Preoperative β-Blocker Use in Coronary Artery Bypass Grafting Surgery
National Database Analysis

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**IMPORTANCE** Use of preoperative β-blockers has been associated with a reduction in perioperative mortality for patients undergoing coronary artery bypass grafting (CABG) surgery in observational research studies, which led to the adoption of preoperative β-blocker therapy as a national quality standard.

**OBJECTIVE** To determine whether preoperative β-blocker use within 24 hours of CABG surgery is associated with reduced perioperative mortality in a contemporary sample of patients.

**DESIGN, SETTING, AND PARTICIPANTS** Retrospective analysis of the Society of Thoracic Surgeons National Adult Cardiac database for 1107 hospitals performing cardiac surgery in the United States from January 1, 2008, through December 31, 2012. Participants included 506 110 patients 18 years and older undergoing nonemergent CABG surgery who had not experienced a myocardial infarction in the prior 21 days or any other high-risk presenting symptom. We used logistic regression and propensity matching with a greedy 5-to-1 digit-matching algorithm to examine the association between β-blocker use and the main outcomes of interest.

**EXPOSURES** Preoperative β-blocker use.

**MAIN OUTCOMES AND MEASURES** Incidence of perioperative mortality, permanent stroke, prolonged ventilation, any reoperation, renal failure, deep sternal wound infection, and atrial fibrillation.

**RESULTS** Among the 506 110 patients undergoing CABG surgery who met the inclusion criteria, 86.24% received preoperative β-blockers within 24 hours of surgery. In propensity-matched analyses that included 138 542 patients, we found no significant difference between patients who did and did not receive preoperative β-blockers in rates of operative mortality (1.12% vs 1.17%; odds ratio [OR], 0.96 [95% CI, 0.87-1.06]; P = .38), permanent stroke (0.97% vs 0.98%; OR, 0.99 [95% CI, 0.89-1.10]; P = .81), prolonged ventilation (7.01% vs 6.86%; OR, 1.02 [95% CI, 0.98-1.07]; P = .26), any reoperation (3.60% vs 3.69%; OR, 0.97 [95% CI, 0.92-1.03]; P = .35), renal failure (2.33% vs 2.24%; OR, 1.04 [95% CI, 0.97-1.11]; P = .30), and deep sternal wound infection (0.29% vs 0.34%; OR, 0.86 [95% CI, 0.71-1.04]; P = .12). However, patients who received preoperative β-blockers within 24 hours of surgery had higher rates of new-onset atrial fibrillation when compared with patients who did not (21.50% vs 20.10%; OR, 1.09 [95% CI, 1.06-1.12]; P < .001). Results of logistic regression analyses were broadly consistent.

**CONCLUSIONS AND RELEVANCE** Preoperative β-blocker use among patients undergoing nonemergent CABG surgery who have not had a recent myocardial infarction was not associated with improved perioperative outcomes.

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β-Blockers have been used perioperatively in cardiovascular surgery for more than 40 years. Strategies for the use of β-blockers before cardiac surgery have changed over time. For many years these therapies were stopped before surgery owing to concerns about negative inotropic effects. However, in the late 1990s, multiple retrospective analyses demonstrated benefits of preoperative β-blockade use. Since 2007, the use of preoperative β-blockers has been used as a quality standard for patients undergoing coronary artery bypass grafting (CABG) surgery4–5; hospital and surgeon reimbursements may be affected by meeting goals for this standard.

Although initial studies (based on CABG data from the 1990s) provided support, no randomized prospective analyses of the use of preoperative β-blockers in CABG have been performed. Retrospective and prospective randomized studies in the noncardiac surgical literature have failed to show a benefit with their routine empirical application. Some investigators have hypothesized that the benefit of β-blockers observed in early studies may be driven by those with recent myocardial infarctions (MIs), a cohort known to benefit from aggressive β-blockade. A meta-analysis of 69 studies by Wiesbauer et al reported that perioperative β-blockers “had no effect on the frequency of hard end-points like myocardial infarction, mortality, or length of hospitalization” in cardiac and noncardiac surgery. A recent analysis of Society of Thoracic Surgeons National Adult Cardiac database (STS-NCD) data collected from a group of North Texas hospitals demonstrated no benefit associated with empirical preoperative β-blocker use before CABG in a cohort that excluded these patients. In addition, the principal data used for mortality benefit associated with β-blockade in noncardiac surgery, the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography (DECREASE), has been shown recently to be falsified and was retracted in a highly publicized episode of academic misconduct. The present study assessed whether administration of β-blockers in patients without a recent MI (ie, within 21 days from CABG) was associated with reduced operative mortality and in general reduced incidence of postoperative adverse outcomes.

