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Association Between Smoking Status, Preoperative Exhaled Carbon Monoxide Levels, and Postoperative Surgical Site Infection in Patients Undergoing Elective Surgery

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IMPORTANCE Cigarette smoking is a risk factor for many perioperative complications, including surgical site infection (SSI). The duration of abstinence from smoking required to reduce this risk is unknown.

OBJECTIVES To evaluate if abstinence from smoking on the day of surgery is associated with a decreased frequency of SSI in patients who smoke cigarettes and to confirm that smoking is significantly independently associated with SSI when adjustment is made for potentially relevant covariates, such as body mass index.

DESIGN, SETTING, AND PARTICIPANTS In this observational, nested, matched case-control study, 2 analyses were performed at an academic referral center in the upper Midwest. Cases included all patients undergoing elective surgical procedures at Mayo Clinic, Rochester, Minnesota, between January 1, 2009, and July 31, 2014 (inclusive) who subsequently developed an SSI. Controls for both analyses were matched on age, sex, and type of surgery.

EXPOSURES Smoking status and preoperative exhaled carbon monoxide level, assessed by nurses in the preoperative holding area. Patients were classified as smoking on the day of surgery if they self-reported smoking or if their preoperative exhaled carbon monoxide level was 10 ppm or higher.

MAIN OUTCOMES AND MEASURES Surgical site infection after a surgical procedure at Mayo Clinic, Rochester, as identified by routine clinical surveillance using National Healthcare Safety Network criteria.

RESULTS Of the 6919 patients in the first analysis, 3282 (47%) were men and 3637 (53%) were women; median age (interquartile range) for control and SSI cases was 60 (48-70). Of the 392 patients in the second analysis, 182 (46%) were men and 210 (54%) were women; median age (interquartile range) for controls was 53 (45-49) and for SSI cases was 51 (45-60). During the study period, approximately 2% of surgical patients developed SSI annually. In the first analysis (evaluating the influence of current smoking status), there were 2452 SSI cases matched to 4467 controls. The odds ratio for smoking and SSI was 1.51 (95% CI, 1.20-1.90; $P < .001$), which remained statistically significant after adjusting for covariates. In the second analysis (evaluating the influence of smoking on the day of surgery), there were 137 SSI cases matched to 255 controls. The odds ratio for smoking on the day of surgery and SSI was 1.96 (95% CI, 1.23-3.13; $P < .001$), which remained statistically significant after adjusting for covariates. Preoperative exhaled carbon monoxide level was not associated with the frequency of SSI, suggesting that the association between smoking on the day of surgery and SSI was not related to preoperative exhaled carbon monoxide levels.

CONCLUSIONS AND RELEVANCE Current smoking is associated with the development of SSI, and smoking on the day of surgery is independently associated with the development of SSI. These data cannot distinguish whether abstinence per se reduces risk or whether it is associated with other factors that may be causative.

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Invited Commentary
Supplemental content

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Cigarette smoking is a risk factor for many perioperative complications, including cardiovascular and respiratory conditions and surgical site infection (SSI).[1-3] This increased risk may result from both an increased prevalence of smoking-related diseases and the acute effects of smoking,[4-7] which increases exposure to several toxins. For example, carbon monoxide not only binds to hemoglobin but also shifts the oxyhemoglobin dissociation curve to the left.[8] The resulting decrease in oxygen supply could contribute to the development of SSI.[5,9]

Although preoperative smoking abstinence reduces the risk of wound-related complications, the duration of abstinence needed for the reduction is unknown, with most studies[10-13] using at least 4 weeks of preoperative abstinence. However, postoperative abstinence alone may also reduce the risk of postoperative complications.[14] It is plausible that brief preoperative abstinence could be beneficial because the half-life of compounds like nicotine (approximately 1 hour) and carbon monoxide (approximately 4 hours) is short, and because tissue oxygenation, one of the primary determinants of SSI risk, rapidly increases with abstinence.[2] However, the association between brief abstinence and the frequency of SSI is unknown.

