Smoking and the Risk of Mortality and Vascular and Respiratory Events in Patients Undergoing Major Surgery

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IMPORTANCE The effects of smoking on postoperative outcomes in patients undergoing major surgery are not fully established. The association between smoking and adverse postoperative outcomes has been confirmed. Whether the associations are dose dependent or restricted to patients with smoking-related disease remains to be determined.

OBJECTIVE To evaluate the association between current and past smoking on the risk of postoperative mortality and vascular and respiratory events in patients undergoing major surgery.

DESIGN Cohort study using the American College of Surgeons National Surgical Quality Improvement Program database. We obtained data on smoking history, perioperative risk factors, and 30-day postoperative outcomes. We assessed the effects of current and past smoking (>1 year prior) on postoperative outcomes after adjustment for potential confounders and effect mediators (eg, cardiovascular disease, chronic obstructive pulmonary disease, and cancer). We also determined whether the effects are dose dependent through analysis of pack-year quintiles.


MAIN OUTCOMES AND MEASURES The primary outcome measure was 30-day postoperative mortality; secondary outcome measures included arterial events (myocardial infarction or cerebrovascular accident), venous events (deep vein thrombosis or pulmonary embolism), and respiratory events (pneumonia, unplanned intubation, or ventilator requirement >48 hours).

RESULTS The sample included 125,192 current (20.6%) and 78,763 past (13.0%) smokers. Increased odds of postoperative mortality were noted in current smokers only (odds ratio, 1.17 [95% CI, 1.10-1.24]). When we compared current and past smokers, the adjusted odds ratios were higher in the former for arterial events (1.65 [95% CI, 1.51-1.81]) vs 1.20 [1.09-1.31], respectively) and respiratory events (1.45 [1.40-1.51]) vs 1.13 [1.08-1.18], respectively). No effects on venous events were observed. The effects of smoking mediated through smoking-related disease were minimal. The increased adjusted odds of mortality in current smokers were evident from a smoking history of less than 10 pack-years, whereas the effects of smoking on arterial and respiratory events were incremental with increased pack-years.

CONCLUSIONS AND RELEVANCE Smoking cessation at least 1 year before major surgery abolishes the increased risk of postoperative mortality and decreases the risk of arterial and respiratory events evident in current smokers. These findings should be carried forward to evaluate the value and cost-effectiveness of intervention in this setting. Our study should increase awareness of the detrimental effects of smoking—and the benefits of its cessation—on morbidity and mortality in the surgical setting.

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Smoking remains a leading preventable cause of morbidity and mortality that is responsible for almost half a million deaths and about $200 billion in added costs for health care and lost productivity each year in the United States alone.1 The role of long-term tobacco dependence in increasing the risks of cancer and cardiovascular and pulmonary disease are well established. However, the effect of smoking on surgical outcomes has not been evaluated extensively. Until recently, most available clinical studies were small, reported data from a single surgical specialty, or evaluated only a few postoperative outcomes.2-12 However, 2 recent large multicenter studies13,14 confirmed the association between smoking and adverse postoperative outcomes. Turan and colleagues13 showed higher adjusted odds of postoperative mortality and major morbidity in 82,304 current smokers compared with those who never smoked (approximately 30% higher odds) using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP). However, the authors did not evaluate the association between past smoking and the observed outcomes. Knowledge of whether smoking cessation modifies (reverses) the adverse effects of smoking remains crucial to promote smoking control measures. The effect of past smoking on postsurgical outcomes was evaluated recently through another large (n = 393,794) multicenter study using the Veterans Affairs Surgical Quality Improvement Program14 that reported that past smokers also have increased odds of 30-day postoperative mortality and major morbidity (approximately 20% higher odds). However, the authors did not adjust for several potential confounders that could have affected outcome rates and the patient’s decision to quit smoking and did not assess the effect of smoking that is not mediated by related disorders (eg, smoking leads to cardiac disease, which in turn leads to adverse postsurgical outcomes), and their study mainly involved men.14

With these previous reports in mind, the purpose of our study was to determine the effects of current as well as past smoking on the incidence of postoperative mortality and arterial, venous, and respiratory events using a large data set from the ACS NSQIP. We also aimed to evaluate whether the observed associations are dose dependent and to establish whether they are restricted to patients who had already acquired smoking-related disease.