Methods

The STS-NCD was established in 1989 for the purpose of outcome assessment after cardiac surgery. Data are collected quarterly from participating hospitals in the United States and Canada, with strict data quality standards. These data are then warehoused at the Duke Clinical Research Institute and used to generate site-level quality assurance and quality improvement feedback reports. Regular audits of the participating centers are used to measure data accuracy and integrity. To assess the association between preoperative β-blocker use and postoperative adverse outcomes, we used STS-NCD data.

Study Cohort

The study cohort consisted of patients 18 years and older who underwent nonemergency isolated CABG surgery at STS-NCD-participating hospitals from January 1, 2008, through December 31, 2012. From a starting population undergoing 756 215 operations, we excluded patients with prior MI within 21 days (211 715 [28.00%]); patients with high-risk presenting symptoms, including shock, prior percutaneous coronary intervention within 6 hours, or preoperative intra-aortic balloon pump or inotropes (18 894 [2.50%]); patients with a documented contraindication to β-blocker therapy (18 881 [2.50%]); and patients with missing data on key variables, including age, sex, and β-blocker reimbursement (615 [0.08%]). The final study cohort included 506 110 patients from 1107 participating centers. The type of analyses presented in this study has been reviewed and approved by the Duke University Health System institutional review board under protocol number CR1_Pro00005876. Informed consent was waived.

Exposure Definition

Preoperative β-blocker use was defined as receiving a dose of a β-blocker within 24 hours preceding surgery (as per STS-NCD definition); STS data definitions for all data fields are found at http://www.sts.org/sites/default/files/documents/word/STSAdultCVDataSpecificationsV2.73%20with%20correction.pdf for version 2.73 and at http://www.sts.org/sites/default/files/documents/pdf/trainingmanuals/adult2.61/V-c-AdultCVDataSpecifications2.61.pdf for version 2.61). According to STS-NCD data definitions, contraindications to β-blocker therapy were only counted if they were documented in the medical record by a physician, a nurse practitioner, or a physician assistant.

Outcome Definitions

The following outcomes (defined by the STS-NCD, version 2.73) were considered for this study. Operative mortality included (1) all deaths occurring during the acute episode of care in which the operation was performed and (2) those deaths occurring after discharge from the hospital, but within 30 days of the procedure. Stroke was defined as any confirmed neurologic deficit of abrupt onset caused by a disturbance in the blood supply to the brain that did not resolve within 24 hours. Prolonged ventilation included any pulmonary ventilator use for longer than 24 hours. Any reoperation included reoperation for bleeding, graft occlusion, valvular dysfunction, or other cardiac reasons. Renal failure included acute or worsening renal function resulting in (1) an increase of serum creatinine level to at least 3 times the most recent preoperative level or a serum creatinine level of at least 4.0 mg/dL with an minimum increase of 0.5 mg/dL relative to the last preoperative value (to convert to micromoles per liter, multiply by 88.4) and/or (2) a new postoperative requirement for dialysis. Deep sternal wound infection included any wound infection within 30 postoperative days involving muscle, bone, and/or mediastinum requiring operative intervention or a positive culture finding requiring antibiotic treatment. Atrial fibrillation included a new onset of atrial fibrillation/flutter requiring treatment, excluding recurrence of previously documented preoperative atrial fibrillation/flutter.
Continuous covariates were imputed by stratifying patients by categorical variables except ejection fraction (3.22%), unstable angina (0.78%), and mitral insufficiency (0.67%). Missing values for categorical covariates listed above for the regression-based analyses. For ejection fraction, the propensity model was augmented to include a missing data indicator variable. Inclusion of this variable ensured an equal prevalence of missing data for ejection fraction for patients with and without β-blockers in the propensity-matched sample. After estimating propensity scores, we matched patients using a greedy 5-to-1 digit-matching algorithm. Before analyzing outcomes, we assessed the success of the propensity-matching procedure by comparing the distribution of patient characteristics in the matched sample. Finally, odds ratios (ORs) comparing the frequency of each end point for patients receiving vs not receiving β-blockers were estimated using univariable logistic regression and reported with 95% CIs.

