Risk of Respiratory Complications and Wound Infection in Patients Undergoing Ambulatory Surgery

Smokers versus Nonsmokers

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Background: Smoking is considered to be a risk factor for patients undergoing surgery and anesthesia, but it is unclear whether this is applicable to patients undergoing ambulatory surgery. The aim of this study was to determine the risk of respiratory complications and wound infection among smokers.

Methods: The authors studied a random selection of 489 adult patients undergoing ambulatory surgery. Smoking status was determined by self-report and confirmed with end-expired carbon monoxide analysis. The risk of respiratory complications (i.e., desaturation, cough, laryngospasm, bronchospasm, breath-holding, or apnea) and wound infection (i.e., wound redness or discharge ± positive microbial culture, requiring antibiotic therapy) in smokers versus nonsmokers was ascertained. Odds ratios were estimated from multivariable logistic regression and adjusted for age, gender, body mass index, partner's smoking status, domiciliary smoking exposure, and extent and duration of surgery.

Results: Most smokers continued to smoke up until the day of surgery. Smokers had a higher rate of respiratory complications (32.8% vs. 25.9%; adjusted odds ratio, 1.71; 95% confidence interval, 1.03–2.84; P = 0.038) and wound infection (3.6% vs. 0.6%; odds ratio, 4.3; 95% confidence interval, 1.58–17.5; P = 0.019). Odds ratios comparing current plus ex-smokers with nonsmokers were of similar magnitude for most of these complications.

Conclusions: Smoking was associated with an increased risk of respiratory complications and postoperative wound infection in ambulatory surgery patients. These findings warrant increased efforts at promoting smoking avoidance and cessation.

Most previous studies of perioperative risk associated with smoking were based on self-reporting and did not control for additional risk factors. Also, they may not represent current surgical and anesthetic practice. For example, there has been a marked increase in the proportion of surgery performed on an ambulatory (day-stay) basis, and this important group has not been previously studied. We therefore studied a broad range of patients undergoing ambulatory surgery and confirmed their smoking status with end-expired carbon monoxide (COexp) analysis.

Materials and Methods

Subjects

We studied 489 adult patients undergoing ambulatory surgery at a university teaching hospital from March 1999 to November 2000. Sequential eligible patients were identified each day, and a random selection, determined by a table of random numbers, was approached for inclusion in the study. Participation and refusal rates were recorded. Their smoking status was based on self-report and COexp analysis (Bedfont Micro Breathalyzer, Kent, United Kingdom) on the day of surgery. The COexp analyzer was recalibrated at 6-month intervals according to the manufacturer’s instructions, using 50 ppm CO gas; before each use the analyzer was set to zero in room air. Nonsmokers were those who had never smoked and had a COexp of ≤10 ppm, ex-smokers were those who reported having stopped smoking for more than 28 days, and current smokers were defined by self-report or a COexp greater than 10 ppm. Two analyses were undertaken: current smokers versus nonsmokers, and all-time (current plus ex-) smokers versus nonsmokers. A reduction in smoking was defined by the patients’ self-reported recent smoking history. All subjects provided informed consent, and the study protocol was approved by both the hospital and university ethics committees. Patients were identified and recruited on the day of surgery. Anesthesia was provided by specialist or trainee anesthesiologists in a university teaching hospital.

Study Design and Endpoints

This was a cohort study comparing smokers with nonsmokers. A preliminary estimate of sample size was based on an expected difference in respiratory compli-
cations between smokers (20%) and nonsmokers (10%) of 10%.9 We anticipated a study of 500 patients would provide a power of 90% (type I error 0.05, type II error 0.1; GraphPad StatMate V1.01, San Diego, CA). The primary endpoints were perioperative respiratory complications and postoperative wound infection.

Respiratory complications occurring intraoperatively and postoperatively in the postanesthesia care unit (PACU) were recorded onto a study case report form that included a definition for each complication, similar to that used previously8:

1. Arterial desaturation: pulse oximetry (SpO₂) less than 92% for more than 1 min
2. Severe coughing: more than two paroxysms or coughing more than 5 s
3. Laryngospasm: audible stridor or airway obstruction not relieved by airway manipulations
4. Bronchospasm: audible wheeze or unexplained increase in airway pressure
5. Recurrent apnea: more than 60 s
6. Use of an opioid antagonist (naloxone) in the PACU
7. Unplanned hospital admission caused by any respiratory event or condition.