Methods

Study Design and Sample
This nested-cohort study used data from the ACS NSQIP database. Details of the ACS NSQIP (http://acsnsqip.org) have been recently described15 and are summarized in eTable 1 in Supplement. The database is a validated outcomes registry designed to provide feedback to participating hospitals on 30-day risk-adjusted surgical mortality and morbidity.16,17 The database includes de-identified data on demographics, perioperative variables, and 30-day postoperative outcomes for adult patients undergoing major surgery in participating non-Veterans Affairs hospitals.16 Trained surgical clinical review-ers collect patient data on admission from the medical record, operative log, anesthesia record, interviews with the attending surgeon, and telephone interviews with the patient.16 Data quality is ensured through comprehensive training of the nurse reviewers, an intrarater reliability audit of participating sites, regular conference calls, and an annual meeting.18

Included in this study were patients undergoing major surgery performed at participating ACS NSQIP medical centers during 2008 (271,368 patients from 211 sites) and 2009 (336,190 patients from 237 sites). In accordance with the American University of Beirut’s guidelines (which follow the US Code of Federal Regulations for the Protection of Human Subjects), institutional review board approval was not needed or sought for our analysis because the data were collected as part of a quality assurance activity.

Smoking History
Data on smoking history are included in the ACS NSQIP as part of the preoperative risk assessment. Patients were categorized into 3 groups on the basis of their smoking status. If the patient has smoked cigarettes in the year before admission for surgery, the patient was considered a current smoker. This definition excluded patients who smoked cigars or pipes or used chewing tobacco. If the patient had ever been a smoker, smoking history measured in pack-years for this patient (the number of packs of cigarettes smoked per day × the number of years the patient smoked) was also retrieved. In this study, patients with a record of pack-years who were not current smokers were categorized as past smokers. Patients who never smoked (ie, never smokers) were defined as patients who were classified as no for the current smoker variable and whose value for the pack-years variable was equal to 0 (325,434 patients [80.6% of never smokers]) or missing (78,169 [19.4% of never smokers]). We decided to classify those patients who had a no for current smoker and a missing for pack-years as never smokers because this approach was more conservative for the analysis of the relationship of smoking with surgical outcomes as determined by others.14 However, we also undertook 2 sensitivity analyses: one with such patients excluded and another with them considered past smokers.

Postoperative Outcomes
Evaluated outcomes included 30-day postoperative mortality, arterial events (myocardial infarction or cerebrovascular accident), venous events (deep vein thrombosis or pulmonary embolism), and respiratory events (pneumonia, unplanned intubation, or ventilator requirement > 48 hours). The diagnoses were defined as described in eTable 2 in Supplement.

Statistical Analysis
Descriptive data are given as mean (SD) or percentage. The primary study outcome was death within 30 days of the index surgery in the current and past smokers groups compared with the never smokers group. The secondary study outcome was the occurrence of arterial, venous, or respiratory events within 30 days of the index surgery in the current and past smokers groups compared with the never smokers group. We esti-
mated unadjusted odds ratios (OR) and 95% confidence intervals for outcomes in the current and past smokers groups. We then constructed 2 multivariate logistic regression models for each outcome to adjust the association between smoking (current and past) and outcomes for 2 types of a priori–defined variables. In model 1 (ORadj-1), we adjusted for variables that are potential confounders but not mediators (ie, factors that could affect the decision of the patient to continue smoking, stop smoking, or never smoke but cannot be caused by smoking). In model 2 (ORadj-2), we adjusted for the variables included in model 1 plus variables that are potential mediators (ie, diseases that may have been caused by smoking). In such analyses, ORadj-1 would represent the true overall effect of current and past smoking on outcomes that is mediated and not mediated by smoking-related diseases; ORadj-2, the true effect of current and past smoking on outcomes that is not mediated by smoking-related diseases. The difference between ORadj-2 and ORadj-1 would represent the true effect of current and past smoking that is mediated by smoking-related diseases. We also stratified data from model 2 per demographics and different surgical settings.

