ONLINE FIRST

β-Blocker Continuation After Noncardiac Surgery

A Report From the Surgical Care and Outcomes Assessment Program

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Background: Despite limited evidence of effect, β-blocker continuation has become a national quality improvement metric.

Objective: To determine the effect of β-blocker continuation on outcomes in patients undergoing elective noncardiac surgery.

Design, Setting, and Patients: The Surgical Care and Outcomes Assessment Program is a Washington quality improvement benchmarking initiative based on clinical data from more than 55 hospitals. Linking Surgical Care and Outcomes Assessment Program data to Washington's hospital admission and vital status registries, we studied patients undergoing elective colorectal and bariatric surgical procedures at 38 hospitals between January 1, 2008, and December 31, 2009.

Main Outcome Measures: Mortality, cardiac events, and the combined adverse event of cardiac events and/or mortality.

Results: Of 8431 patients, 23.5% were taking β-blockers prior to surgery (mean [SD] age, 61.9 [13.7] years; 63.0% were women). Treatment with β-blockers was continued on the day of surgery and during the postoperative period in 66.0% of patients. Continuation of β-blockers both on the day of surgery and postoperatively improved from 57.2% in the first quarter of 2008 to 71.3% in the fourth quarter of 2009 (*P* value <.001). After adjusting for risk characteristics, failure to continue β-blocker treatment was associated with a nearly 2-fold risk of 90-day combined adverse event (odds ratio, 1.97; 95% CI, 1.19-3.26). The odds were even greater among patients with higher cardiac risk (odds ratio, 5.91; 95% CI, 1.40-25.00). The odds of combined adverse events continued to be elevated 1 year postoperatively (odds ratio, 1.66; 95% CI, 1.08-2.55).

Conclusions: β-Blocker continuation on the day of and after surgery was associated with fewer cardiac events and lower 90-day mortality. A focus on β-blocker continuation is a worthwhile quality improvement target and should improve patient outcomes.

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CARDIAC COMPLICATIONS are common after surgery. A recent study of more than 8300 patients demonstrated that myocardial infarction (MI) after noncardiac surgery occurred in 5% of patients, with nearly 75% of those happening in the first 48 hours.[1] Patients with a perioperative myocardial infarction had a nearly 6-fold increased risk of death at 30 days compared with those without myocardial infarction. Several studies have demonstrated reductions in perioperative cardiac events and mortality when high-risk patients take β-blockers before surgery.[2-7] At least 1 randomized study demonstrated sustained survival benefit with continuation of β-blockers up to 2 years postoperatively,[2] but more recent studies showing adverse effects from high-dose metoprolol succinate before surgery have tempered the interest in initiating β-blockade for at-risk patients.[8]

Distinct from the issue of β-blocker initiation, a far less controversial issue is the immediate withdrawal or discontinuation of β-blockers after surgery in patients taking β-blockers at home. β-Blocker continuation is considered a quality improvement metric based on very limited evidence. Immediate β-blocker withdrawal may cause a reflex tachycardia and increased cardiac demand. Independent of reflex tachycardia, β-blocker withdrawal may also create a deleterious perturbation of the physiological milieu created by β-blockers during a critical period of surgical stress.[9-11] Studies that have examined β-blocker withdrawal in the peri-

operative period have had small sample sizes, have been conducted in a limited number of settings, and have focused on patients undergoing vascular or cardiac surgical procedures.[12-16] The continuation of β-blockers in the perioperative setting is a measure in the Surgical Care Improvement Project (SCIP), which mandates that all surgical patients who take a β-blocker preoperatively receive a β-blocker on the day of surgery (defined as 24 hours prior to surgical incision through discharge from the postanesthesia care unit).[17] However, it has been unclear whether this quality improvement metric is sufficiently associated with improved outcomes in noncardiac surgery to make investment in accomplishing universal β-blocker continuation an effective use of resources. To evaluate the relationship of β-blocker withdrawal among intermediate-risk surgery across a broad spectrum of practice settings, we studied patients in Washington's Surgical Care and Outcomes Assessment Program (SCOAP, http://www.scoap.org), which is a prospectively gathered clinical quality improvement activity implemented at nearly all hospitals statewide where surgery is performed (n = 55 hospitals).[18,19] The purpose of this study was to evaluate the relationship among the continuation of β-blockers, survival, and cardiac complications in elective colorectal and bariatric surgical procedures.