The criteria for wound infection were modeled on those of the Centers for Disease Control and Prevention13 and included purulent discharge, redness, or serous discharge with positive microbial culture or requiring antibiotic therapy. In each case, independent verification by a health care provider was required. Pneumonia was defined by any new infiltrate on chest radiograph postoperatively, but no cases were reported in this study. Infection data were obtained via 7-day telephone follow-up of the patient, followed by review of the patient’s medical record or direct contact with the patient’s medical practitioner. Research staff conducting the follow-up were unaware of the patient’s smoking status.

Perioperative Measurements

Preoperative demographic, health, and smoking history data were recorded. Chronic obstructive pulmonary disease was defined by a history of emphysema or chronic bronchitis. On the day of surgery, each patient was instructed about the procedure of obtaining a CO_exp measurement and asked to provide an end-expired breath sample. Their SpO₂ while breathing room air was also obtained. SpO₂ cannot distinguish carboxyhemoglobin from oxyhemoglobin and so may overestimate arterial oxygen saturation in smokers. We therefore used CO_exp measurements to calculate adjusted SpO₂ using the conversion factor, 0.01(100 − CO_exp/6), to adjust for carboxyhemoglobin concentration (Bedfont Micro Breathalyser). Surgical data included extent and duration of surgery. The patient’s postoperative analgesia regimen was recorded because pain and opioid drugs may impair postoperative respiratory function.

Statistical Analysis

The potential association of smoking with protocol-defined respiratory complications and wound infection was evaluated using a chi-square test or Fisher exact test. Crude odds ratios (ORs) were calculated to measure the degree of association but do not account for differences in additional risk factors (confounding). For this reason we estimated adjusted ORs using multivariable logistic regression. Regression models included factors that were known or suspected of being associated with respiratory complications or wound infection. These factors included age, gender, body mass index, partner’s smoking status, domiciliary smoking exposure, and extent and duration of surgery. Selected interaction terms between age, gender, and previous smoking were explored but were not significant. Numerical data were compared using unpaired t test (two-tailed) or Wilcoxon rank sum test, as appropriate. The correlation between CO_exp and cigarette consumption was calculated using Spearman ρ. All statistical analyses were performed using SPSS for Windows V10.1 (SPSS Ltd., Chicago, IL). A P value < 0.05 was considered significant.

Results

We approached 537 patients, and 521 (97%) consented to the study; 18 patients were excluded because of canceled or ineligible surgery (e.g., endoscopy), and 14 patients were excluded because their procedure was performed with local anesthesia. This left 489 patients in the study. Five patients had stopped smoking within 28 days of surgery, a further patient was found to have a CO_exp greater than 10 ppm; these were reclassified as current smokers. The prevalence of current smokers in our study population was 41%. Current smokers were younger, less well-educated, more likely to live with a smoker, and their partner was more likely to be a smoker (table 1). Current smokers had a lower adjusted SpO₂ when compared with nonsmokers and were more likely to have a history of chronic obstructive pulmonary disease, chronic cough, and coronary artery disease. Nonsmokers, ex-smokers, and current smokers underwent similar types of surgical procedures, of similar extent and duration. They received equivalent perioperative analgesia.

Current smokers had a higher rate of respiratory complications (adjusted OR, 1.71; 95% confidence interval [CI], 1.03–2.84; P = 0.038) and postoperative wound infection (adjusted OR, 16.3; 95% CI, 1.58–175; P = 0.019; table 2). Two patients (both ex-smokers) were treated with naloxone in the PACU, but the event rate was too low to calculate reliable risk estimates. There were no unplanned hospital admissions caused by any respiratory event in the study cohort. ORs comparing current smokers and ex-smokers with nonsmokers were of similar magnitude for most respiratory complications.
and wound infection (table 3). Nonsmokers with a partner who was a smoker had increased risk of respiratory complications (adjusted OR, 2.65; 95% CI, 0.95–7.36), but this was not statistically significant (P/H110050.061).