Exhaled carbon monoxide is an objective indicator of smoking status in studies of smoking cessation, providing a simple method of assessing recent smoking behavior. Preoperative carbon monoxide monitoring is now a standard of care at Mayo Clinic, Rochester, or patients who report current smoking. The primary aim of this prospective, observational, nested, matched case-control study was to test the hypothesis that the frequency of SSI is reduced in smokers who abstain from smoking on the day of elective surgery. The secondary aim was to confirm prior studies that current smokers are more likely to develop SSI using a cohort in which smoking status was systematically ascertained immediately before surgery and covariates potentially affecting the frequency of SSI were accounted for in the model.

Key Points

Question Is abstinence from smoking on the day of elective surgery associated with a reduction in the frequency of surgical site infection?

Findings In this case-control study that included 137 cases of surgical site infection and 255 matched controls among smokers who underwent surgery at an academic referral center, surgical site infection was significantly less likely in those who abstained from smoking on the day of surgery.

Meaning These findings raise the possibility but do not yet prove that efforts to promote abstinence from smoking on the day of surgery may reduce the risk of surgical site infection.

Methods

This study was approved by the Mayo Clinic, Rochester, Institutional Review Board. This study reviewed medical records only, so patients who declined having their records used for research were excluded. Informed consent was waived by the institutional review board.

Overview

This observational, nested, matched case-control study included 2 analyses. For both, cases were drawn from patients undergoing elective surgical procedures at Mayo Clinic, Rochester, between January 1, 2009, and July 31, 2014 (inclusive) who subsequently developed an SSI. In the first analysis, SSI cases were matched (on age, sex, and type of surgery) with up to 2 controls who did not develop SSI to evaluate if being a current smoker was independently associated with the frequency of SSI. The second analysis was restricted to those who reported current smoking, matching (on age, sex, and type of surgery) SSI cases with up to 2 controls who did not develop SSI to evaluate if smoking on the day of surgery was independently associated with the frequency of SSI (**Figure 1**).

Determination of Smoking Status

Since September 2009, all patients undergoing elective surgery at Mayo Clinic, Rochester, have had smoking status ascertained by nurses in the preoperative holding area. Patients are asked if they currently smoke cigarettes. For those who respond affirmatively, the number of cigarettes smoked on a typical day is noted (1-10, 11-20, or ≥21), preoperative exhaled carbon monoxide levels are measured (Micro Smokerlyzer; Bedfont Scientific), and patients are asked whether they have smoked that day. This information is routinely included in the clinical record. Carbon monoxide analyzers are maintained by the Division of Respiratory Care at Mayo Clinic, Rochester, including regular calibration and in-servicing of nursing personnel. Patients were classified as smoking on the day of surgery if they self-reported smoking or if their preoperative exhaled carbon monoxide level was 10 ppm or higher, a threshold consistent with recommendations by the Society for Research on Nicotine and Tobacco.[15] Those patients who had surgery between January 1 and September 1, 2009, before preoperative smoking status was being routinely confirmed, were considered to have an unknown smoking status.

Identification of SSI Cases

Surgical site infection cases after surgical procedures at Mayo Clinic, Rochester, are identified by Mayo Clinic Infection Prevention and Control as a part of vigilant clinical surveillance using the National Healthcare Safety Network criteria published by the Centers for Disease Control and Prevention.[16] Identification includes review of all potential cases by infection preventionists, with case validation by infectious disease specialists. Cases were classified as associated with either type 1 surgical procedures (clean) or type 2 surgical procedures (clean-contaminated, with the respiratory, gastrointestinal, or genitourinary tract entered). Patients who declined to have their Mayo Clinic, Rochester, electronic medical record used for research purposes (approximately 4% of Mayo Clinic, Rochester, patients[17]) were excluded from the study. Patients who did not have their surgical procedures performed in the main operating rooms at Mayo Clinic, Rochester (ie, at

Mayo Clinic outpatient surgical centers) were also excluded because smoking status and preoperative exhaled carbon monoxide level measurements were not available. Finally, patients younger than 18 years were excluded because of concerns about the accuracy of self-reported smoking. If an individual patient developed more than 1 SSI, only the first incidence of SSI was analyzed unless the incident dates were separated by more than 1 year.

