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Underuse of statins for secondary prevention of atherosclerotic cardiovascular disease events among ambulatory surgical patients

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ABSTRACT

Although statins are highly effective for reducing cardiovascular disease events, prior studies demonstrate their significant underuse in the US population, including among those with known atherosclerotic disease. It is unknown whether this finding applies to the subset of patients who present for outpatient surgery, as such patients would be expected to have recent exposures to healthcare providers during the preoperative referral period. The primary aim of this manuscript was to ascertain the prevalence of statin underuse and associated risk-factors for such underuse among ambulatory surgical patients with documented atherosclerotic cardiovascular disease.

This was a retrospective observational study of a random sample of 600 patients ages 40–75 years presenting for ambulatory surgery within a 6-month period in 2016, at one of three ambulatory surgical centers affiliated with a large, tertiary care hospital. Compilation and analysis of data occurred in 2018–2019. Of the 600 subjects, 117 (19.5%) had documented atherosclerotic cardiovascular disease. Within this high-risk group, only 71 (60.7%) carried a prescription for any statin, and only 30 (25.6%) were prescribed a recommended high intensity statin dose for secondary prevention. In a multivariable logistic regression analysis, older age, male sex, and treatment for hypertension were positively associated with statin use.

In conclusion, statin underuse among ambulatory surgical patients is common and mirrors what has been observed in non-surgical populations. Future trials are needed to investigate the possible role of surgical teams to promote guideline-based statin therapy, including the role of preoperative screening interventions to impact long term cardiovascular morbidity and mortality.

1. Introduction

Among patients with atherosclerotic cardiovascular disease (ASCVD), statins substantially reduce morbidity and mortality from cardiovascular disease (Stone et al., 2014). Nevertheless, the Medical Expenditure Panel Survey estimates that 41.9% of Americans with documented ASCVD are not prescribed a statin (Salami et al., 2017). Among those taking a statin for secondary prevention, approximately two-thirds are not taking the recommended high-intensity dose recommended by major guidelines and other supporting evidence (Rodriguez et al., 2017).

Despite the importance of statins, patterns of statin utilization in the perioperative setting remain largely unknown. Given that ambulatory surgery is increasingly common (Cullen et al., 2006), the possibility of harnessing these care episodes to address long-term cardiovascular disease risk carries potentially large public health benefits (Schonberger et al., 2012; Schonberger et al., 2015; Schonberger et al., 2018; Warner, 2009; Warner et al., 2011; Warner et al., 2008). However, leveraging the surgical encounter to improve adherence to statin guidelines requires an understanding of the patterns of underuse specific to this population. The primary aim of this manuscript was thus to describe the prevalence of statin underuse for secondary prevention of ASCVD among ambulatory surgical patients and to identify demographic, comorbid, and procedural characteristics that are associated with lack of statin use.

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2. Methods

2.1. Study design and setting

After IRB approval including a waiver of consent, we queried data from a randomly selected sample of 600 patients age 40–75 years presenting for ambulatory surgery within a 6-month period (June 1 - December 30, 2016) at three ambulatory centers affiliated with the Yale School of Medicine. Compilation and analysis of data occurred in 2018–2019.

2.1.1. Data extraction

Demographic data for cohort identification were obtained from our local Perioperative Data Repository (Kheterpal, 2011). The repository also forms the local dataset for our site participation in the Multicenter Perioperative Outcomes Group (MPOG) consortium (Larach et al., 2019; Lee et al., 2017). The MPOG data collection methods have been previously described (see www.mpog.org) (Kheterpal, 2011), but briefly include automated collection of structured data into a dedicated perioperative data repository that incorporates case by case validation of a random sample of data by subject-matter experts on a monthly basis. The cohort was selected from among the index ambulatory surgical case of any patients age 40–75 who received ambulatory surgery during the chosen timeframe. The resulting cohort was then randomly ordered using the "newid()" SQL function to create an unbiased, randomly ordered sample. After random ordering was achieved, the first 600 cases were selected for the analytic dataset.

For each encounter, the following information was collated and then confirmed via manual chart review: demographics (age, gender, self-identified race), the scheduled procedure including subspecialty of the proceduralist, and American Society of Anesthesiologists Physical Status score (ASA score) (Dripps et al., 1961), and insurance status recorded as Medicaid, Medicare, or private/other insurance. ASCVD status was ascertained based on the presence of one of the following conditions: coronary artery disease, history of myocardial infarction, congestive heart failure, peripheral vascular disease, stroke, and/or transient ischemic attack. Hypertension history and treatment were also recorded, as was the presence or absence of a preoperative statin prescription.

2.1.2. Analytic plan

Descriptive statistics are reported, including number (%), mean (SD), or median (IQR) as appropriate. Any patient with documented ASCVD who was not prescribed a statin was coded as a "likely statin underuser" because we recognize that the preoperative evaluations that were reviewed lacked documentation of statin intolerance.

