Risk of Perioperative Respiratory Complications and Postoperative Morbidity in a Cohort of Adults Exposed to Passive Smoking

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Objective: To evaluate the risks of perioperative respiratory complications and postoperative morbidity associated with active and passive cigarette smoking.

Background: Environmental tobacco smoke is associated with perioperative respiratory events in children, but its effect in adults is unknown.

Methods: We conducted a cohort study of 736 adult patients receiving general anesthesia for major elective surgery. Patients were classified according to their self-reported smoking history and urinary cotinine concentration within 48 hours before surgery. The main outcomes were composite measures of perioperative respiratory complications and postoperative morbidity on the third day after surgery.

Results: There were 313 (42.5%) never-smokers (reference group), 92 (12.5%) passive nonsmokers, 157 (21.3%) ex-smokers without environmental tobacco smoke exposure, 53 (7.2%) passive ex-smokers, and 121 (16.4%) smokers. The incidence of perioperative respiratory complications and postoperative morbidity was 9.5% [95% confidence interval (CI), 7.5–11.8] and 29.2% (95% CI, 26.0–32.6), respectively. Smoking was significantly associated with an increased risk of perioperative respiratory complications [relative risk (RR), 4.40; 95% CI, 2.20–8.80] and postoperative morbidity (RR, 1.86; 95% CI, 1.22–2.83). Although passive smoking was not associated with the risk of perioperative respiratory complications, the risk of postoperative morbidity was increased in passive nonsmokers (RR, 1.51; 95% CI, 1.04–2.21) and passive ex-smokers (RR, 2.21; 95% CI, 1.39–3.50).

Conclusions: One in 5 adults was exposed to environmental tobacco smoke before surgery. Passive cigarette smoking showed very little, if any, increased risk of perioperative respiratory complications. Both active exposure and passive exposure to cigarette smoke increased the risk of postoperative morbidity.

Keywords: cohort study, environmental tobacco smoke, postoperative outcomes, respiratory, risk

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Cigarette smoking is a preventable cause of perioperative respiratory complications, wound infection, myocardial infarction, stroke, and mortality.[1–3] Postoperative respiratory complications in smokers contribute to marginally higher inpatient costs than in never-smokers [relative cost, 1.04; 95% confidence interval (CI), 1.00–1.07].[4] Many smokers (17%) deny recent tobacco use before surgery.[5] As most perioperative smoking studies[1,3,6,7] have relied on self-reported smoking history, the risks of perioperative complications are likely to be underestimated.

Previous studies have established a strong association between environmental tobacco smoke (ETS) exposure in children receiving general anesthesia and respiratory complications.[8,9] However, the effect of passive smoking before surgery in adults on perioperative outcomes has not been evaluated extensively.

The main objective of this study was to evaluate the association between active and passive cigarette smoking on the risk of perioperative respiratory complications and postoperative morbidity. The secondary objectives were to determine whether there were differences in the quality of recovery (QoR) and health-related quality of life on the third day after surgery between the different smoking status groups.

METHODS

Study Design and Sample

The Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee approved the research protocol for this prospective cohort study at the Prince of Wales Hospital, a large university teaching hospital in Hong Kong. All patients gave written informed consent before surgery.

Patients were included if they were undergoing major and complex elective orthopedic surgery, general surgery, urological surgery, and cardiac surgery. The specific types of surgical procedures included in this study were the same as those in previous studies that had validated the Postoperative Morbidity Survey (POMS) tool.[10,11] Patients undergoing other types of surgery, given only regional anesthesia, unable to give written informed consent, receiving nicotine replacement therapy, having chronic renal failure, or were younger than 18 years were not included. We also excluded patients with urine samples collected more than 48 hours before surgery to minimize bias in exposure assessment.

Assessment of Smoking

Patients were interviewed by the research staff within 48 hours before surgery using a standardized questionnaire. The patients were asked about their current ("Do you currently smoke?") and past smoking history ("Did you smoke in the past?"). Current smokers and ex-smokers were also asked to recall when they smoked their last cigarette.