To determine whether the observed effects of current and past smoking in model 2 are dose dependent, we also constructed multivariate logistic regression models with the current and past smokers groups divided into 5 equal quintiles according to pack-years of smoking. Data on pack-years were

### Table 1. Patient Demographics and Preoperative Medical Histories

<table>
<thead>
<tr>
<th>Variable</th>
<th>Never (n = 403,603)</th>
<th>Past (n = 78,763)</th>
<th>Current (n = 125,192)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>55.5 (17.7)</td>
<td>63.6 (13.7)</td>
<td>51.1 (15.2)</td>
</tr>
<tr>
<td>Male sex</td>
<td>39.2</td>
<td>52.3</td>
<td>48.3</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>76.7</td>
<td>83.6</td>
<td>76.3</td>
</tr>
<tr>
<td>Black or African American</td>
<td>9.8</td>
<td>6.9</td>
<td>12.8</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>13.5</td>
<td>9.5</td>
<td>10.9</td>
</tr>
<tr>
<td>ASA class&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I or II</td>
<td>59.7</td>
<td>39.4</td>
<td>51.0</td>
</tr>
<tr>
<td>III</td>
<td>34.2</td>
<td>50.5</td>
<td>40.4</td>
</tr>
<tr>
<td>IV or V</td>
<td>6.1</td>
<td>10.1</td>
<td>8.6</td>
</tr>
<tr>
<td>Functional status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>93.5</td>
<td>92.8</td>
<td>93.0</td>
</tr>
<tr>
<td>Partially dependent</td>
<td>4.7</td>
<td>5.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Totally dependent</td>
<td>1.9</td>
<td>1.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Alcohol consumption&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.4</td>
<td>3.6</td>
<td>6.3</td>
</tr>
<tr>
<td>Diabetic using oral agents or insulin</td>
<td>14.5</td>
<td>21.1</td>
<td>13.3</td>
</tr>
<tr>
<td>BMI ≥30</td>
<td>39.8</td>
<td>42.4</td>
<td>34.2</td>
</tr>
<tr>
<td>Hypertension requiring medication</td>
<td>44.8</td>
<td>61.3</td>
<td>42.0</td>
</tr>
<tr>
<td>Currently undergoing dialysis</td>
<td>1.9</td>
<td>2.3</td>
<td>1.8</td>
</tr>
<tr>
<td>History of chronic obstructive pulmonary disease</td>
<td>2.3</td>
<td>10.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Dyspnea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>91.4</td>
<td>81.9</td>
<td>86.8</td>
</tr>
<tr>
<td>With moderate exertion</td>
<td>7.5</td>
<td>16.1</td>
<td>11.4</td>
</tr>
<tr>
<td>At rest</td>
<td>1.1</td>
<td>2.0</td>
<td>1.9</td>
</tr>
<tr>
<td>Congestive heart failure in 30 d prior</td>
<td>0.8</td>
<td>1.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Angina in 30 d prior</td>
<td>0.8</td>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Myocardial infarction in 6 mo prior</td>
<td>0.6</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Previous percutaneous coronary intervention</td>
<td>4.4</td>
<td>10.2</td>
<td>6.2</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>5.0</td>
<td>11.2</td>
<td>4.8</td>
</tr>
<tr>
<td>History of peripheral vascular disease&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.4</td>
<td>6.9</td>
<td>7.2</td>
</tr>
<tr>
<td>Rest pain/gangrene</td>
<td>1.5</td>
<td>3.1</td>
<td>4.2</td>
</tr>
<tr>
<td>History of transient ischemic attack</td>
<td>2.5</td>
<td>4.9</td>
<td>3.2</td>
</tr>
<tr>
<td>History of cerebrovascular accident with neurologic deficit</td>
<td>2.0</td>
<td>3.3</td>
<td>2.8</td>
</tr>
<tr>
<td>History of cerebrovascular accident without neurologic deficit</td>
<td>1.8</td>
<td>3.0</td>
<td>2.3</td>
</tr>
<tr>
<td>Disseminated cancer</td>
<td>1.8</td>
<td>2.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Tumor involving central nervous system</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0.3</td>
<td>0.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

**Abbreviations:** ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

<sup>a</sup> Unless otherwise indicated, data are expressed as percentage of patients. Percentages have been rounded and might not total 100.