Post hoc analysis identified obesity (body mass index > 30 kg/m²) as a significant covariate for respiratory complications (OR, 1.78; 95% CI, 1.1–2.9; P = 0.023) and wound infection (OR, 4.27; 95% CI, 1.3–14; P = 0.011). Partner’s smoking status was also a significant covariate (smoker OR, 1.62; 95% CI, 1.02–2.57; P = 0.043).

Most current smokers had their elective ambulatory surgery booked within 6 weeks of assessment by their surgeon and had subsequently received advice to stop smoking (table 4). In most cases this occurred through their hospital notification letter advising them of their date of surgery. Only 6 patients (3.0%) recalled receiving such advice from their general practitioner and 13 (6.5%) from their surgeon. Despite this, only five smokers reported they had stopped smoking after being informed they were to undergo elective surgery.

In our cohort, 71% of current smokers and 42% of ex-smokers had undergone previous surgery as a smoker (table 5). Most (64%) current smokers had attempted to stop smoking on at least one occasion. There was a
strong correlation between CO_{ex}p and reported current daily cigarette consumption ($p = 0.74$, $P < 0.0005$). All patients who reported they were nonsmokers had a CO_{ex}p level of 10 ppm or less (sensitivity of self-reporting 100%). Of the 200 patients who reported they were current smokers, 101 had a CO_{ex}p level greater than 10 ppm (sensitivity of CO_{ex}p 51%).

Three of seven patients (43%) who reported they had stopped smoking within 1 month of surgery had respiratory complications.

### Discussion

We found that smokers undergoing ambulatory surgery do indeed have a higher rate of perioperative complications. They were more likely to suffer respiratory complications in the operating room and in the PACU; these consisted mainly of coughing, laryngospasm, bronchospasm, apnea, and breath-holding. Nevertheless, these adverse respiratory events were not associated with arterial desaturation in the operating room or PACU. This could possibly be explained by the immediate, expert attention by the anesthesiologist and PACU staff available in these areas, who were able to avoid more serious morbidity. This study was not designed to identify a difference in rates of serious events that are known to be rare in contemporary anesthetic practice, and so we cannot exclude an increased risk in smokers.

Our findings are consistent with previous reports of patients undergoing more extensive surgery1-11,14 and offer greater surety in view of CO_{ex}p confirmation of current smoking status. We could find little benefit for those who had stopped smoking in the past (other than a reduction in risk of laryngospasm and bronchospasm). In view of a median duration of smoking in ex-smokers of 10 yr, this may reflect irreversible lung damage and propensity to respiratory complications in many ex-smokers.

We also found an increased risk of wound infection, despite this being uncommon after ambulatory surgery. The marked increase in risk is consistent with findings from several other studies.6,7,15 Kurz et al.,7 in an exploratory analysis of a randomized trial of maintenance normothermia, found that smokers were more likely to have wound infection after colorectal surgery (OR, 10.5; 95% CI, 3.2-34; $P = 0.004$). Fawcett et al.,15 also in patients undergoing colorectal surgery, found that anastomotic breakdown was more common in smokers (OR, 7.3; $P < 0.005$). Moller et al.11 tested the effect of a 6-8-week smoking intervention program on smokers undergoing orthopedic joint replacement surgery and found a significant reduction in wound infection (OR,

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**Table 2. Incidence of Respiratory Complications in the Operating Theater and Postanesthesia Care Unit and 7-day Postoperative Wound Infection: Current Smokers versus Nonsmoker**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Nonsmokers (n = 173)</th>
<th>Current Smokers (n = 200)</th>
<th>Univariate OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coughing</td>
<td></td>
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<tr>
<td>Arterial desaturation (SpO_2 &lt; 92%)</td>
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<tr>
<td>Laryngospasm or bronchospasm</td>
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<tr>
<td>Apnea or breath-holding</td>
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<tr>
<td>Any respiratory complication</td>
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<tr>
<td>Wound infection</td>
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</table>

Data are presented as number (%).

OR = odds ratio (adjusted for age, gender, partner’s smoking status, domiciliary smoking exposure, and extent and duration of surgery); SpO_2 = pulse oximetry oxygen saturation.