For ETS exposure at work, we asked patients, "In the place you work (in the same office, shop floor, or about 10 feet around you), does anyone smoke (including coworkers and other people)? If yes, how many (not including you)?"[12] Similarly, ETS exposure at home was ascertained by asking the patient, "In the past month, among those who lived with you in the same household or unit, did anyone

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smoke in the household or unit? If yes, how many (not including you)?"[12] The laboratory staff and the anesthesiologist were blinded to the smoking history data collected by the research staff.

Urinary cotinine, a biomarker for tobacco smoke exposure, has a relatively long half-life (~20 hours).[13] However, it is not routinely measured as part of the preoperative anesthesia consultation. A sample of urine was obtained on the same day after the questionnaire was completed. The urinary cotinine concentration was measured using liquid chromatography–tandem mass spectrometry analysis (API 2000 system; AB SCIEX, Foster City, CA). When a patient's cotinine concentration was below 0.20 ng/mL (lowest limit of detection), we assumed that nondetects were 0.10 ng/mL (half of detection limit).[14] We also adjusted the cotinine level for creatinine concentration.[15] We used thresholds at 50 and 550 ng/mL of urinary cotinine for discriminating between nonsmokers, passive smokers, and current smokers.[16] Because a recent systematic review found that smoking cessation more than 8 weeks before surgery greatly reduced the risk of respiratory complications to a level comparable with nonsmokers,[17] we used this cutoff to define current smokers and ex-smokers.

Smoking Status

We used patients' self-reported smoking exposure and the adjusted urinary cotinine concentration to classify the patients into one of the following groups:

1. Never-smoker (urinary cotinine <50 ng/mL with no ETS history) as the reference group for statistical analyses.
2. Passive nonsmoker (never-smoker with an adjusted urinary cotinine concentration of <550 ng/mL and a positive ETS history).
3. Ex-smoker with no ETS exposure (ex-smoker with smoking cessation >2 months before surgery with an adjusted urinary cotinine concentration of <550 ng/mL and no ETS history).
4. Passive ex-smoker (ex-smoker with smoking cessation >2 months before surgery with an adjusted urinary cotinine concentration of <550 ng/mL and a positive ETS history).
5. Smoker (no smoking cessation within 2 months before surgery or had an adjusted urinary cotinine concentration of ≥550 ng/mL).

Perioperative Outcomes Measures

Primary Composite Measures

The first primary outcome was a composite measure of perioperative respiratory complications (arterial desaturation, severe coughing, laryngospasm, bronchospasm, recurrent apnea, airway secretions, new chest radiographical changes, use of naloxone, unplanned intensive care unit admission).[2] The procedural anesthesiologist recorded any respiratory events during surgery or in the postanesthesia care unit (PACU) (Table 1) using a standardized collection form and was unaware of the urinary cotinine concentration results.

The research staff collected the second composite outcome-POMS[10,11] on postoperative day 3. The POMS included pulmonary, infectious, renal, gastrointestinal, cardiovascular, neurological, hematological, wound, and pain events (Table 1) that occurred on postoperative day 3.

Secondary Measures

We measured the QoR score on postoperative day 3 using the 9-item Quality of Recovery questionnaire.[18,19] The QoR score ranged from 0 to 18, with higher scores reflecting better recovery. In addition, the health-related quality of life was measured on postoperative day 3 using the Chinese version (Hong Kong) EuroQol EQ-5D. The patients were asked to rate 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension had 3 response levels: no problems, some problems, and extreme problems.[20] Patients were also asked to rate how good or bad their health state was on a visual analog scale from 0 (worst imaginable) to 100 (best imaginable).[20] The EQ-5D index, a preference/utility-based measure, was estimated by using the descriptive responses and applying the US set of reference weights.[21]