Risk-factors for likely statin underuse among secondary prevention patients were examined in accordance with prior data from outside the perioperative period, including univariate associations between statin underuse and age, gender, race, and insurance status (Salami et al., 2017). Additionally, we examined possible associations between likely statin underuse and ASA score, procedure type, and treatment for hypertension. After univariate analyses, we then performed a multivariable logistic regression in which likely statin underuse for secondary prevention was the dependent variable and the above putative risk-factors were entered as the independent variables. A p-value of 0.05 was considered statistically significance. SAS version 9.4 (NC, Cary) was utilized for all analyses.

Finally, during the peer review process, additional analyses were undertaken including univariate comparisons of secondary prevention patients taking high-intensity vs. other intensity statins and a description of 6-month mortality postoperatively.

Statistical Power: As our primary aim was descriptive (i.e. observed prevalence of statin underuse) rather than inferential, sample size was based on the confidence with which the prevalence of statin underuse could be specified. Assuming that 20% of our cohort would have ASCVD, and further assuming a true prevalence of statin underuse of 41% (consistent with prior literature) our sample should have been sufficient to specify a 95% confidence interval of the prevalence of statin underuse between 32.2% and 50%. For the secondary aim of identifying predictors of statin underuse, we expected to have sufficient numbers to follow the rule of thumb of maintaining at least 10 events per predictor variable in the multivariable logistic regression modeling as has been described previously (Peduzzi et al., 1996).

3. Results

3.1. Baseline characteristics

Of the 600 participants, the mean (± SD) age was 59.2 (± 9.6) and 360 (60%) were female. 117 (19.5%) had documented ASCVD. For those with ASCVD, the mean (SD) age was 63.8 (± 8.1) of whom 59 (50.4%) were female, and 22 (18.8%) were African American. Within the high-risk ASCVD group, 71 of 117 (60.7%) carried a prescription for any statin, and only 30 of 117 (25.6%) were prescribed a recommended high intensity statin dose. On univariate analysis, ASCVD patients who lacked a statin prescription were younger than those who had prescriptions (61 ± 8.6 years vs. 65.6 ± 7.3.; p for difference = 0.002). Those without a statin prescription were also more likely female (54.2% vs 45.8%, $p < 0.001$). Further, those who were treated for hypertension were more likely to have a statin prescription than those who lacked hypertension treatment (72.5% of treated hypertensives vs. 27.5% of those not treated for hypertension; $p < 0.001$). Regarding Black or African-American race, although the point estimate for statin non-use was higher among this group, the difference was not statistically significantly (54.5% vs 45.5%, $p = 0.10$). A description of the secondary prevention population, stratified by statin-use is listed in Table 1.

In a multivariable logistic regression analysis including age, sex, race, ASA Physical Status, payer source, type of procedure, and anti-hypertensive treatment, we found that older age, male sex, and treatment with anti-hypertensive medication were strongly and independently associated with likelihood of statin use (see Table 2).

Table 1
Summary Univariate Comparisons of Patients with Atherosclerotic Cardiovascular Disease Prescribed vs. not Prescribed a Statin for Secondary Prevention (N = 117).

	Statin			
	No (N = 46, 39.3%)	Yes (N = 71, 60.7%)	Total (N = 117)	P Value
Age				
Mean (SD)	61.0 (8.6)	65.6 (7.3)	63.8 (8.1)	0.002
Insurance				
Medicaid	07 (33.3%)	14 (66.7%)	21 (18.3%)	0.66
Medicare	16 (38.1%)	26 (61.9%)	42 (36.5%)	
Private/Other	23 (44.2%)	29 (55.8%)	52 (45.2%)	
ASA				
1–2	15 (60.0%)	10 (40.0%)	25 (21.4%)	0.017
3–4	31 (33.7%)	61 (66.3%)	92 (78.6%)	
Sex				
Female	32 (54.2%)	27 (45.8%)	59 (50.4%)	< 0.001
Male	14 (24.1%)	44 (75.9%)	58 (49.6%)	
Race				
Not black	34 (35.8%)	61 (64.2%)	95 (81.2%)	0.10
Black	12 (54.5%)	10 (45.5%)	22 (18.8%)	
Surgery Subgroup				
Gastroenterology	08 (24.2%)	25 (75.8%)	33 (28.2%)	0.017
General Surgery	04 (30.8%)	09 (69.2%)	13 (11.1%)	
Orthopedic	09 (75.0%)	03 (25.0%)	12 (10.3%)	
Other	25 (42.4%)	34 (57.6%)	59 (50.4%)	
Any Anti-Hypertensive Rx				
No	21 (80.8%)	05 (19.2%)	26 (22.2%)	< 0.001
Yes	25 (27.5%)	66 (72.5%)	91 (77.8%)	

Table 2
Results of multivariable logistic regression analysis showing relative odds of statin use among 117 ambulatory surgical patients with ASCVD.