METHODS

STUDY DESIGN

This study was approved by the University of Washington Human Subject Review Committee and the Washington State Department of Health. We conducted a retrospective cohort study using a linked in-hospital clinical registry (SCOAP), the Washington Comprehensive Health Abstract Reporting System (CHARS), and the state's vital records system. The Surgical Care and Outcomes Assessment Program draws data from medical records by trained, audited abstractors using standardized definitions (http://www.scoap.org/documents/index.html). Yearly auditing assured more than 98% data validity for all involved metrics. Data from patients at 38 SCOAP hospitals were available during the evaluation period. The state's hospital administrative discharge database (CHARS) includes administrative information on all hospitalizations and patient identifiers that allow for the tracking of subsequent hospitalizations. The CHARS data set also contains *International Classification of Diseases, Ninth Revision* procedure and diagnosis codes. The linked database allowed for identification of those patients who were rehospitalized at any medical center after a SCOAP index admission for any diagnoses. To determine mortality, CHARS and SCOAP were linked to the state's vital statistics records. Records of inpatient hospitalizations between the first quarter of 2008 and fourth quarter of 2009 at 38 hospitals across Washington were used to identify patients with a history of taking a β-blocker who were undergoing elective colon/rectal or bariatric procedures. Using this cohort, we assessed outcomes among those patients who did and did not receive perioperative β-blockers during their hospitalizations.

VARIABLE DEFINITIONS

Patient Risk Factors

The Surgical Care and Outcomes Assessment Program records were used to obtain sociodemographic and clinical characteristics, laboratory values, and operative type using a set of standard definitions. We used the Deyo modification of the Charlson Comorbidity Index to calculate a weighted index of comorbid conditions for each patient with the information gathered from clinical records.[20] Scores range from 0 to 3, where 0 indicates the absence of comorbid conditions and the score was truncated at 3 and greater.

Cardiac Risk Factors

We used Revised Cardiac Risk Index criteria to stratify patients by cardiac risk.[4] Of the 6 criteria (ischemic cardiac disease, congestive heart failure, cerebrovascular disease, insulin-dependent diabetes, chronic renal insufficiency, and high-risk surgery), we did not have information on cerebrovascular disease or congestive heart failure. Any patient with more than 2 Revised Cardiac Risk Index criteria was identified as a high-risk patient.

Types of Operation

Bariatric operations included laparoscopic and open Roux-en-y gastric bypass, laparoscopic gastric band placement, sleeve gastrectomy, biliopancreatic bypass with and without duodenal switch, vertical band gastroplasty, and revision of gastric bypass. Colon operations included right/transverse and left hemicolectomy, low anterior resection, abdominal perineal resection, total abdominal colectomy, stoma takedown, perineal proctectomy, and abdominal proctectomy. Methods of operation were specified as laparoscopic, open, laparoscopic converted to open, and laparoscopic/hand assisted.

β-Blocker Administration

We limited our cohort to those patients known to be taking a β-blocker preoperatively based on medication and narrative reports. We identified patients who were administered β-blockers on the day of surgery (preoperatively within 24 hours of surgery or before leaving the postanesthesia care unit) and those who were prescribed β-blockers on postoperative day 1. Patients with contraindications of β-blocker use such as hypotension, critical bradycardia, or vasopressor use were excluded from the analysis.

We compared those who were not given β-blockers either on the day of surgery or postoperatively with those who were given β-blockers in both periods. In a secondary analysis, we evaluated the effect of missing just the preoperative dose of β-blockers compared with the effect of missing postoperative dosing.

Outcomes

The primary outcomes were 90-day mortality, cardiac complications, and combined adverse events (CAEs). Ninety-day mortality was defined as all-cause death 90 or fewer days after the procedure as ascertained from Washington vital records. Cardiac complications were defined as either a documented myocardial infarction and/or specific *International Classification of Diseases, Ninth Revision* codes as previously described related to cardiac events.[21] Readmissions for cardiac complications were defined as any hospital admission within 90 days of discharge from the index hospitalization using the same *International Classification of Diseases, Ninth Revision* codes. We also looked at the rate of these CAEs at 30 days and 1 year from the day of the procedure. Lastly, given the previous finding of an increased risk of stroke with preoperative β-blocker initiation,[8] we looked at the rate of inpatient cerebrovascular accident.