TABLE 1. Definitions of Outcomes Adapted From Previous Studies

Perioperative respiratory	
Arterial saturation	Pulse oximetry Spo_2 <92% for >1 min[2]
Severe coughing	>2 paroxysms or coughing >5 s[2]
Laryngospasm	Audible stridor or airway obstruction not relieved by airway manipulations[2]
Bronchospasm	Audible wheeze or unexplained increase in airway pressure[2]
Recurrent apnea	>1 min[2]
Airway secretions	Secretions requiring suctioning of endotracheal tube or laryngeal mask airway
Chest X-ray changes	New perioperative chest radiographical changes
Use of opioid antagonist	Use of naloxone[2]
Unplanned ICU admission	Direct emergency admission to the ICU from the operating theatre or PACU
POMS events	
Pulmonary	Patient has developed a new requirement for oxygen or respiratory support[10]
Infectious	Currently on antibiotics/or has had a temperature of >38°C in the last 24 h[10]
Renal	Presence of oliguria <500 mL/24 h; increase serum creatinine (>30% from preoperative level); urinary catheter in-situ[10]
Gastrointestinal	Unable to tolerate an enteral diet for any reason including nausea, vomiting, and abdominal distension (use of antiemetics)[10]
Cardiovascular	Diagnostic tests or therapy within the last 24 h for any of the following: new myocardial infarction or ischaemia, hypotension (requiring fluid therapy >200 mL/h or pharmacological therapy), atrial or ventricular arrhythmias, cardiogenic pulmonary oedema, thrombotic event (requiring anticoagulation)[10]
Neurological	New focal neurological deficit, confusion, delirium, or coma[10]
Hematological	Requirement for any of the following within the last 24 h: pack erythrocytes, platelets, fresh frozen plasma, or cryoprecipitate[10]
Wound	Wound dehiscence requiring surgical exploration or drainage of pus from the operation wound with or without isolation of organisms[10]
Pain	New postoperative pain significant enough to require parenteral opioids or regional analgesia[10]

From Myles et al[2] and Grocott et al.[10]
ICU indicates intensive care unit; Spo_2, oxygen saturation as measured by pulse oximetry.

Statistical Analysis

Descriptive data are given as percentages, mean with standard deviation, and median with interquartile range. Ninety-five percent CIs were calculated around the prevalence estimates for passive smokers. Analysis of variance was used to compare the mean age, duration of anesthesia, and duration of PACU stay between smoking status groups. An independent-samples Jonckheere-Terpstra test was used to examine the dose-response relationship of the median adjusted cotinine concentration among the 5 smoking status groups. An appropriate χ^2 test or exact test was used to compare the incidence of individual components of perioperative respiratory complications and POMS between the smoking status groups. A Bonferroni correction was used to adjust for multiple testing of individual events. The significance criterion for individual perioperative respiratory complications and POMS components was set at $P < 0.0042$ (ie, 0.05/12) and $P < 0.0056$ (ie, 0.05/9), respectively.

Poisson regression models were used to estimate the association between smoking status and the composite endpoints of perioperative respiratory complications and POMS without adjustment to covariates. A generalized estimating equation (GEE) model with a Poisson distribution, log-link function, and exchangeable correlation was used to obtain a common-effect relative risk (RR) of perioperative respiratory complications associated with smoking status after adjusting for demographic (age, sex) and clinical characteristics (American Society of Anesthesiologists' Physical Status,[22] magnitude of surgery, surgical specialty, and preexisting respiratory disease). These covariates in the GEE model were chosen for clinical relevance and on the basis of uncorrected *P* value less than 0.10 of the univariate tests. The common-effect RR from the GEE model[23] assumes that there is a single common exposure effect across all components used in the perioperative respiratory composite endpoint. A similar GEE model was used to estimate the common-effect RR of POMS associated with smoking status. Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test. The discrimination of the model was assessed by estimating the area under the receiver operating characteristic curve (AUROC). We also examined the dose-response relationship between the adjusted urinary cotinine concentration and the common-effect RR of the primary outcomes using GEE models.

We compared the mean QoR and health-related quality-of-life (EQ-5D) scores between smoking status groups using analysis of variance after adjusting for age, sex, American Society of Anesthesiologists' Physical Status, and magnitude of surgery. If significant, a Student *t* test was used to compare the different smoking groups with never-smokers. STATA (version 12.1) software (STATA Corp, College Station, TX) was used for all analyses.