Variables	Odds ratio (95% CI)	P-value
Age*	1.12 (1.04–1.21)	0.004
Sex, male vs. female	4.98 (1.70–14.57)	0.003
Race, black vs. non-black	0.41 (0.12–1.46)	0.17
ASA 3–4 vs. 1–2	1.29 (0.32–5.32)	0.72
Insurance		0.31
Private/other	0.25 (0.04–1.47)	0.12
Medicare	0.36 (0.07–1.87)	0.22
Medicaid	ref	Ref
Procedural group		0.14
Gastroenterology	2.34 (0.33–16.69)	0.40
Orthopedic surgeries	0.21 (0.02–2.10)	0.19
Other surgical subspecialty (cardiac, ENT, gyn, neuro, ophtho, plastics, ECT, thoracic, urology, vascular)	0.89 (0.16–4.79)	0.89
General surgery	ref	ref
On anti-hypertensive, Yes	16.80 (3.91 – 72.14)	< 0.001

*: OR (95% CI) = 1.79 (1.21–2.64) for every 5 year increase in age.

Regarding high-intensity statins, only 30 (25.6%) of all secondary prevention patients were prescribed a guideline-adherent statin dose. Restricting the analysis to the 71 secondary prevention patients who were taking at least some dose of statin, the 30 high-intensity patients represented 42.3% of the subset taking a statin while 41 (57.7%) of this group were taking some other dose of statin. In univariate analyses, both statin-receiving groups appeared similar with the exception that male patients were more likely than female patients to be taking the high-intensity dose (31 of 44 males vs.10 of 27 females, p = 0.006; see Supplemental Table).

In response to manuscript review, a supplementary descriptive analysis was conducted to look at postoperative, 6-month mortality outcomes. A total of 4 patients out of the full 600-patient cohort died within 6-months, two of whom were among the 116 secondary prevention patients. Neither of these higher risk patients was taking guideline-adherent statin therapy at the time of surgery.

4. Discussion

The present study provides an estimate of likely statin underuse among ambulatory surgical patients with documented ASCVD. Our finding that 39.3% of this population lacked a statin prescription accords very well with prior literature documenting that 41% of American adults with ASCVD outside of the perioperative population lack a statin prescription, and it suggests that the perioperative period may be an opportunity to screen for and address poorly controlled cardiovascular risk factors (Schonberger et al., 2012; Schonberger et al., 2015; Schonberger et al., 2018; Schonberger et al., 2014; Schonberger et al., 2014). While the present manuscript is descriptive in nature rather than interventional, it provides a potentially important foundation for future interventional work by improving our understanding of statin use in this population.

Our study has several limitations. As a retrospective observation study using healthcare records, it is subject to inaccuracies stemming from unmeasured or poorly measured data (Schonberger et al., 2014; Schonberger, 2014). Second, we lacked information regarding reasons for statin non-adherence, including statin intolerance. However, a recent study of Medicare beneficiaries estimates the rate of statin intolerance to be < 2% among post-MI patients (Serban et al., 2017), and there is no literature to suggest that perioperative patients would demonstrate higher rates of statin intolerance than other groups. Even allowing for a plausible degree of statin intolerance, our underlying findings of significant rates of statin underuse in this population persist. Third, while we document a clear gap in preventive care, our study does not answer the question of what to do about it. The degree to which ambulatory surgical patients may be amenable to interventions to improve modifiable cardiovascular disease risk deserves further study.

Although we are not aware of prior studies examining likely statin underuse in ambulatory surgery, other investigators have shown poor rates of statin adherence in limited, higher-risk surgical populations such as patients with peripheral arterial disease undergoing major vascular procedures (Meltzer et al., 2018; Williams et al., 2018). These data further highlight the fact that even among surgical patients - who typically undergo repeated interactions with the healthcare system – a significant proportion remain in need of improved treatment for persistently uncontrolled cardiovascular risk-factors.

5. Conclusions

In conclusion, the present study demonstrates levels of likely statin underuse among ASCVD patients presenting for ambulatory surgery that are similar to the general US non-surgical population. These findings underscore the need for future studies investigating potential interventions during perioperative healthcare visits to address modifiable cardiovascular risk factors that may impact long-term morbidity and mortality.

CRediT authorship contribution statement

Robert B. Schonberger: Conceptualization, Methodology, Investigation, Resources, Supervision, Project administration, Writing - original draft, Writing - review & editing. **Vivek Vallurupalli:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing. **Hollie Matlin:** Investigation. **Daina Blitz:** Investigation. **Adambeke Nwozuzu:** Investigation. **Brian Barron:** Investigation. **Yuemei Zhang:** Investigation. **Feng Dai:** Methodology, Software, Validation, Formal analysis, Resources, Data curation, Visualization. **Daniel Jacoby:** Conceptualization, Methodology, Investigation. **Khurram Nasir:** Conceptualization, Methodology, Investigation. **Amit Bardia:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing.

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Conflicts of interest

Dr. Schonberger discloses that he holds an equity stake in Johnson & Johnson, a publicly traded, diversified manufacturer of healthcare products. No industry funding was obtained for the present research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2020.101085.

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