STATISTICAL ANALYSIS

Patient characteristics were summarized using frequency distributions for categorical variables and using means and standard deviations for continuous variables stratified by continuation of β-blockers perioperatively. With the same stratification, the 30-day, 90-day, and 1-year mortality; 90-day index and readmission cardiac complications; inpatient cerebrovascular accidents; and 90-day CAEs were summarized using frequency distributions. Pearson χ^2 statistics were used to compare characteristics and unadjusted event rates. Logistic regression models were created to evaluate the association between missing a dose of β-blocker perioperatively and outcomes adjusting for patient, clinical, and operative characteristics identified as statistically significant ($P < .05$) on univariate evaluation or found to be important in previous studies.

We evaluated the importance of missing β-blockers on the day of surgery by comparing patients who were not administered β-blockers only on the day of surgery with those who continued receiving β-blockers throughout the perioperative period using the same adjusted logistic regression model. We then repeated this evaluation for patients who were not administered β-blockers only during the postoperative period. We used Stata version 11 statistical software (StataCorp) for all analyses.

RESULTS

There were 8431 patients who underwent elective colorectal and bariatric procedures at 38 SCOAP hospitals between January 1, 2008, and December 31, 2009 (**Table 1**). Of those, 1976 patients (23.4%; mean [SD] age, 61.9 [13.7] years; 63.0% women) were using β-blockers prior to admission. During the study, (**Figure**), continuation of β-blockers throughout the perioperative period increased (57.2% [107 of 187 patients] in the first quarter of 2008 to 71.3% [221 of 310 patients] in the fourth quarter of 2009) and postoperative β-blocker use increased from 75.9% (142 of 187 patients) to 93.4% (282 of 302 patients). Patients who received β-blockers throughout the perioperative period (n=1303 [65.9%]) and those who did not (n=673 [34.1%]) were similar with respect to sex; smoking status; body mass index; comorbidities such as hypertension, diabetes mellitus, and coronary artery disease; use of certain medications including statins and anticoagulants; cardiac risk index; American Society of Anesthesiologists classification; Charlson Comorbidity Index scores; and type of procedure (Table 1). Subjects who had β-blocker withdrawal were more likely to have disability qualifying Medicare, were less likely to be taking angiotensin-converting enzyme inhibitors, and had lower albumin levels (Table 1).

The unadjusted rates of 90-day mortality were higher among those who had a missed dose of β-blockers at any point in the perioperative period (**Table 2**). Unadjusted rates of inpatient mortality, 30-day mortality, 1-year mortality, 90-day index cardiac complications, and 90-day readmissions with cardiac complications were not significantly different in the group who missed a dose of β-blockers (Table 2).

After adjustment for calendar year, age, sex, coronary artery disease, and Charlson Comorbidity Index score, the odds of a 90-day CAE were almost 2-fold higher among those missing a dose of β-blockers on the day of surgery or postoperatively (odds ratio [OR], 1.97; 95% CI, 1.19-3.26) (**Table 3**). The risk was even higher for those who were identified as high-risk patients using Revised Cardiac Risk Index criteria (OR, 5.91; 95% CI, 1.40-25.00) (Table 3). There was an increased risk of CAEs in the 30-day period (OR, 2.10; 95% CI, 1.15-3.84) as well as in the 1-year period (OR, 1.66; 95% CI, 1.08-2.55), and an even greater risk among those with more Revised Cardiac Risk Index characteristics (Table 3).

In a secondary analysis, we looked at the effect of not administering β-blockers on the day of surgery but continuation in the postoperative period. We found a 90-day CAE rate of 5.4% (19 of 349 patients) in this group, compared with 2.8% (36 of 1304 patients) in those who continued β-blocker treatment throughout the periopera-

Table 1. Patient Demographic Characteristics and Procedures by β-Blocker Administration