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**Table 3. Incidence of Respiratory Complications in the Operating Theater and Postanesthesia Care Unit and 7-day Postoperative Wound Infection: Ex-smokers and Current Smokers versus Nonsmokers**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Ex (n = 116)</th>
<th>Current (n = 200)</th>
<th>Univariate OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coughing</td>
<td></td>
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<tr>
<td>Arterial desaturation (SpO_2 &lt; 92%)</td>
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<td>Apnea or breath-holding</td>
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<tr>
<td>Any respiratory complication</td>
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<tr>
<td>Wound infection</td>
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</tbody>
</table>

Data are presented as number (%).

OR = odds ratio (adjusted for age, gender, body mass index, partner’s smoking status, domiciliary smoking exposure, and extent and duration of surgery); SpO_2 = pulse oximetry oxygen saturation.
Table 4. Advice to Stop Smoking Given to Current Smokers and Their Preoperative Smoking Behavior

<table>
<thead>
<tr>
<th>Advice to stop smoking by:</th>
<th>Current Smokers (n = 200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration on the waiting list (days)</td>
<td>26 (8–48)</td>
</tr>
<tr>
<td>No. of smokers waiting &gt; 6 weeks</td>
<td>56 (28%)</td>
</tr>
<tr>
<td>Advised to stop smoking by:</td>
<td></td>
</tr>
<tr>
<td>General practitioner</td>
<td>131 (66%)</td>
</tr>
<tr>
<td>Surgeon</td>
<td>6 (3.0%)</td>
</tr>
<tr>
<td>Hospital letter</td>
<td>121 (61%)</td>
</tr>
<tr>
<td>Other</td>
<td>19 (9.5%)</td>
</tr>
<tr>
<td>Had a cigarette in last 2 days</td>
<td>193 (96.5%)</td>
</tr>
</tbody>
</table>

Data presented as median (interquartile range) or number (%).

0.16; 95% CI, 0.05–0.52; P = 0.001). The cost of surgical wound infection in more extensive surgery has been estimated to be more than US$3,000 per episode, accurate cost data are not available for ambulatory surgery.

It is noteworthy that we also identified obesity as a risk factor for respiratory complications and wound infection. We adjusted for this in our analyses and each group were of similar body mass index, and so concurrent obesity does not explain the adverse effects of smoking. However, it supports the view that the prevention and treatment of obesity is another factor that could reduce the risks associated with anesthesia and surgery. Non-smokers with a partner who was a smoker had a higher risk of respiratory complications, suggesting a possible adverse effect of passive smoking.

Forrest et al. compared four anesthetic regimens in a randomized trial of 17, 201 patients and noted that self-reported smoking was a risk factor (adjusted OR, 1.54) for severe respiratory adverse events that required therapeutic intervention. Schwilk et al., in a retrospective analysis of a database of 26,961 adult patients undergoing general anesthesia, reported a relative risk of 1.8 for perioperative respiratory adverse events for smokers. The risk was increased in young smokers and those who were obese. Bluman et al. surveyed the smoking habits of 410 adult (mostly male) patients undergoing noncardiac surgery and found a greater than fourfold increased risk of respiratory complications. These reports are consistent with other smaller studies. One of the main deficiencies of most previous studies is that they did not adjust for confounding or verify reported smoking status, and so our study provides reliable data.

A patient’s personal smoking history is not the only relevant factor. Skolnick et al. measured urine cotinine concentrations, a nicotine metabolite and marker of passive smoking, in 602 children undergoing general anesthesia and found a greater than twofold increased risk of respiratory complications in those children exposed to environmental tobacco smoke. In our study we found that the patients’ partner’s smoking status is an independent risk factor for perioperative respiratory complications, suggesting an adverse effect of passive smoking in our setting.

One of the interesting findings from the studies of Warner et al. and Bluman et al. was that smokers who had stopped smoking within a few weeks of their elective surgery were more likely to develop perioperative respiratory complications. This has previously been attributed to a transient increased sputum production. Kotani et al. recently found that smokers may require more than 6 months to regain alveolar macrophage antimicrobial function, including gene expression of proinflammatory cytokines, equivalent to that of nonsmokers. This is one explanation of why smokers have higher rates of respiratory complications and require at least a 2-month smoke-free interval. But there may be a selection bias in studies reporting recent quitters having an increased risk of respiratory complications, in that smokers who were most at risk were perhaps more likely to be advised to stop or reduce their smoking behavior preoperatively—this bias will overestimate risk. In our study, patients who reported they had stopped smoking within 1 month of surgery appeared to have a similar rate of respiratory complications, but conclusions regarding this factor cannot be determined because of the small numbers involved (n = 3).