In addition to comparing overall outcomes for patients receiving vs not receiving β-blockers, we further examined whether the association between β-blockers and mortality differed across prespecified subgroups based on age, sex, congestive heart failure, ejection fraction, diabetes mellitus, and chronic lung disease. For each subgroup, the association with mortality was estimated in a logistic regression model that included a treatment group indicator (0, no β-blockers; 1, β-blockers), an indicator variable for the subgroup of interest, and the interaction between the treatment group and subgroup indicators. Subgroup-specific ORs were estimated and displayed with 95% CIs, and we used a test of treatment-by-subgroup interaction to assess whether differences in the estimated ORs across subgroups were consistent with chance.

**Table 1. β-Blocker Use Overall and by Year of Operation**

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of patients</th>
<th>No. (%) receiving β-blockers</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>111 059</td>
<td>89 012 (80.15)</td>
</tr>
<tr>
<td>2009</td>
<td>109 178</td>
<td>90 819 (83.18)</td>
</tr>
<tr>
<td>2010</td>
<td>103 234</td>
<td>89 425 (86.62)</td>
</tr>
<tr>
<td>2011</td>
<td>93 322</td>
<td>84 403 (90.44)</td>
</tr>
<tr>
<td>2012</td>
<td>89 317</td>
<td>82 817 (92.72)</td>
</tr>
<tr>
<td>All</td>
<td>506 110</td>
<td>436 476 (86.24)</td>
</tr>
</tbody>
</table>

**Definition of Baseline Covariates**

Body surface area (BSA) was calculated by the following Du Bois formula:

\[
\text{BSA} = \text{Weight (in Kilograms)}^{0.425} \times \text{Height (in Centimeters)}^{0.725}
\]

Other clinical factors were defined according to STS-NCD data specifications, using version 2.61 (January 1, 2008, through June 30, 2011) or version 2.73 (July 1, 2011, through December 31, 2012). Atrial fibrillation was defined as preoperative fibrillation or flutter within 2 weeks of operation using version 2.61 or within 30 days of operation using version 2.73. Other preoperative factors had identical definitions across the 2 data versions or were mapped based on established conventions for the STS risk models.

**Statistical Analysis**

Baseline demographic and clinical characteristics were summarized for patients receiving and not receiving β-blockers (β-blocker and non-β-blocker groups, respectively). Baseline factors were summarized as percentages for categorical variables and as mean (SD) for continuous variables. Statistical testing was not conducted for baseline factors because the very large sample size causes even small differences to be highly statistically significant. Analysis was performed using commercially available software (SAS, version 9.3; SAS Institute Inc). We used the following 2 techniques to adjust for selection bias when comparing outcomes of the β-blocker vs non-β-blocker groups: multivariable regression modeling and propensity matching. For the regression-based analyses, the association between β-blocker use and each clinical end point was estimated in a logistic regression model with adjustment for the following patient-level covariates: age, body surface area, sex, Hispanic or nonwhite race, dyslipidemia, prior CABG, prior percutaneous coronary intervention, 2 or more prior cardiovascular operations, hypertension, immunosuppressive therapy, peripheral vascular disease, unstable angina, left main coronary artery disease, number of diseased vessels (<2, 2, or 3), cerebrovascular disease, prior cerebrovascular accident, diabetes mellitus (types 1 or 2 or none), urgent status, congestive heart failure (New York Heart Association class IV, classes I-III, or none), atrial fibrillation, ejection fraction, chronic lung disease (severe, moderate, mild, or none), dialysis, creatinine level, and prior MI. In addition to patient-level covariates, each logistic model also included year of surgery to account for temporal trends in outcomes and β-blocker use and a set of fixed-effect hospital-specific intercept variables to control for potential confounding by center effects. Missing data occurred in fewer than 0.5% of records for all model covariates except ejection fraction (3.22%), unstable angina (0.78%), and mitral insufficiency (0.67%). Missing values for continuous covariates were imputed by stratifying patients by combinations of related risk factors and then imputing stratum-specific medians. Missing values for categorical covariates were imputed to the most common category. Alternative sophisticated missing data techniques (ie, multiple imputation) were not used for this analysis owing to the low rate of missing data and because multiple imputation has had a negligible effect on previous analyses of the STS-NCD.