<sup>b</sup> Class I indicates healthy; II, mild systemic disease but no functional limitations; III, severe systemic disease with definite functional limitations; IV, severe systemic disease that is a constant threat to life; and V, moribund and unlikely to survive 24 hours with or without operation.

<sup>c</sup> Indicates more than 2 drinks/d in the 2 weeks prior.

<sup>d</sup> Requiring revascularization, angioplasty, or amputation.
available for all past smokers (part of the definition) and for 84,338 current smokers (67.4%).

Data were nearly complete, with missing values only for body mass index (16,343 patients [2.7%]), which were imputed by the respective means of similar sex and age groups. All analyses were performed using commercially available software (SAS, version 9.2; SAS Institute, Inc.).

### Results

We included data for 607,558 patients. Their mean age was 55.7 (SD, 17.1; range, 16–90) years, and 42.7% were men. A total of 125,192 patients (20.6%) were current smokers; 78,763 (13.0%), past smokers; and 403,603 (66.4%), never smokers. 

#### Table 2. Association Between Smoking and 30-Day Postoperative Outcomes

<table>
<thead>
<tr>
<th>Outcome*</th>
<th>Never (n = 403,603)</th>
<th>Past (n = 78,763)</th>
<th>Current (n = 125,192)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, No. (%)</td>
<td>6194 (1.5)</td>
<td>1636 (2.1)</td>
<td>2200 (1.8)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.36 (1.29–1.44)</td>
<td>1.15 (1.09–1.21)</td>
</tr>
<tr>
<td>Adjusted model 1</td>
<td>1 [Reference]</td>
<td>1.00 (0.94–1.06)</td>
<td>1.21 (1.14–1.28)</td>
</tr>
<tr>
<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>0.91 (0.85–0.97)</td>
<td>1.17 (1.10–1.24)</td>
</tr>
<tr>
<td>Arterial events, No. (%)</td>
<td>1915 (0.5)</td>
<td>701 (0.9)</td>
<td>898 (0.7)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.88 (1.73–2.06)</td>
<td>1.52 (1.40–1.64)</td>
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<tr>
<td>Adjusted model 1</td>
<td>1 [Reference]</td>
<td>1.28 (1.17–1.40)</td>
<td>1.78 (1.63–1.93)</td>
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<tr>
<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>1.20 (1.09–1.31)</td>
<td>1.65 (1.51–1.81)</td>
</tr>
<tr>
<td>Myocardial infarction, No. (%)</td>
<td>1039 (0.3)</td>
<td>425 (0.5)</td>
<td>503 (0.4)</td>
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<tr>
<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>2.10 (1.88–2.35)</td>
<td>1.56 (1.41–1.74)</td>
</tr>
<tr>
<td>Adjusted model 1</td>
<td>1 [Reference]</td>
<td>1.40 (1.24–1.57)</td>
<td>1.92 (1.72–2.16)</td>
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<tr>
<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>1.28 (1.14–1.44)</td>
<td>1.77 (1.57–1.99)</td>
</tr>
<tr>
<td>Cerebrovascular accident, No. (%)</td>
<td>907 (0.2)</td>
<td>289 (0.4)</td>
<td>416 (0.3)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.64 (1.43–1.87)</td>
<td>1.48 (1.32–1.66)</td>
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<tr>
<td>Adjusted model 1</td>
<td>1 [Reference]</td>
<td>1.14 (1.00–1.31)</td>
<td>1.63 (1.44–1.84)</td>
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<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>1.10 (0.96–1.26)</td>
<td>1.55 (1.36–1.76)</td>
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<tr>
<td>Venous events, No. (%)</td>
<td>3643 (0.9)</td>
<td>966 (1.2)</td>
<td>1086 (0.9)</td>
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<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.36 (1.27–1.46)</td>
<td>0.96 (0.90–1.03)</td>