Matching

A nested, matched case-control design was used because of the low incidence of SSI, with cases defined as surgical patients who developed SSI during the study period and controls selected from among patients without SSI. The index surgical procedure was considered the last procedure before SSI diagnosis. In both the first analysis and the second analysis, up to 2 controls were selected for each case, matched according to age (within 10 years), sex, the date of surgery (within 5 years), and the case index surgical procedure using measures of the duration of surgery and procedure codes. The control surgery was required to be between 0.5 and 2.0 times the duration of the case surgery, with an absolute limit of no more than 100 minutes in either direction (whichever boundary was greater). For example, a 30-minute surgery could be matched with a surgical procedure that was 15 to 60 minutes.

Each surgery could have multiple procedure codes. A primary procedure code was specified for each case as part of the SSI surveillance procedure but was not specified for potential controls. For surgical procedures with multiple procedure codes, controls were matched on as many codes as possible but had to include the primary procedure code for the case. All surgical procedures with multiple procedure codes were manually reviewed by [2] of us (M.B.N. and D.O.W.) to ensure that the primary procedures of cases and controls were comparable. If at least 1 appropriate control could not be identified for a case, it was excluded from analysis. Separate matching procedures were conducted for the 2 analyses.

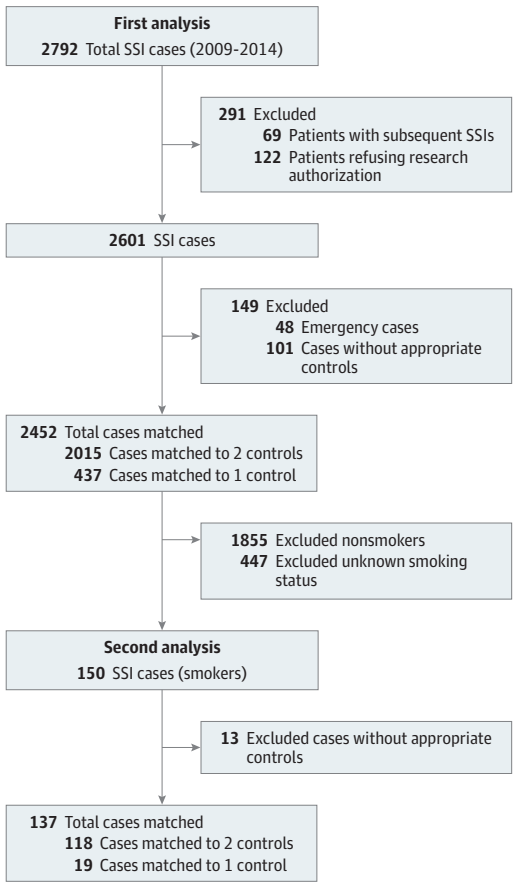
Measurement of Potentially Relevant Covariates

Several factors other than smoking status have been associated with SSI risk.[1,6,7,18,19] A clinical data warehouse constructed from the Mayo Clinic, Rochester, electronic medical record was used to ascertain several of these potentially relevant factors for each case and control, including the duration of surgery, body mass index (BMI), American Society of Anesthesiologists physical status (ASA PS), and median intraoperative body temperature (measured as esophageal or bladder temperature).

Statistical Analysis

Demographic information and other characteristics were summarized for cases and controls. The first analysis examined whether SSI was more frequent in those who self-reported being current smokers compared with those who were not currently smoking (either never or former smokers). This comparison was restricted to cases and controls with smoking status information available. The second analysis examined whether SSI was more frequent among patients who reported current smoking and who smoked on the day of surgery, with SSI as the dependent variable and smoking on the day of surgery (self-reported smoking or preoperative exhaled carbon monoxide level ≥10 ppm) as the factor of interest. Both analyses were performed using conditional logistic regression taking into account the 1:2 matched set study design. Covariates in this analysis were the BMI, ASA PS, duration of surgery, and median intraoperative body temperature. Separate analyses were conducted for type 1, type 2, and all (either type 1 or 2) procedures. The second analysis was also repeated with preoperative exhaled carbon monoxide level measured as a continuous variable, substituted for smoking on the day of surgery as the factor of interest. For the first analysis, this study had statistical power of 80.0% to detect an odds ratio (OR) of 1.40 or greater. For the second analysis, this study had statistical power of 80% to detect an OR of 1.77 or greater.