Using PASS (version 8.06) software (NCSS, Kaysville, UT), a Poisson regression of respiratory complications on smoking exposure (of which 10% are in the group of passive smokers at home or at work and 90% are not passive smokers at home or at work)[12] with a sample size of 726 observations will achieve 80% power at a 5% significance level to detect a change in baseline rate of 19% (nonsmokers) to 43% (expected risk in passive smokers), a change corresponding to an RR of 2.25.[24] Adjusting for some loss to follow-up (2%), the total sample size estimated was 750 patients.

RESULTS

Of the 888 consecutive patients screened for inclusion between January 5, 2011, and January 14, 2013, 136 were not eligible (32 refusals, 26 unable to provide written informed consent, 24 provided no urine sample before surgery, 23 not available in the ward at the time of recruitment, 16 had renal impairment, and 15 already participated in the study). After 752 patients provided written informed consent for the study, 16 patients had surgery cancelled on the day of surgery after providing a sample of urine. Of the 736 patients with perioperative data, 711 (96.6%) were able to rate their QoR score and the level of health-related quality of life on postoperative day 3.

There were 313 (42.5%) never-smokers, 92 (12.5%) passive nonsmokers, 157 (21.3%) ex-smokers without ETS exposure, 53 (7.2%) passive ex-smokers, and 121 (16.4%) smokers. The demographic and perioperative characteristics are shown in Table 2. More than half of the smokers (52.1%) reported having smoked a cigarette within 24 hours of surgery.

The prevalence of passive smoking was 19.7% (95% CI, 16.9–22.7). Of the 145 patients exposed to ETS, 101 (69.7%) were exposed at home and 50 (34.5%) at work. Six patients (4.1%) were exposed to ETS at both places. The median number of smokers both at home and at work was 1 (interquartile range, 1–1) and 2.5 (interquartile range, 2–4), respectively. There was a significant trend ($P < 0.001$) in the median cotinine concentration (ng/mL) between smoking status groups (Table 2).

The individual perioperative respiratory events are shown in Table 3. Only intraoperative airway secretions met our a priori criteria for statistical significance (Table 3). Compared with never-smokers, smokers had an increased risk of intraoperative airway secretions (RR, 4.85; 99.6% CI, 1.33–21.24). No intraoperative new chest radiographical changes or PACU bronchospasm was recorded. The overall incidence of perioperative respiratory complications was 9.5% (95% CI, 7.5–11.8).

The individual POMS events on postoperative day 3 are shown in Table 4. The most common postoperative morbidity was gastrointestinal, mostly postoperative nausea and vomiting. However, none of the individual POMS events met our a priori criteria for statistical significance in the comparison of smoking status groups (Table 4). The overall incidence of POMS events was 29.2% (95% CI, 26.0–32.6).

The estimated unadjusted RR and common-effect RR for the association between smoking status and perioperative respiratory complications are shown in Table 5. Overall, smoking status was associated with an increased risk of perioperative respiratory complications using the univariate ($P = 0.002$) and multivariate models ($P < 0.001$). Compared with never-smokers, smokers had a significantly increased risk of perioperative respiratory complications after adjusting for covariates (common-effect RR, 4.40; 95% CI, 2.20–8.80) whereas passive nonsmokers and passive ex-smokers did not (Table 5). The multivariate GEE model had adequate fit (Hosmer-Lemeshow test, 9 *df*; $P = 0.61$) and good discrimination (AUROC = 0.84; 95% CI, 0.79–0.89). The dose-response relationship between adjusted urinary cotinine concentration and adjusted risk of perioperative respiratory complications was significant ($P < 0.001$) and is shown in Figure 1.

Smoking status was not associated with POMS events on univariate Poisson regression analysis ($P = 0.20$). However, there was a significant difference between smoking status groups in the multivariate GEE model ($P = 0.004$). Compared with never-smokers, active and passive smokers had a significantly increased risk of POMS events after adjusting for covariates (Table 5). The multivariate model had adequate fit (Hosmer-Lemeshow test, 9 *df*; $P = 0.37$) and good discrimination (AUROC = 0.80; 95% CI, 0.77–0.83). However, the dose-response relationship between adjusted urinary cotinine concentration and adjusted risk of POMS events was not significant ($P = 0.13$).