The second method of adjusting for selection bias involved matching patients with similar estimated probability of receiving β-blockers (ie, their propensity score). To estimate the propensity score, a logistic regression model predicting the use of preoperative β-blockers was developed using the same covariates listed above for the regression-based analyses. With the exception of ejection fraction, handling of missing data was identical to that for the regression-based analyses. For ejection fraction, the propensity model was augmented to include a missing data indicator variable. Inclusion of this variable ensured an equal prevalence of missing data for ejection fraction for patients with and without β-blockers in the propensity-matched sample. After estimating propensity scores, we matched patients using a greedy 5-to-1 digit-matching algorithm. Before analyzing outcomes, we assessed the success of the propensity-matching procedure by comparing the distribution of patient characteristics in the matched sample. Finally, odds ratios (ORs) comparing the frequency of each end point for patients receiving vs not receiving β-blockers were estimated using univariable logistic regression and reported with 95% CIs.

In addition to comparing overall outcomes for patients receiving vs not receiving β-blockers, we further examined whether the association between β-blockers and mortality differed across prespecified subgroups based on age, sex, congestive heart failure, ejection fraction, diabetes mellitus, and chronic lung disease. For each subgroup, the association with mortality was estimated in a logistic regression model that included a treatment group indicator (0, no β-blockers; 1, β-blockers), an indicator variable for the subgroup of interest, and the interaction between the treatment group and subgroup indicators. Subgroup-specific ORs were estimated and displayed with 95% CIs, and we used a test of treatment-by-subgroup interaction to assess whether differences in the estimated ORs across subgroups were consistent with chance.

**Results**

The study cohort included 506 110 patients who underwent non-emergency isolated CABG from January 1, 2008, through December 31, 2012, and did not have a prior MI within 21 days of operation or other high-risk presenting symptoms. The use of preoperative β-blockade in the STS-NCD changed from 80.15% in 2008 to 92.72% in 2012 (Table 1). Rates of use varied from 20% to 99% across years.
to 100% (median, 87.1%) across all individual reporting units and from 53% to 100% (median, 87.5%) in the subset of units that had at least 500 records in the study database.

Clinical characteristics of the study cohort are summarized in Table 2. Patients not receiving β-blockers were less likely to have a prior MI, prior revascularization, urgent status, and operation after 2010. Hypertension, dyslipidemia, diabetes mellitus, congestive heart failure, history of unstable angina, and dialysis were more common in patients who received preoperative β-blockers.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (n = 506 110)</th>
<th>No (n = 69 634)</th>
<th>Yes (n = 436 476)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y [No. with data]</td>
<td>65.0 (10.3) [506 110]</td>
<td>65.7 (10.1) [69 634]</td>
<td>64.9 (10.3) [436 476]</td>
</tr>
<tr>
<td>Male sex</td>
<td>374 526/506 110 (74.00)</td>
<td>52 698/69 634 (75.68)</td>
<td>321 828/436 476 (73.73)</td>
</tr>
<tr>
<td>Nonwhite race or Hispanic ethnicity</td>
<td>83 843/504 707 (16.61)</td>
<td>11 329/69 636 (16.33)</td>
<td>72 514/435 331 (16.66)</td>
</tr>
<tr>
<td>Operation after 2010</td>
<td>182 639/506 110 (36.09)</td>
<td>15 419/69 634 (22.14)</td>
<td>167 220/436 476 (38.31)</td>
</tr>
<tr>
<td>BSA, mean (SD), m² [No. with data]</td>
<td>2.0 (0.2) [504 328]</td>
<td>2.0 (0.2) [69 264]</td>
<td>2.0 (0.2) [435 067]</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>213 301/505 898 (42.16)</td>
<td>27 483/69 620 (39.48)</td>
<td>185 818/436 278 (42.59)</td>
</tr>
<tr>
<td>Portion treated with insulin</td>
<td>71 068/505 622 (14.06)</td>
<td>8416/69 578 (12.10)</td>
<td>62 652/436 044 (14.37)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>443 990/505 966 (87.75)</td>
<td>57 612/69 508 (82.89)</td>
<td>382 587/435 894 (87.77)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11 605/504 396 (2.30)</td>
<td>1275/69 392 (1.84)</td>
<td>10 330/435 004 (2.37)</td>
</tr>
<tr>
<td>Last creatinine level, mean (SD), mg/dL [No. with data]</td>
<td>1.1 (0.4) [493 559]</td>
<td>1.0 (0.4) [68 056]</td>
<td>1.1 (0.4) [425 503]</td>
</tr>
<tr>
<td>Chronic lung disease, moderate or worse</td>
<td>45 596/505 311 (9.02)</td>
<td>6037/69 530 (8.68)</td>
<td>39 559/435 781 (9.08)</td>
</tr>
</tbody>
</table>