Figure 1. Flow Diagram Showing the Derivation of Cases and Controls for Analyses of Surgical Site Infection (SSI)



The first analysis evaluated the influence of current smoking status on SSI. The second analysis evaluated the influence of smoking on the day of surgery on SSI.

Results

During the study period, approximately 23 000 type 1 procedures and 6200 type 2 procedures were performed annually

Table 1. Demographics and Surgical Characteristics of Surgical Site Infection (SSI) Cases and Matched Controls With Matching Performed Without Regard to Smoking Status (First Analysis)

Variable	Type 1 Surgical Procedures (Clean)		Type 2 Surgical Procedures (Clean-Contaminated)		Overall	
	Controls (n = 2367)	SSI Cases (n = 1288)	Controls (n = 2100)	SSI Cases (n = 1164)	Controls (n = 4467)	SSS Cases (n = 2452)
Age, median (IQR), y	60 (49-70)	60 (49-70)	59 (48-69)	59 (48-69)	60 (48-70)	60 (48-70)
Sex, No. (%)						
Male	1151 (48.6)	627 (48.7)	965 (46.0)	539 (46.3)	2116 (47.4)	1166 (47.6)
Female	1216 (51.4)	661 (51.3)	1135 (54.0)	625 (53.7)	2351 (52.6)	1286 (52.4)
BMI, median (IQR) (n = 6901)	28.9 (24.9-33.5)	30.1 (25.8-35.6)	27.1 (23.6-31.6)	27.7 (23.8-32.6)	28.1 (24.3-32.6)	28.9 (24.8-34.3)
Smoker, No. (%)						
Unknown	381 (16.1)	216 (16.8)	346 (16.5)	231 (19.8)	727 (16.3)	447 (18.2)
No	1888 (79.8)	999 (77.6)	1652 (78.7)	856 (73.5)	3540 (79.2)	1855 (76.7)
Yes	98 (4.1)	73 (5.7)[a]	102 (4.9)	77 (6.6)[a]	200 (4.5)	150 (6.1)[a]
Cigarettes per day, No./total No. (%)[b]						
Unknown	21/98 (21.4)	17/73 (23.3)	22/102 (21.6)	12/77 (15.6)	43/200 (21.5)	29/150 (19.3)
1-10	39/98 (39.8)	39/73 (53.4)	45/102 (44.1)	39/77 (50.6)	84/200 (42.0)	78/150 (52.0)
11-20	35/98 (35.7)	15/73 (20.5)	32/102 (31.4)	25/77 (32.5)	67/200 (33.5)	40/150 (26.7)
>21	3/98 (3.1)	2/73 (2.7)	3/102 (2.9)	1/77 (1.3)	6/200 (3.0)	3/150 (2.0)
Smoked today, No./total No. (%)[b,c]	63/98 (64.3)	53/73 (72.6)[a]	58/102 (56.9)	48/77 (62.3)[a]	121/200 (60.5)	101/150 (67.3)[a]
Preoperative exhaled carbon monoxide level among smokers only, median (IQR), ppm	9 (4-16)	10 (6-16)	9 (5-16)	10 (5-16)	9 (5-16)	10 (5-16)
ASA physical status, No. (%)						
1-2	1293 (54.6)	600 (46.6)	1174 (55.9)	570 (49.0)	2467 (55.2)	1170 (47.7)[a]
3-4	1074 (45.4)	688 (53.4)	926 (44.1)	594 (51.0)	2000 (44.8)	1282 (52.3)
Type of surgery, No./total No. (%) (n = 6916)						
Breast or chest	116/2365 (4.9)	59/1287 (4.6)	0/2100	0/1164	116/4465 (2.6)	59/2451 (2.4)
Cardiac	313/2365 (13.2)	171/1287 (13.3)	0/2100	0/1164	313/4465 (7.0)	171/2451 (7.0)
General	235/2365 (9.9)	131/1287 (10.2)	1272/2100 (60.6)	708/1164 (60.8)	1507/4465 (33.8)	839/2451 (34.2)
Gynecologic	0/2365	0/1287	286/2100 (13.6)	159/1164 (13.7)	286/4465 (6.4)	159/2451 (6.5)
Miscellaneous	160/2365 (6.8)	90/1287 (7.0)	59/2100 (2.8)	33/1164 (2.8)	219/4465 (4.9)	123/2451 (5.0)
Multiple types	32/2365 (1.4)	17/1287 (1.3)	20/2100 (1.0)	11/1164 (0.9)	52/4465 (1.2)	28/2451 (1.1)
Neurologic	452/2365 (19.1)	243/1287 (18.9)	0/2100	0/1164	452/4465 (10.1)	243/2451 (9.9)
Orthopedic	751/2365 (31.8)	406/1287 (31.5)	0/2100	0/1164	751/4465 (16.8)	406/2451 (16.6)
Plastics	143/2365 (6.0)	78/1287 (6.1)	0/2100	0/1164	143/4465 (3.2)	78/2451 (3.2)
Thoracic	11/2365 (0.5)	6/1287 (0.5)	244/2100 (11.6)	130/1164 (11.2)	255/4465 (5.7)	136/2451 (5.5)
Transplant	2/2365 (0.1)	2/1287 (0.2)	105/2100 (5.0)	57/1164 (4.9)	107/4465 (2.4)	59/2451 (2.4)
Urologic	2/2365 (0.1)	1/1287 (0.1)	114/2100 (5.4)	66/1164 (5.7)	116/4465 (2.6)	67/2451 (2.7)
Vascular	148/2365 (6.3)	83/1287 (6.4)	0/2100	0/1164	148/4465 (3.3)	83/2451 (3.4)
Duration of surgery, median (IQR), h	2.9 (1.8-4.7)	3.0 (1.8-4.9)	4.2 (2.8-5.7)	4.3 (2.8-6.0)	3.6 (2.2-5.3)	3.6 (2.2-5.4)
Intraoperative body temperature, median (IQR), °C	36.2 (35.8-36.6)	36.3 (35.8-36.7)	36.1 (35.7-36.6)	36.1 (35.6-36.6)	36.2 (35.7-36.6)	36.2 (35.7-36.6)