There was a significant difference between smoking status groups in the adjusted mean QoR score ($P < 0.001$) and EQ-5D index ($P = 0.002$) but not for EQ-5D visual analog scale score ($P = 0.11$). Compared with never-smokers, the adjusted mean QoR score was significantly lower in all groups (all *P*s < 0.01; Table 6). The adjusted mean EQ-5D index in ex-smokers with or without ETS exposure and smokers were lower than never-smokers (all *P*s < 0.03;

TABLE 2. Demographic and Perioperative Characteristics by Smoking Status

Characteristics	Never-smoker (n = 313)	Passive Nonsmoker (n = 92)	Ex-smoker (n = 157)	Passive Ex-smoker (n = 53)	Smoker (n = 121)	*P*
Age, mean (SD), yr	61.8 (11.6)	57.4 (12.8)	65.4 (9.8)	56.5 (11.2)	56.5 (10.5)	<0.001
Male, n (%)	152 (49)	39 (42)	149 (95)	49 (92)	108 (89)	<0.001
Education level, n (%)						
No formal/primary	125 (40)	41 (45)	89 (57)	20 (38)	65 (54)	
Secondary	140 (45)	39 (42)	62 (39)	31 (58)	48 (40)	<0.001
College/university	48 (15)	12 (13)	6 (4)	2 (4)	8 (7)	
Asthma or COPD	7 (2)	5 (5)	12 (8)	3 (6)	8 (7)	0.04
Adjusted cotinine, median (IQR),* ng/mL	0.56 (0.19–0.95)	1.04 (0.29–1.88)	0.71 (0.27–1.57)	1.36 (0.57–2.79)	570 (83–1457)	<0.001
ASA Physical Status, n (%)						
I	59 (19)	18 (20)	10 (6)	7 (13)	26 (21)	
II	179 (57)	56 (61)	93 (59)	24 (45)	71 (59)	<0.001
III/IV	75 (24)	18 (20)	54 (34)	22 (42)	24 (20)	
Type of surgery, n (%)						
General	153 (49)	46 (50)	89 (57)	21 (40)	78 (64)	
Orthopedic	69 (22)	22 (24)	15 (10)	9 (17)	17 (14)	0.001
Cardiac	51 (16)	12 (13)	34 (22)	16 (30)	10 (8)	
Urology	40 (13)	12 (13)	19 (12)	7 (13)	16 (13)	
Magnitude of surgery, n (%)						
Major	50 (16)	22 (24)	24 (15)	6 (11)	30 (25)	0.06
Complex	263 (84)	70 (76)	133 (85)	47 (89)	91 (75)	
Duration of anesthesia, mean (SD), min	260 (122)	253 (109)	282 (119)	272 (86)	272 (114)	0.27
Duration of PACU, mean (SD), min	70 (35)	66 (28)	72 (33)	75 (34)	72 (40)	0.74

*Adjusted for urine creatinine concentration.
ASA indicates American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; IQR, interquartile range.

TABLE 3. Incidence of Individual Components of Perioperative Respiratory Complications in the Operating Theatre and PACU by Smoking Status