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<td>Adjusted model 1</td>
<td>1 [Reference]</td>
<td>1.05 (0.98–1.13)</td>
<td>0.94 (0.87–1.00)</td>
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<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>1.05 (0.98–1.13)</td>
<td>0.94 (0.87–1.01)</td>
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<td>Deep vein thrombosis, No. (%)</td>
<td>2661 (0.7)</td>
<td>708 (0.9)</td>
<td>802 (0.6)</td>
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<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.37 (1.26–1.49)</td>
<td>0.97 (0.90–1.05)</td>
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<td>1.05 (0.96–1.14)</td>
<td>0.91 (0.84–0.99)</td>
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<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>1.05 (0.96–1.14)</td>
<td>0.92 (0.85–1.00)</td>
</tr>
<tr>
<td>Pulmonary embolism, No. (%)</td>
<td>1274 (0.3)</td>
<td>352 (0.4)</td>
<td>343 (0.3)</td>
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<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.42 (1.26–1.60)</td>
<td>0.87 (0.77–0.98)</td>
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<tr>
<td>Adjusted model 1</td>
<td>1 [Reference]</td>
<td>1.12 (0.99–1.26)</td>
<td>0.91 (0.81–1.03)</td>
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<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>1.10 (0.98–1.25)</td>
<td>0.91 (0.80–1.03)</td>
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<td>Respiratory events, No. (%)</td>
<td>11,422 (2.8)</td>
<td>3571 (4.5)</td>
<td>5691 (4.5)</td>
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<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.63 (1.57–1.69)</td>
<td>1.64 (1.58–1.69)</td>
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<tr>
<td>Adjusted model 1</td>
<td>1 [Reference]</td>
<td>1.21 (1.17–1.27)</td>
<td>1.53 (1.47–1.58)</td>
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<tr>
<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>1.13 (1.08–1.18)</td>
<td>1.45 (1.40–1.51)</td>
</tr>
<tr>
<td>Pneumonia, No. (%)</td>
<td>4826 (1.2)</td>
<td>1605 (2.0)</td>
<td>2572 (2.1)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.72 (1.62–1.82)</td>
<td>1.73 (1.65–1.82)</td>
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<tr>
<td>Adjusted model 1</td>
<td>1 [Reference]</td>
<td>1.25 (1.18–1.33)</td>
<td>1.63 (1.55–1.72)</td>
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<td>Adjusted model 2</td>
<td>1 [Reference]</td>
<td>1.16 (1.09–1.23)</td>
<td>1.50 (1.43–1.59)</td>
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<td>Unplanned intubation, No. (%)</td>
<td>4247 (1.1)</td>
<td>1551 (2.0)</td>
<td>2179 (1.7)</td>
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<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.90 (1.78–2.00)</td>
<td>1.67 (1.58–1.76)</td>
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<td>Adjusted model 1</td>
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<td>1.35 (1.27–1.43)</td>
<td>1.63 (1.54–1.72)</td>
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<td>1 [Reference]</td>
<td>1.25 (1.17–1.32)</td>
<td>1.51 (1.43–1.60)</td>
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<tr>
<td>Ventilator requirement for &gt;48 h, No. (%)</td>
<td>7249 (1.8)</td>
<td>2185 (2.8)</td>
<td>3663 (2.9)</td>
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<tr>
<td>Unadjusted</td>
<td>1 [Reference]</td>
<td>1.56 (1.49–1.64)</td>
<td>1.65 (1.58–1.72)</td>
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<td>1 [Reference]</td>
<td>1.14 (1.08–1.20)</td>
<td>1.43 (1.36–1.50)</td>
</tr>
</tbody>
</table>