Abbreviations: BSA, body surface area; CABG, coronary artery bypass surgery; CHF, congestive heart failure; CVA, cerebrovascular accident; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

S² conversion factor: To convert creatinine to micromoles per liter, multiply by 88.4.

*Unless otherwise indicated, data are expressed as number (percentage) of patients.

*Excludes patients undergoing dialysis.
Table 3 summarizes the clinical end points and risk-adjusted ORs in the nonpropensity-matched sample for patients receiving vs not receiving preoperative β-blockers. The observed frequency of operative mortality was similar for both cohorts (1.22% vs 1.17% for the β-blocker vs non–β-blocker groups; adjusted OR, 0.96 [95% CI, 0.88-1.04]). Compared with patients not receiving β-blockers, those receiving β-blockers had a higher frequency of new-onset postoperative atrial fibrillation (21.38% for the β-blocker group vs 20.10% for the non–β-blocker group; adjusted OR, 1.11 [95% CI, 1.09-1.14]) and a lower frequency of deep sternal wound infection (0.30% for the β-blocker vs 0.34% for the non–β-blocker groups; 0.81 [0.70-0.94]). For other end points, estimated ORs ranged from 0.96 to 1.03 and were not statistically distinguishable from the null value of 1.00 (for each, P > .10).

After propensity matching, comparable groups of 69,271 patients each were created. As shown in the eTable in the Supplement, the distribution of measured risk factors was similar for the β-blocker compared with the non–β-blocker groups. For each variable in the eTable (Supplement), the difference in prevalence across the 2 groups was less than 0.5%.

Clinical end points for propensity-matched patients receiving vs not receiving β-blockers are summarized in Table 4. The frequency of operative mortality was similar for the 2 groups (1.12% in the β-blocker vs 1.17% in the non–β-blocker groups; adjusted OR, 0.96 [95% CI, 0.87-1.06]). Compared with patients not receiving β-blockers, those receiving β-blockers had a higher frequency of new-onset postoperative atrial fibrillation (21.50% in the β-blocker vs 20.10% in the non–β-blocker groups; adjusted OR, 1.09 [95% CI, 1.06-1.12]). We found no significant statistical difference in the rate of deep sternal wound infection (0.29% for the β-blocker group vs 0.34% for the non–β-blocker group; adjusted OR, 0.86 [95% CI, 0.71-1.04]). For other end points, estimated ORs ranged from 0.97 to 1.04 and were not statistically distinguishable from the null value of 1.00 (for each, P > .25).

Table 5 summarizes operative mortality as a function of β-blocker use for prespecified subgroups in the propensity-matched cohort. For each subgroup, the 95% CI for the OR overlapped unity, and the interaction P value was not significant (P ≥ .10), indicating that observed differences across subgroups were consistent with chance.

Discussion

Summary of Findings

We studied perioperative outcomes in 506,110 patients from 1107 centers who did not have an MI within 21 days of an isolated CABG operation and who underwent surgery from January 1, 2008, through December 31, 2012. After propensity matching, comparable groups of 69,271 patients each were created. We performed analyses on the unmatched and propensity-matched data sets, controlling for the preoperative risk factors. No statistical mortality benefit was associated with the use of preoperative β-blockers. Other end points were equal between groups except for new-onset postoperative atrial fibrillation, which was significantly higher in the β-blocker group. On the surface, these observational study data stand in contrast to the endorsed National Quality Forum standards5 that mandate preoperative β-blocker use before CABG procedures.