Events	Never-smoker (n = 313)	Passive Nonsmoker (n = 92)	Ex-smoker (n = 157)	Passive Ex-smoker (n = 53)	Smoker (n = 121)	*P**
During surgery						
Arterial desaturation, n (%)	1 (0.3)	0	3 (1.9)	0	2 (1.7)	0.22
Severe coughing, n (%)	1 (0.3)	0	0	0	2 (1.7)	0.29
Laryngospasm, n (%)	1 (0.3)	1 (1.1)	0	0	0	0.44
Bronchospasm, n (%)	5 (1.6)	0	4 (2.5)	1 (1.9)	6 (5.0)	0.14
Airway secretions, n (%)	8 (2.6)	5 (5.4)	8 (5.1)	3 (5.7)	15 (12.4)	0.002
During PACU						
Arterial desaturation, n (%)	1 (0.3)	0	0	0	0	0.79
Severe coughing, n (%)	0	0	1 (0.6)	0	2 (1.7)	0.14
Laryngospasm, No. (%)	1 (0.3)	0	0	0	0	0.79
Airway secretions, n (%)	1 (0.3)	1 (1.1)	0	0	4 (3.3)	0.03
New chest x-rays changes, n (%)	1 (0.3)	0	1 (0.6)	1 (1.9)	0	0.36
Naloxone administration, n (%)	0	1 (1.1)	0	0	1 (0.8)	0.14
Unplanned ICU admission, n (%)	0	0	1 (0.6)	0	2 (1.7)	0.14

*To control for type I error at 0.05 from multiple comparisons, $P < 0.004$ was considered significant.
ICU indicates intensive care unit.

Table 6). One never-smoker and 1 passive ex-smoker had died at 30 days after surgery.

DISCUSSION

Using a combination of self-reported smoking exposure and adjusted urinary cotinine concentration, 1 in 5 adult patients undergoing major and complex elective surgery in Hong Kong had been exposed to ETS, mainly from other smokers living at home. The adjusted cotinine concentrations in the passive nonsmokers and passive ex-smokers appeared higher than never-smokers and ex-smokers, suggesting that the smoking status misclassification was likely to be minimal.

Passive smoking was not associated with a higher risk of perioperative respiratory complications. This finding is in contrast to previous studies, where passive smoking was associated with respiratory events occurring at the induction of anesthesia (unadjusted RR, 2.25; 95% CI, 1.02–4.98)[24] or likely to be associated with respiratory complications in the perioperative period (adjusted OR, 2.65; 95% CI, 0.95–7.36; $P = 0.061$).[2] Differences in the surgical population, classification of smoking status groups, and the underlying smoking prevalence may account for these different findings.

Our results suggest that the association between ETS and perioperative respiratory complications is weaker than previous studies.[2,24] Decreasing smoking prevalence and daily cigarette

TABLE 4. Incidence of Individual Components of POMS on Third Day After Surgery by Smoking Status

Events	Never-smoker (n = 313)	Passive Nonsmoker (n = 92)	Ex-smoker (n = 157)	Passive Ex-smoker (n = 53)	Smoker (n = 121)	P*
Pulmonary, n (%)	1 (0.3)	0	5 (3.2)	0	3 (2.5)	0.03
Infectious, n (%)	21 (6.7)	5 (5.4)	10 (6.4)	4 (7.5)	11 (9.1)	0.85
Renal, n (%)	4 (1.3)	0	1 (0.6)	1 (1.9)	3 (2.5)	0.47
Gastrointestinal, n (%)	45 (14.4)	25 (27.2)	28 (17.8)	15 (28.3)	27 (22.3)	0.02
Cardiovascular, n (%)	3 (1.0)	2 (2.2)	6 (3.8)	0	2 (1.7)	0.21
Neurological, n (%)	7 (2.2)	1 (1.1)	4 (2.5)	1 (1.9)	2 (1.7)	0.97
Hematological, n (%)	11 (3.5)	2 (2.2)	5 (3.2)	2 (3.8)	6 (5.0)	0.87
Wound, n (%)	2 (0.6)	0	1 (0.6)	0	1 (0.8)	0.96
Pain, n (%)	2 (0.6)	1 (1.1)	3 (1.9)	0	2 (1.7)	0.60

*To control for type I error at 0.05 from multiple comparisons, $P < 0.006$ was considered significant.