Characteristic	β-Blocker Continued (n=1303)	β-Blocker Missed Day of Surgery, Postoperatively, or Both (n=673)	*P* Value
Age, mean (SD), y	62.4 (13.4)	60.9 (14.0)	.02
Female, No. (%)	802 (61.5)	442 (65.8)	.06
Insurance, No. (%)			
Medicaid	70 (5.4)	21 (3.1)	.02
Medicare	535 (41.4)	312 (46.7)	.02
Private	793 (61.3)	335 (50.1)	<.001
Uninsured	17 (1.3)	4 (0.6)	.14
Smoker, No (%)	169 (13.0)	96 (14.3)	.41
ASA classification, No. (%)			.03
1	17 (1.3)	7 (1.1)	
2	363 (28.4)	179 (26.8)	
3	790 (61.7)	4455 (66.6)	
4	110 (8.6)	35 (5.2)	
Mean (SD)	2.8 (0.6)	2.8 (0.6)	.91
Currently taking, No. (%)			
Statin	631 (48.4)	311 (46.2)	.36
ACE	585 (44.9)	249 (37.0)	.001
Anticoagulant	139 (10.7)	68 (10.1)	.71
Comorbidities, No. (%)			
HTN	1187 (91.0)	609 (90.5)	.66
DM	490 (37.6)	270 (40.1)	.27
CAD	318 (24.4)	144 (21.5)	.15
Charlson Comorbidity Index score			
No (%)			.14
0	536 (41.1)	270 (40.1)	
1	504 (38.7)	274 (40.7)	
2	212 (16.3)	91 (13.5)	
≥3	52 (4.0)	38 (5.7)	
Mean (SD)	0.8 (0.8)	0.9 (0.9)	.69
Revised cardiac risk index in high-risk group, No. (%)	68 (5.2)	25 (3.7)	.14
BMI	36.8 (11.0)	37.3 (11.5)	.36
Albumin, mean (SD), g/dL	4.0 (0.6)	3.8 (0.7)	<.001
Procedure, No. (%)			.87
Bariatric	613 (47.0)	319 (47.4)	
Colon	691 (53.0)	354 (52.6)	

Abbreviations: ACE, angiotensin-converting enzyme; ASA, American Society of Anesthesiologists, BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CAD, coronary artery disease; DM, diabetes mellitus; HTN, hypertension.

SI conversion factor: To convert albumin to grams per liter, multiply by 10.

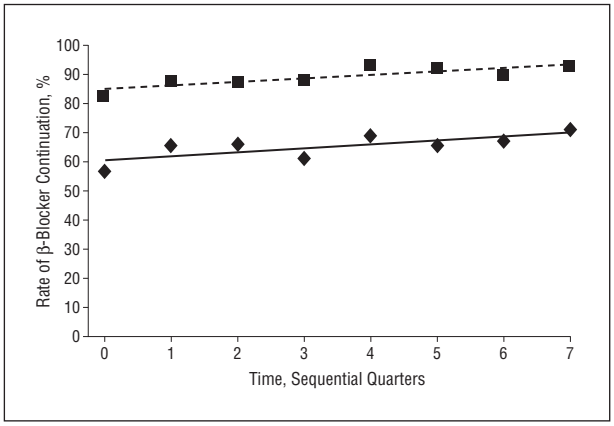

Figure. Trend of β-blocker continuation over sequential quarters from the first quarter of 2008 (labeled 0) to the fourth quarter of 2009 (labeled 7). Solid line indicates the rate of β-blocker continuation throughout the perioperative period and dashed line, the rate of β-blocker continuation in the postoperative period (Surgical Care and Outcomes Assessment Program metric).

Table 2. Outcomes by β-Blocker Administration

Outcome	No (%)		*P* Value
	β-Blocker Continued (n=1303)	β-Blocker Missed Day of Surgery, Postoperatively, or Both (n=673)	
In-hospital mortality	14 (1.1)	11 (1.6)	.29
Mortality			
30 d	16 (1.2)	15 (2.2)	.09
90 d	26 (2.0)	24 (3.6)	.04
1 y	39 (3.0)	30 (4.5)	.09
90-d readmission with cardiac complications	5 (0.4)	7 (1.0)	.11
90-d cardiac complications	11 (0.8)	10 (1.5)	.21
Stroke	1 (0.1)	0	.50
90-d combined adverse events	36 (2.8)	32 (4.8)	.02

tive period (*P*=0.01). After adjusting for relevant covariates, we found a doubling of the odds of 90-day CAE if β-blockers were not administered only on the day of surgery (OR, 2.02; 95% CI, 1.11-3.68) (**Table 4**).

COMMENT

In this statewide evaluation of the continuation of β-blockers in patients undergoing colorectal and bariatric surgery, we found that a missed dose of β-blockers on the day of surgery and afterward was associated with significantly higher 90-day and 1-year mortality, cardiac complications, and CAEs. Our findings, based on the clinical records of patients from most hospitals in Washington across all types of medical centers and communities, suggest that β-blocker continuation is critical to avoiding cardiac complications. To our knowledge, this is the first large-scale study evaluating the comparative effectiveness of this key SCIP cardiac metric in noncardiac surgery.