*Adjustment in model 1 was undertaken for the following potential confounders: age, sex, race (white, black, or African American, or other), American Society of Anesthesiologists class (described in footnote b of Table 1), functional status (totally dependent, partially dependent, or independent), alcohol consumption (>2 drinks/d in 2 weeks prior), diabetes mellitus (receiving oral agents or insulin), obesity (body mass index [calculated as weight in kilograms divided by height in meters squared] >30), and pregnancy. Adjustment in model 2 was undertaken for the variables listed for model 1 plus the following potential mediators: hypertension (requiring medication), renal failure (currently undergoing dialysis), chronic obstructive pulmonary disease, dyspnea (at rest, on moderate exertion, or none), congestive heart failure (in 30 days prior), angiina (in 30 days prior), myocardial infarction (in 6 months prior), previous percutaneous coronary intervention, previous cardiac surgery, peripheral vascular disease (requiring revascularization, angioplasty, or amputation), rest pain, transient ischemic attack, cerebrovascular accident without or with neurologic deficit, disseminated cancer, and tumor involving the central nervous system.
increased odds of death (OR adj-2, 1.17 [95% CI, 1.10-1.24]). More- 
tality associated with current smoking dropped by only 4% 

timates of 30-day postoperative arterial and respiratory events 
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tavior American Society of Anesthesiologists class and had 
the highest prevalence of diabetes mellitus, obesity, hyper-
tension, renal failure, chronic obstructive pulmonary dis-
ease, cardiovascular disease, and cancer (Table 1). 

The crude rates (cumulative incidence) of postoperative outcomes plus the potential confounders and mediators for which we adjusted the models are summarized in Table 2. Current and past smokers had increased unadjusted odds of 30-
day postoperative mortality and arterial and respiratory events compared with never smokers. However, on adjustment for po-
tential confounders, only current smokers had increased odds of mortality after surgery (OR adj-2, 1.21 [95% CI, 1.14-1.28]). On further adjustment for potential mediators, the odds of mor-
tality associated with current smoking dropped by only 4% 
(smoking-related disease effect), and patients maintained an 
increased odds of death (OR adj-2, 1.17 [95% CI, 1.10-1.24]). Moreover, on adjustment for potential confounders, the effect es-
timates of 30-day postoperative arterial and respiratory events were higher in current smokers (OR adj-2, 1.78 [95% CI, 1.63-
1.93]) and 1.52 [1.47-1.58], respectively) than in past smokers 
(1.28 [1.17-1.40] and 1.21 [1.17-1.27], respectively) when com-
pared with never smokers. On further adjustment for poten-
tial mediators, a similar minimal effect of smoking-related dis-
ease on arterial and respiratory events was noted for current 
smokers (OR adj-2, 1.65 [95% CI, 1.51-1.81]) and 1.45 [1.40-1.51], respectively) and past smokers (1.20 [1.09-1.31] and 1.13 [1.08-
1.18], respectively). Current and past smokers did not have in-
creased adjusted odds of 30-day venous events compared with 
never smokers (Table 2).

In the sensitivity analyses of patients who were not cur-
rent smokers but had missing past pack-years data, results did not differ for the primary and secondary study outcomes 
whether they were considered past smokers rather than never 
smokers (eTable 3 in Supplement) or were excluded (eTable 4 
in Supplement).

The increased adjusted odds of mortality and arterial and respiratory events in current smokers were generally noted 
across all age groups (mostly in those >40 years), in both sexes, 
in inpatients and outpatients, in those who underwent sur-
gery with general or other types of anesthesia, in elective and 
emergency cases, and in various surgical subspecialties (eTable 
5 in Supplement). We also stratified the analyses for postop-
erative arterial and respiratory events according to the pres-
ence of preoperative cardiovascular or chronic obstructive pul-
ymonary disease, respectively (Figure 1).

When we considered history of cigarette smoking in pack-
year data (dose-dependent effect), the increased adjusted odds 
of mortality in current smokers were evident in light (<10 pack-
years) and heavy (>50 pack-years) smokers. Past smokers did 
not have increased odds of mortality even with a cigarette 
smoking history of at least 50 pack-years (Figure 2A). The in-
creased adjusted odds for arterial and respiratory events were 
incremental with increased pack-years, with current smok-
ers generally having higher effect estimates across the whole 
range of pack-years of smoking. In fact, increased odds of ar-
terial and respiratory events were noted only in past smokers 
who had smoking histories of at least 50 and at least 20 pack-
years, respectively (Figure 2B and C). A similar trend was ob-
served for venous events in current smokers, although the ef-
fect estimates remained minimal (eFigure in Supplement).