TABLE 5. Association Between Active and Passive Smoking and Composite Endpoints

	Incidence (%)	Unadjusted RR (95% CI)*	Common-Effect RR (95% CI)	P
Perioperative respiratory complications				
Nonsmoker	17 (5.4)	1.00	1.00	
Passive nonsmoker	7 (7.6)	1.40 (0.58–3.38)	1.13 (0.47–2.73)†	0.79
Ex-smoker without ETS exposure	17 (10.8)	1.99 (1.02–3.90)	1.72 (0.85–3.49)†	0.13
Passive ex-smoker	5 (9.4)	1.74 (0.64–4.71)	1.48 (0.54–4.05)†	0.44
Smoker	24 (19.8)	3.65 (1.96–6.80)	4.40 (2.20–8.80)†	<0.001
POMS events				
Nonsmoker	77 (24.6)	1.00	1.00	
Passive nonsmoker	31 (33.7)	1.37 (0.90–2.08)	1.51 (1.04–2.21)‡	0.03
Ex-smoker without ETS exposure	44 (28.0)	1.13 (0.79–1.65)	1.56 (1.00–2.41)‡	0.05
Passive ex-smoker	21 (39.6)	1.61 (0.99–2.61)	2.21 (1.39–3.50)‡	0.001
Smoker	42 (34.7)	1.41 (0.97–2.05)	1.86 (1.22–2.83)‡	0.004

*The estimates are from univariate Poisson regression models.

†The estimates are from the GEE model, adjusted for American Society of Anesthesiologists Physical Status, elderly (age >65 years), sex, magnitude of surgery, surgical specialty, and preoperative asthma/chronic obstructive pulmonary disease.

‡The estimates are from the GEE model, adjusted for American Society of Anesthesiologists Physical Status, elderly (age >65 years), sex, and magnitude of surgery.

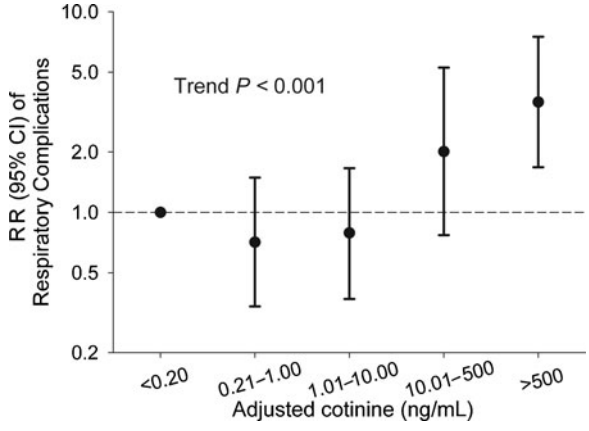

FIGURE 1. Association between adjusted urinary cotinine concentration and risk (95% CI) of perioperative respiratory complications in 736 patients. The RR was adjusted for American Society of Anesthesiologists Physical Status, elderly (age >65 years), sex, magnitude of surgery, surgical specialty, and preoperative asthma/chronic obstructive pulmonary disease.

consumptions over the last 4 decades,[25] implementation of smoking legislations, and the current low prevalence of daily smoking in the Hong Kong population (11.1%)[26] may account for this observation. Therefore, caution should be exercised when interpreting the negative finding because the study may be underpowered to detect a small effect of passive smoking on perioperative respiratory complications. The applicability of our results to other surgical settings with higher smoking prevalence is uncertain.

As expected, there was a strong association between smoking and perioperative respiratory complications, with a significant dose-response relationship shown in Figure 1 using adjusted cotinine concentration groups. Our population etiological fraction[27] for perioperative respiratory complications caused by smoking before surgery was 32%. Thus, 32% of perioperative respiratory complications were attributed to cigarette smoking. Cigarette smoking decreases mucociliary clearance and alters the mucus volume and composition by inducing an inflammatory lung state.[28] Our smokers were 5 times more likely to have increased airway secretions than never-smokers. This is comparable with previous studies, where current smokers had 2 times[29] to 12 times[30] the risk of increased secretions versus never-smokers.