Smoking impairs mucus transport and pulmonary macrophage function, increases bronchial reactivity, reduces the closing capacity of the lung, and increases arterial carbon monoxide levels. These adverse effects can explain the increased susceptibility to pulmonary complications. Our study confirms that smokers have higher rates of wound infection. Tobacco smoke contains many toxic substances known to impair wound healing. Nicotine is a potent vasoconstrictor and can induce wound ischemia. Carbon monoxide reduces oxygen transport and metabolism. Cyanide inhibits mitochondrial oxidative metabolism. These, and others, would be major contributing factors to tissue ischemia, wound breakdown, and infection.

Table 5. Number of Quit Attempts and Previous Operations in Smokers

<table>
<thead>
<tr>
<th>No. of quit attempts</th>
<th>Ex-smokers (n = 116)</th>
<th>Current Smokers (n = 200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>71 (36%)</td>
</tr>
<tr>
<td>1–2</td>
<td>85 (72%)</td>
<td>82 (41%)</td>
</tr>
<tr>
<td>3–4</td>
<td>20 (17%)</td>
<td>23 (12%)</td>
</tr>
<tr>
<td>5–8</td>
<td>8 (7%)</td>
<td>14 (7%)</td>
</tr>
<tr>
<td>≥ 9</td>
<td>5 (4%)</td>
<td>8 (4%)</td>
</tr>
</tbody>
</table>

Data presented as number (%).

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In our setting, self-reporting of smoking status was reliable in that all self-reported nonsmokers and ex-smokers had a COexp level ≤10 ppm. This is of interest in that an earlier observation reporting experience of subjects volunteering for phase I clinical trials found that 25% of self-reported nonsmokers were positive for cotinine, indicating recent exposure to tobacco smoke. Naturally these represent two very different populations, but it appears that ambulatory surgical patients can be relied on to accurately report their smoking status.

Many smokers in this study had undergone previous operations as smokers, and so opportunities existed to counsel smoking cessation. The original condition leading to hospitalization and surgery may also be related to smoking-related disease. It has been estimated that 20 million anesthetics are administered each year in the United States; approximately 25% of surgical patients smoke and a further 25% are ex-smokers. This suggests that a significant amount of perioperative morbidity can be prevented, a view supported by a recent randomized trial. There are several limitations to our study. The patient’s smoking status was generally known by the clinical staff, and as the adverse respiratory event data were collected by the anesthesiologist intraoperatively and by the nursing staff in the PACU, this introduces the potential for detection and reporting bias. However, we did not make explicit to these staff the purpose of our study, and each adverse event was clearly defined on the case report form. Pulse oximetry data were equivalent, which we attribute to prompt and expert attention within the operating room and PACU; this supports minimal detection bias. All 7-day septic complication data were collected by research staff who were masked to smoking status and guided by the predetermined criteria. There were no serious adverse events reported, which is to be expected in relatively well patients undergoing ambulatory surgery. This study was not designed to estimate the risk of these rare events. The low rate of wound infection does not allow reliable estimation of adjusted ORs. Observational studies are not the best method to identify causative factors. We have found that smoking is associated with a number of perioperative complications, but there may be other explanations of why such a relation exists. Nevertheless, other than the expected imbalance of demographic factors (education level, cohabitation with a smoker, existence of smoking-related conditions), there were no other significant differences between smokers and nonsmokers. Relevant factors, other than American Society of Anesthesiologists physical status and smoking-related conditions (which are directly affected by smoking), were included in the multivariable models. Clearly there are compelling explanations of why smoking may cause such respiratory complications.

In conclusion, a history of current or previous smoking was associated with respiratory complications and postoperative wound infection in ambulatory surgical patients. Most smokers continue to smoke up until the time of surgery. A realization that smoking is associated with increased risks, even in young smokers, warrants increased efforts at promoting smoking avoidance and cessation.

References
25. Hill D, Borland R: Are doctors doing enough to stop their patients smoking? Med J Aust 1989; 150:413–4

Anesthesiology, V 97, No 4, Oct 2002