### Discussion

In this large multicenter study, we demonstrated that current 
but not past smoking is associated with an increased risk of 
mortality in patients undergoing major surgery. Moreover, al-
though past smokers remain at risk of increased arterial and 
respiratory events after surgery, the effect is milder than that
Figure 2. Odds Ratios for the Main Study Outcomes in Past and Current Smokers

The odds are adjusted for potential confounders and mediators described in Table 2 (ORadj). With never smokers as the reference group. Smoking history is divided into quintiles of pack-years. A, Thirty-day postoperative mortality. B, Arterial events. C, Respiratory events.

observed in current smokers. These findings encourage ongoing efforts to implement smoking cessation programs across various health care systems. Early intervention in heavy smokers is warranted, especially because the effect of smoking on postoperative arterial and respiratory morbidity seems to be dose dependent. However, because smokers with a cigarette smoking history of less than 10 pack-years are also at risk of postoperative death, recent and light smokers should also be targeted.

The prevalence of current smokers presenting for major surgery in our study (approximately 20%) is close to that reported by Turan et al.13 but lower than that reported by Hawn et al.14 (approximately 35%), who used data from the Veterans Affairs Surgical Quality Improvement Program involving mostly male veterans. However, the effects of current smoking on mortality and arterial, venous, and respiratory events echoed those reported by both studies, although they used more strict exclusion criteria (eg, excluding patients with the most severe disease, those undergoing cardiac surgery, or emergency cases).13,14 We chose to include all patients, apply extensive adjustment, and stratify outcomes per different patient groups. The adverse effects of current smoking were noted across several patient groups and surgical settings, although with varying effect estimates and uncertainties. This study should help to better target subpopulations who may benefit most from smoking cessation intervention trials.

In the study by Hawn et al.14 the authors found that past smokers remain at increased risk of mortality compared with never smokers and have similar or sometimes even higher odds of certain morbidities (eg, myocardial infarction) than current smokers when compared with never smokers. However, the authors in that study did not adjust the association for mediators, and the reported effect also includes that attributed to smoking-related disease. Moreover, only minimal adjustment for confounding was undertaken, which excluded some clinical conditions (not smoking related) that could cause the patient to stop smoking, while leaving him or her at higher risk of adverse outcomes (eg, obesity and diabetes mellitus). The key strengths of our study lie in the large number of patients and the reliable and comprehensive data collection tool of the ACS NSQIP, which provides more than 60 demographic and preoperative variables available for adjustment. Our study established that past smoking does not increase the risk of postoperative mortality and poses lower risks of arterial and respiratory events compared with those found in current smokers, which is in agreement with smaller studies on select patient groups.6,19

Our study demonstrates that smoking is associated with adverse postoperative outcomes irrespective of the presence of smoking-related disease (eg, cardiovascular disease, chronic obstructive pulmonary disease, and cancer). The effect of smoking on adverse postoperative outcomes mediated by smoking-related disease (the difference between ORadj and ORadj) was minimal. This finding suggests that smoking may exert its effect on adverse postoperative outcomes through acute or subclinical chronic vascular and respiratory pathologic mechanisms. Smoking has acute exposure and chronic cumulative effects on pulmonary function. Toxins and particles in tobacco smoke activate the inflammatory system, ultimately leading to the destruction of alveoli and reduction of the surface area for gas exchange.20 Smoking impairs mucus transport, provokes goblet cell hyperplasia and thus causes stimulation of mucus overproduction,20 impairs pulmonary macrophage function,22 and increases bronchial reactivity by stimulation of airway inflammation.23 Moreover, animal studies show that exposure to tobacco smoke leads to an increased bacterial load and delayed bacterial clearance, demonstrating that cigarette smoke suppresses the respiratory antibacterial host defense and potentially increases the risk for pneumonia.24 The effects of smoking on vessel wall patho-
logic changes, progression of atherosclerosis, and thrombo-
sis potential are numerous. Smoking increases oxidative stress
and inflammation; promotes endothelial activation, dysfunc-
tion, and damage; alters the endothelium-mediated vascular
tone control; increases hypercoagulability and platelet acti-
vation; and reduces fibrinolysis. A direct necrotic action on card-
diomyocytes is also believed to exist.25 The contribution of
smoking to venous thrombosis is still a matter of debate, and
studies with a positive association reported effects smaller than
those consistently observed in arterial thrombosis.26-27 Many
of the smoking-induced effects on respiratory and vascular
pathologic changes are at least partially reversible on cessa-
tion of exposure, usually within 1 year.28-31