The POMS outcome measure is a composite of mild, transient, and serious complications. One in 3 patients had POMS events on postoperative day 3, which was less than those reported in other studies.[10,11] This may be due to local differences in postoperative care and the underlying severity of preoperative coexisting morbidities patients had. All components of POMS, except pain, were similar to the major and minor perioperative smoking-related outcomes included in previous studies.[3,31] Notably, a smoking cessation trial using

TABLE 6. Adjusted Mean (95% CI) Quality of Recovery Scores and Health-related Quality-of-life Measure on the Third Day After Surgery by Smoking Status

Smoking Status	QoR*	EQ-5D VAS*	EQ-5D Index*
Never-smoker	15.1 (14.9–15.3)	67 (66–69)	0.70 (0.66–0.73)
Passive nonsmoker	14.4 (14.0–14.8)	68 (65–71)	0.64 (0.57–0.70)
Ex-smoker with no ETS exposure	14.2 (13.9–14.6)	66 (64–68)	0.58 (0.53–0.64)
Passive ex-smokers	14.1 (13.6–14.7)	65 (61–69)	0.59 (0.51–0.67)
Smoker	14.2 (13.9–14.6)	63 (60–66)	0.60 (0.54–0.65)

*Adjusted for age, sex, American Society of Anesthesiologists Physical Status, and magnitude of surgery.
VAS indicates visual analog scale.

POMS-based defined complications showed that smoking cessation therapy starting 4 weeks before general and orthopedic surgery reduced postoperative complications in the first month after surgery by half (RR, 0.51; 95% CI, 0.27–0.97).[31] Active smoking and passive smoking were also associated with an increase in postoperative pain intensity levels.[32] Our study showed that active smoking and passive smoking were associated with a 2-fold increased risk of POMS events in the multivariate GEE model. However, there was no significant dose-response relationship between adjusted cotinine concentration and the risk of POMS events on day 3 after surgery. Cotinine measured only short-term exposure to tobacco and did not necessarily reflect the cumulative long-term exposure of tobacco on the risk of POMS events.

Our study showed that direct or indirect exposure to tobacco smoke reduced the QoR after surgery. Lower recovery scores were associated with lower patient satisfaction.[33] Using a minimal important difference of 0.03,[34] we found that any exposure to tobacco smoke was associated with a lower health-related quality of life (EQ-5D index) after surgery.

Our results imply that it is worthwhile to also include self-reported passive smoking in the preoperative history. Nonsmokers and ex-smokers exposed to ETS need to be informed about the risks of postoperative morbidity and the expected poorer QoR and be motivated to take steps to achieve a smoke-free environment at home before surgery. Our results reiterate the need for clinicians to make concerted efforts to help patients quit smoking before surgery. A recent systematic review of randomized controlled trials and observational studies showed that patients should stop smoking at least 4 weeks, and preferably 8 weeks, before surgery to reduce postoperative respiratory and wound-healing complications.[17]

The first limitation of this study was that the common-effects GEE analysis was influenced by components with a higher frequency. Although we tried to addressed this limitation with an average relative-effect GEE analysis,[23] the models did not converge, as the data set was too small to model the interaction term between smoking status and individual components adequately. Second, we did not measure preoperative lung function in our patients. Quantification of the effect of passive smoking on lung function and its subsequent relationship with perioperative respiratory complications would further our understanding of the possible harmful effects of ETS in surgery. We did not collect pack-years because of concerns about its moderate validity when calculated retrospectively; individual differences between prospectively calculated pack-years and retrospectively calculated pack-years were large in subjects with an exposure of tobacco smoke of 5.2 pack-years or more.[35]

As with all nonrandomized studies, there is a potential for residual confounding despite the use of multivariate analyses. Post hoc sensitivity analyses did not show a significant interaction effect between smoking status and type of surgery on the risks of perioperative respiratory event ($P = 0.98$) and postoperative morbidity ($P = 0.64$), suggesting that the smoking status effect was consistent among the heterogeneous surgical groups.

CONCLUSIONS

In a setting of low-smoking prevalence, a substantial number of patients were exposed to ETS before major and complex elective surgery. Although passive cigarette smoking showed very little, if any, increased risk of perioperative respiratory complications, it was associated with a higher risk of POMS events and lower QoR after surgery. The association between passive cigarette smoking and perioperative respiratory complications may be weaker than previously believed.

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