The use of preoperative β-blockers before CABG has been established as a quality indicator by the National Quality Forum.5 These data are then used to assess the performance of physicians and hospitals participating in public reporting via the STS-NCD. The present report builds on a previous analy-
sis of β-blocker administration before CABG conducted using STS-NCD data from a large institution. In that analysis of 12,855 patients, investigators were unable to show any benefit with the empirical use of preoperative β-blockers. A prior analysis of STS-NCD data in 2002 showed contrasting results. In the present study we analyzed more recent national data (2008-2012) from the STS-NCD for more than 500,000 patients undergoing isolated CABG surgery. In 2002 Ferguson et al reported rates of β-blocker use before coronary bypass procedures at 50% to 60% for the study period ending in 1999. Since then, the emphasis on meeting this quality standard has led to an increase in β-blocker use, with the STS-NCD reporting a rate of 86.24% for the use of β-blockers before CABG in the 2008-2012 data. Because the use of β-blockers is well established after acute MI, we decided to remove that patient population from our analysis. Our motivating question was “Do physicians have to give β-blockers to their patients just because they are scheduled for an elective CABG?”

Empirical Preoperative β-Blocker Use in Noncardiac Surgery

In 2006, the results of the Metoprolol After Vascular Surgery (MaVS) trial, a double-blinded placebo-controlled study, were published. Hypotension and bradycardia were more common in the treatment group. No difference in cardiac events (ie, cardiac death, nonfatal MI, unstable angina, congestive heart failure, or arrhythmia requiring treatment) was demonstrated. The MaVS trial showed no benefit of perioperative β-blocker use; of greater concern, it showed potential harm. Other studies have mirrored this finding of the MaVS trial. In 2008 the Perioperative Ischemic Evaluation (POISE) study published their findings. The POISE study was a prospective randomized trial of 8351 patients with known coronary disease or at risk for coronary disease scheduled to undergo noncardiac surgery. Patients were randomized to extended-release metoprolol succinate or placebo. Analysis of the POISE data revealed that for every 1200 patients treated, metoprolol would prevent 15 MIs at a cost of 8 excess deaths and 5 disabling strokes. They suggested that the therapy may benefit only small selective groups of patients. A recent meta-analysis reviewed 22 trials involving 2437 randomized patients undergoing noncardiac surgery. The authors reported that perioperative use of β-blockers was not associated with statistically significant benefits on cardiovascular outcomes. Further, they reported an increased risk for bradycardia and hypotension with empirical β-blockade use. In their view, “the evidence for perioperative β-blockade was ‘insufficient and inconclusive,’ especially in those at low to moderate risk of adverse cardiovascular outcomes.”

Of greater concern, data used to support previous guidelines for perioperative β-blockade use appear to have been at least partially corrupt. This issue has come to light with the discrediting of the DECREASE family of studies. In light of this problem, Bouri et al in 2013 performed a meta-analysis of randomized clinical trials of initiation of β-blocker therapy before noncardiac surgery that excluded the DECREASE data. Their conclusions stated that “The well-conducted trials indicate a statistically significant 27% increase in mortality from the initiation of perioperative β-blockade.”

Empirical Preoperative β-Blocker Use in Cardiac Surgery

In 2002, Ferguson et al reported an observational study assessing β-blocker use and outcomes among patients undergoing isolated CABG from 1996 through 1999. More than 600,000 patients underwent analysis using STS-NCD data. Preoperative β-blocker use was associated with “slightly lower mortality after adjusting for patient risk and center effects using both risk adjustment (OR, 0.94; 95% CI, 0.91-0.97) and treatment propensity matching (OR, 0.97; 95% CI, 0.93-1.00).” How-
ever, in patients with left ventricular ejection fractions of less than 30%, preoperative β-blockers were associated with a trend toward an increased mortality rate. The authors stated in their conclusions: “Although these results are quite promising, we believe that, ideally, they should be confirmed in a large, randomized clinical trial of preoperative β-blocker use. Such a trial could also further optimize therapy and better determine the mechanisms underlying this effect.”

