiation and continuation.[3–6,8,9] However, patients with a history of

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coronary artery disease (CAD), particularly those requiring coronary intervention, are often prescribed chronic BB and statin therapy to be continued indefinitely. For this group of patients for whom BB and statin therapy have already been initiated, the important, but less-studied, question is the relationship between postoperative outcomes and continued perioperative therapy.

The purpose of this study was to examine the associations of perioperative BB and statin use with postoperative major adverse cardiac and cerebrovascular events (MACCE) and mortality in a national cohort of Veterans Affairs patients with a history of coronary stenting undergoing non-cardiac surgery. We hypothesized that in this patient population with elevated cardiac risk, perioperative use of BB and statins would be associated with decreased MACCE.

2. Methods

All patients undergoing coronary stenting in the VA between October 1, 2002 and September 30, 2011 were identified either from the VA Clinical Assessment, Reporting, and Tracking (CART) program data or by the occurrence of ICD9 procedure codes of 36.06 for bare metal stents (BMS) and 36.07 for drug-eluting stents (DES) in VA Medical SAS datasets. Non-cardiac surgeries in the 2 years following stent placement were identified by the National Surgery Office. Using VA pharmacy data we limited the cohort to patients who had at least one prescription for both a BB and a statin within 365 days prior to surgery. This included any outpatient prescription or an inpatient prescription with at least a 30-day supply.

The main outcome variable was any major adverse cardiac or cerebrovascular event (MACCE) in the 30-days following surgery; a composite outcome of death, acute MI, a revascularization procedure, or a stroke as identified from the VA Medical SAS Datasets or non-VA healthcare utilization from the VA Information Resource Center's Center for Medicaid and Medicare Services (CMS) data for veterans. Each component of MACCE was considered separately as a secondary outcome. As with postoperative outcomes, preoperative co-morbidities were determined using the VA Medical SAS Datasets in combination with non-VA healthcare utilization captured by CMS. The study population and definition of study variables have been previously described.[10]

The main independent variable reflected the perioperative use of BB and statin therapy and captured whether the patient had current BB or statin usage prior to surgery. For a patient admitted on the day of surgery this was defined as having a prescription with remaining supply at the time of surgery, or which expired within 7 days prior to surgery, after inflating the prescription duration by 20% to account for approximately 80% adherence.[11] For patients admitted on days prior to surgery, exposure was defined from inpatient pharmacy records by the receipt of drugs on the day before or of surgery. Patients' perioperative medications were classified separately as BB, yes or no; Statins, yes or no; and together as neither, BB alone, statin alone, or both. We developed a separate set of variables classifying the patients' general usage patterns for each class of drugs as chronic (no gaps in coverage >90 days during the year prior to surgery); recently initiated (first prescription or inpatient administration within 90 days prior to surgery), and discontinued (medication supply from last prescription exhausted more than 90 days prior to surgery). We also calculated patient's adherence to their BB and Statin therapies separately, as percent of days covered (PDC). PDC was calculated if the patient had at least two prescriptions in the year prior to surgery and was calculated as the percent of days covered between the first and last prescription. To control for potential confounding due to antiplatelet therapy, similar variables were constructed for clopidogrel.

Univariate and bivariate frequencies were used to examine differences in population characteristics and outcomes by BB and statin use, with Chi-square tests and t-tests used to assess statistical significance. Logistic regression was used to calculate odds ratios of study outcomes with respect to medication use with adjustment for usage patterns and PDC. For statistical modeling, we used one indicator variable to indicate that a PDC was calculated, and then included the PDC itself as an interaction term set to be zero when the PDC was not defined. Initial models explicitly tested for interactions between BB and statin usage; finding no suggestion of interactions, final models included both BB and statin use without interaction terms.

The first set of models (MedUse-Adjusted) adjusted only for drug usage and possession variables. Fully-adjusted models included stent type (DES vs BMS), time from most recent stent to surgery, age, revised cardiac risk index, prior stents, clopidogrel usage and possession, procedure specialty, work relative value units, diabetes, chronic kidney disease, acute myocardial infarction in the six months prior to surgery, congestive heart failure in the six months prior to surgery, elective vs. non-elective procedure, and whether the surgery took place before or after the 2008 guidelines regarding appropriate time to surgery after BMS and DES implantation.[12] To explore the possible variation in associations by cardiac risk, models were repeated stratified by the revised cardiac risk index. To further examine associations for patients with elevated cardiac risk, all analyses were repeated using a cohort limited to patients with an acute MI within two years prior to surgery. R version 3.0.1 was used for all analyses.[13]

3. Results

23,537 VA patients underwent surgery within 2 years following stent placement, and 20,579 (87.4%) of these patients had prescriptions for both BB and statins within 365 days prior to surgery. Table 1 shows patient and operative characteristics overall and by medications on hand at the time of surgery. Of those, 7789 (37.8%) had an MI within two years prior to surgery. The majority of patients, 13,509 (65.6%) used both BB and statins prior to surgery, while 2628 (12.8%) used only BB, 2346 (11.4%) used only statins, and 2096 (10.2%) used neither. As seen in Table 1 many factors are significantly associated with preoperative medication use. Patients were most likely to have both medications on-hand and least likely to have neither on hand when their surgery occurred <6 weeks after stent placement compared to patients with surgery more than 3 months after stent placement (77.8% vs. 64.5%, and 5.8% vs. 10.8%, respectively). Fig. 1 shows the probability of beta blocker and statin use by time from stent placement to surgery with the highest probabilities for those with surgery within 6 months of stent placement or more than 18 months after stent placement. This bimodal distribution persisted in fully adjusted models, models limited to the first surgery after stent placement, and models limited to patients who survived at least two years after stent placement.

In unadjusted analyses, perioperative medication use was significantly associated with MACCE, with rates of 5.5% for BB and statin use, 6.0% for BB only, 5.4% for statins only, and 7.1% for neither ($p = 0.03$). Among the MACCE components only 30-day mortality was significantly associated with medication usage, with rates, respectively, of 1.1%, 1.9%, 1.0%, and 1.9%, respectively ($p < 0.001$). Table 2 shows the unadjusted associations of perioperative medication use and overall medication usage patterns with study outcomes.

Table 3 shows the associations between perioperative usage and outcomes using logistic regression both overall and stratified by