Several studies have demonstrated an association of perioperative β-blockers with decreased postoperative cardiac events and mortality.[2-7] The Perioperative Ischemic Evaluation Study trial, the largest randomized, controlled trial of initiating preoperative β-blockers to date,[8] found that starting a high dose of β-blockers on the day of surgery reduced cardiac events and cardiac death but was associated with increased death and stroke. A large observational study looking at the benefit of β-blockers based on patients' Revised Cardiac Risk Index scores found that the benefit of β-blockers appeared greatest among patients with the highest cardiac risk.[7] Updated guidelines from the American College of Cardiology Foundation and the American Heart Association recommend limiting β-blocker initiation to high-risk patients undergoing higher-risk procedures.[22] In comparison, the information supporting perioperative β-blocker continuation in any patient undergoing surgery who is receiving long-term β-blocker treatment for an American College of Cardiology Foundation/American Heart Association class I indication (including coronary disease, angina, symptomatic arrhythmias, and hypertension)[22] is limited. There have been few small case series demonstrating an association of cardiac events subsequent to β-blocker withdrawal in nonoperative populations.[9,11,16,23,24] An early case report in the 1980s suggested that perioperative withdrawal may be detrimental and associated with a rebound syndrome potentially inducing coronary events and arrythmias.[25] In a group of patients undergoing vascular surgery, β-blocker withdrawal was associated with greater in-hospital[14] and 1-year mortality.[12] In the latter study, not receiving β-blockers among all higher-risk patients was associated with mortality, but withdrawal among patients previously receiving a β-blocker was associated with even worse outcomes.[12] To our knowledge, our study is the first to evaluate β-blocker withdrawal in a patient population undergoing intermediate cardiac risk surgery (noncardiac and nonvascular). Moreover, ours is the largest cohort of perioperative patients studied to date (n=1976).

A national campaign to encourage the continuation of β-blockers on the day of surgery has been led by the Centers for Medicare and Medicaid Services through the SCIP initiative,[17] yet the evidence underlying this metric is limited and adherence to it has been limited. This SCIP metric is completed in 93% of patients nationwide, with wide variability between 0% and 100%,[26] suggesting that β-blocker withdrawal is actually quite common even among the Medicare beneficiaries that SCIP reports. Data from SCOAP demonstrate that in the first quarter of 2008, 75.9% (142 of 187) of patients receiving long-term β-blocker treatment prior to undergoing a procedure were administered a β-blocker postoperatively and 57.2% (107 of 187) received it both on the day of surgery and postoperatively. The Surgical Care and Outcomes Assessment Program initiated a β-blocker continuation campaign focusing on all opportunities to continue β-blocker administration (both on the day of surgery and postoperatively). The strategy included a statewide education campaign, quarterly reports demonstrating benchmarked performance data by hospital, and the deployment of a SCOAP surgical checklist (now implemented in 100% of Washington hospitals; http://www.scoapchecklist.org). As part of the checklist, operating

Table 3. Risk-Adjusted Odds Ratio for CAEs Across Different Periods for Overall Number of Patients and Patients With High-Risk Cardiac Index[a]

Covariate	AOR (95% CI)					
	30-d CAE	30-d CAE for High-Risk Patients	90-d CAE	90-d CAE for High-Risk Patients	1-y CAE	1-y CAE for High-Risk Patients
β-Blocker missed	2.10 (1.15-3.84)	4.77 (0.87-26.03)	1.97 (1.19-3.26)	5.91 (1.40-25.0)	1.66 (1.08-2.55)	3.60 (0.97-13.41)
Year[b]	0.98 (0.53-1.83)	2.28 (0.35-14.77)	1.03 (0.62-1.73)	2.27 (0.48-10.74)	0.80 (0.52-1.22)	1.72 (0.43-6.93)
Age	1.07 (1.05-1.10)		1.08 (1.06-1.11)		1.07 (1.05-1.09)	
Sex	2.13 (1.14-4.00)		1.66 (0.99-2.75)		1.95 (1.27-2.99)	
Coronary artery disease	1.47 (0.63-3.44)		1.33 (0.66-2.65)		1.36 (0.78-2.39)	
Charlson Comorbidity Index score						
1	1.59 (0.66-3.83)		1.23 (0.59-2.58)		1.45 (0.80-2.64)	
2	1.52 (0.43-5.28)		2.00 (0.76-5.26)		2.02 (0.94-4.32)	
≥3	6.08 (1.74-21.21)		5.77 (2.03-16.43)		3.97 (1.61-9.78)	

Abbreviations: AOR, adjusted odds ratio; CAE, combined adverse event.
[a] Each variable is adjusted for all other covariates listed.
[b] Year the operation was performed.