In 2007, Wiesbauer et al. published a meta-analysis of perioperative β-blockade use. This analysis included randomized clinical trials comparing perioperative β-blockers with placebo or the standard care in cardiac and noncardiac surgery. The authors concluded: “In our review, we found that β-blockers... had no effect on the frequency of hard end-points like perioperative myocardial infarction, operative mortality, or length of hospitalization.”

In the present study, preoperative β-blocker use in CABG patients was not associated with lower operative mortality in the whole study population (1.22% in β-blocker group vs 1.17% in non-β-blocker group; adjusted OR, 0.96 [95% CI, 0.88-1.04]) or in a propensity-matched group of patients who have not had a recent MI (<21 days) (1.17% in the non-β-blocker group vs 1.12% in the β-blocker group; adjusted OR, 0.96 [95% CI, 0.87-1.06]). Subgroup analysis of the OR for mortality with preoperative β-blocker use showed no benefit for patients in relation to sex, age, presence of diabetes mellitus, congestive heart failure, low ejection fraction (<30%), or chronic lung disease.

We were unable to demonstrate any benefit in regard to the incidence of postoperative atrial fibrillation. In fact, we noted a significant increase in the incidence of postoperative atrial fibrillation in the group that had received a β-blocker. This finding seems counterintuitive and is in contrast to guidelines for the treatment of atrial fibrillation. The guidelines advocate preoperative β-blocker use as a class I (level of evidence, A) recommendation. However, a closer analysis of the studies used to generate this recommendation shows that the timing of initiation of β-blocker therapy varied widely. Essentially, the data used to generate these guidelines were a mix of preoperative, intraoperative, and postoperative administration of β-blockers. A possible explanation for this unexpected finding in our data could be the incidence of β-blocker therapy withdrawal in the non-β-blocker cohort. This effect has been demonstrated previously.

Because the STS-NCD only collects data on preoperative β-blocker use (within 24 hours of the incision) as a yes/no field, we are unable to determine whether the timing, the dose given, or other unrecorded covariates may contribute to this observation. Although we adjusted for recent preoperative atrial fibrillation (version 2.61 records occurrence within 14 days and version 2.73 records it within 30 days before surgery) as a covariate, we were unable to adjust for chronic atrial fibrillation, and the β-blocker group might have contained a higher prevalence of prior atrial fibrillation occurring remotely. Hypotension at the end of surgery due to β-blocker use may also play a role. However, one must keep in mind the preponderance in the medical literature of support for the assertion that perioperative β-blockade is effective for the prevention of arrhythmias after cardiac surgery.

Limitations
The actual β-blocker type, dose, and physiologic response are not available in the STS-NCD. The present findings could be related to inadequate dosing or drug type. The STS-NCD is limited to 30-day perioperative outcomes. Any long-term benefit related to β-blockade would not be demonstrated.

Using the STS-NCD allowed analysis of almost every CABG case in the United States during the sample period. Despite the use of preoperative β-blockers being a National Quality Forum quality indicator, we still see only 86.24% of patients receiving the drug. The nonadherence comes from surgeons who believe it is wrong to force the medication on all patients. In some cases of off-pump revascularization, the surgeons believe that the risks in manipulation of the heart are increased in the presence of β-blockade. The data form does not record reasons for refusal (just verifiable medical contraindications).

Conclusions
In this large cohort study of patients with isolated CABG who have not had an MI within 21 days, the administration of β-blockers before CABG was not associated with improved outcomes in the study group or in equivalent propensity-matched groups. These data are consistent with recent literature regarding the empirical perioperative use of β-blockers in noncardiac surgery that demonstrates no mortality benefit associated with their use.

β-Blockers are an important and effective tool in the care of patients undergoing cardiac surgery in specific clinical scenarios. However, the empirical use of β-blockers as recommended by the National Quality Forum (without physiologic goals, ie, adequate clinical drug levels) in all patients before CABG may not improve outcomes. A prospective randomized trial with careful attention to adequate dosing and specific drug type may help to answer this question.
Preoperative β-Blocker Use in CABG Surgery