One limitation in our study is that we could identify only
past smokers who quit smoking less than 1 year before sur-
gery (otherwise considered current smokers in the ACS NSQIP).
This limitation will not permit any conclusions regarding the
effects of smoking cessation when implemented closer to sur-
gery (eg, at the time of the decision to undergo an elective pro-
cedure), but it does show that the benefits of smoking cessa-
tion on surgical outcomes may start appearing as soon as 1 year
after cessation. This difference may have little importance in
the individual setting but has relevance in the public health
perspective. Studies in this direction had mixed results and de-
pended on the surgical population and the timing and inten-
sity of the intervention.19,32-39 In our multivariate analyses, we
considered preoperative medical diseases that could be caused
by smoking as mediators. However, these conditions may be
confounders rather than mediators in some patients if smok-
ing did not contribute to their causation but influenced the de-
cision of the patient to continue or quit smoking. However, this
confounding does not affect the main estimate in our study,
ORadj = 0.89, which represents the true and nonmediated effect
of smoking.

Another potential limitation of this study was that we were
unable to control for hospital effects owing to the absence
of hospital identifiers in our data. Variability in hospital quality
or in surgical strategy may have confounded the association
between risk factors and outcome. Last, the ORadj of out-
comes that we reported attributable to smoking might be re-
garded as of modest clinical significance because the crude 30-
day outcome rates (cumulative incidence) in never smokers
are low (eg, 0.3% for myocardial infarction). However, such
adjusted increase in outcome rates in a large sample still means
that a considerable number of patients could have acute ad-
verse postoperative outcomes solely from the subclinical dam-
aging effects of smoking (eg, 675 myocardial infarctions dur-
ing the 2 years of the study). Moreover, our data included a wide
variety of patients and surgical procedures from various sur-
gical subspecialties with different crude outcome rates in never
smokers (eTable 4 in Supplement), and the adjusted esti-
mates of increased morbidity and mortality may be of higher
clinical significance in certain patient populations or surgical
procedures. Similarly, we reported adverse outcome rates ap-
plicable in a population with a case mix similar to that generat-
ed by the ACS NSQIP sampling strategy. If our findings are
to be extrapolated to settings with higher adverse outcome
rates, such relative increases would be of more apparent clin-
ical significance.

Studies show that hospitals do not consistently provide
smoking cessation services to their hospitalized patients, and
in most cases these services are restricted to adults admitted
for acute myocardial infarction, congestive heart failure, or
pneumonia.7 Our study should increase awareness of the det-
rimental effects of smoking—and the benefits of its cess-
ation—on morbidity and mortality in the surgical setting.
Surgical teams should thus be more involved in the ongoing
efforts to optimize measures for smoking control. Surgery
provides a teachable environment for smoking cessation.
Unlike the long-term consequences of smoking, the acute
consequences of smoking on patients’ postoperative out-
comes can provide a strong motive for quitting.45 The cost-
effectiveness of such interventions warrants further study.
Finally, the effects of other forms of tobacco smoking, such
as cigars, pipers, and water pipes, on surgical outcomes merit
evaluation.

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REFERENCES

Research  Original Investigation

Smoking and Postoperative Outcomes