Table 4. Risk-Adjusted Odds Ratio for 90-Day CAEs for β-Blocker Missed During Different Perioperative Periods[a]

	90-d CAE, AOR (95% CI)	
	β-Blocker Not Administered Only on Day of Surgery	β-Blocker Not Administered Only in Postoperative Period
β-Blocker missed	2.02 (1.11-3.68)	0.80 (0.17-3.69)
Year[b]	1.02 (0.57-1.81)	0.95 (0.48-1.88)
Age	1.09 (1.06-1.12)	1.10 (1.06-1.14)
Sex	1.28 (0.74-2.22)	2.14 (1.08-4.27)
Coronary artery disease	1.2 (0.57-2.57)	1.05 (0.45-2.42)
Charlson Comorbidity Index score		
1	1.62 (0.72-3.62)	1.96 (0.73-5.27)
2	2.80 (0.95-8.21)	3.89 (1.17-12.88)
≥3	7.95 (2.43-25.97)	8.19 (1.92-34.93)

Abbreviations: AOR, adjusted odds ratio; CAE, combined adverse event.
[a] Each variable is adjusted for all other covariates listed.
[b] Year the operation was performed.

room teams review whether a patient is taking a β-blocker and are asked to formulate a plan for postoperative continuation of β-blockers in patients receiving β-blockers. Consequent to the introduction of the checklist campaign, the rates of β-blocker continuation increased to 71.3% (221 of 310 patients) for β-blocker administered both on the day of surgery and postoperatively and 93.4% (282 of 302 patients) for β-blocker administered postoperatively within 2 years.

Our study is limited in several ways. We used all-cause mortality (both alone and in combination with cardiac events) because most deaths that are directly caused by significant cardiac events occur before a timely diagnosis. The use of all-cause mortality may have included some patients who died of causes unrelated to cardiac complication. For this reason, we performed a sensitivity analysis with and without death included in the end point and found similar results. Some of the limitations of this study arise from the use of administrative data (CHARS) to evaluate postdischarge outcomes by its design (retrospective) and from the way health conditions and interventions are defined (using *International Classification of Diseases, Ninth Revision* diagnostic and procedural codes). Additionally, clinicians within and among hospitals may have variable approaches to caring for patients with cardiac risk. β-Blocker continuation by staff at any single hospital might also be a marker for better implementation of process measures in general, thus reducing cardiac complications and mortality through other causal pathways. We could not disentangle these from the effect of β-blocker continuation. Although SCOAP contains rich clinical data and we adjusted for relevant clinical factors including patient comorbidities and coronary artery disease, there is a possibility that patients who have β-blocker treatment discontinued may have worse outcomes independent of the β-blocker use. The Surgical Care and Outcomes Assessment Program does account for contraindications of β-blocker therapy including hypotension, critical bradycardia, vasopressor use, or any other documentation at the discretion of the clinical teams regarding a contraindication to its use. Patients with contraindications were excluded from the analysis. We did not have information on the route, dose, and brand of β-blocker used, thus limiting the ability to differentiate withdrawal based on medication half-life. β-Blockers have varied half-lives and may be differentially absorbed in the postoperative period when taken orally.[27] Those with a longer half-life may have had continued effect into the postoperative period, limiting the ability to decipher the effect of timing of administration. Lastly, the measure of postoperative β-blocker administration was based on record abstraction of physicians' medication orders rather than the documented administration of β-blockers. Neither the receipt of β-blockers nor the effect on heart rate control could be assessed using the current version of SCOAP.

In conclusion, β-blocker withdrawal was associated with significantly higher rates of mortality, cardiac complications, and CAEs. This association appears to be long lasting, with similar differences in outcomes at 1 year. Our findings provide strong evidence to support the universal continuation of β-blockers in patients undergoing colorectal and bariatric operations. The effect of longer-term

β-blocker continuation and effective heart rate control with β-blocker administration remains to be determined.

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