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

[a] Significant difference from controls ($P < .05$).

[b] Percentages calculated in reference to smokers.

[c] Patients were classified as having smoked on the day of surgery if they self-reported smoking or if their preoperative exhaled carbon monoxide level was 10 ppm or higher.

at Mayo Clinic, Rochester. Between January 1, 2009, and July 31, 2014, the overall crude incidence of SSI was approximately 1.4% for type 1 procedures and 3.4% for type 2 procedures. Of these, a total of 2792 SSI cases were identified in adult patients meeting our surgical criteria. Of this total, 122 cases did not provide research authorization for the use of their electronic medical record, and 69 cases represented episodes of SSI that developed in a patient less than 12 months after a prior

Table 2. Case-Control Analysis Summaries[a]

Variable	Type 1 Surgical Procedures (Clean)		Type 2 Surgical Procedures (Clean-Contaminated)		Overall	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
First Analysis (SSI Cases and Controls Among All Patients)						
Current smoker vs not[b]						
Unadjusted	1.47 (1.06-2.05) (n = 3058)	.02	1.56 (1.13-2.13) (n = 2687)	.007	1.51 (1.20-1.90) (n = 5745)	<.001
Adjusted	1.44 (1.03-2.02) (n = 3035)	.04	1.54 (1.11-2.14) (n = 2685)	.009	1.51 (1.19-1.90) (n = 5720)	<.001
Second Analysis (SSI Cases and Controls Among Current Smokers)						
Smoked today vs not[c]						
Unadjusted	2.29 (1.10-4.76) (n = 190)	.03	1.76 (0.96-3.22) (n = 202)	.07	1.96 (1.23-3.13) (n = 392)	.004
Adjusted	1.90 (0.87-4.18) (n = 184)	.11	1.68 (0.91-3.09) (n = 202)	.10	1.75 (1.09-2.81) (n = 386)	.02
Preoperative exhaled carbon monoxide level measured						
Unadjusted	1.01 (0.97-1.05) (n = 190)	.69	1.02 (0.98-1.05) (n = 202)	.43	1.01 (0.98-1.04) (n = 392)	.40
Adjusted	1.01 (0.96-1.05) (n = 184)	.82	1.02 (0.98-1.06) (n = 202)	.36	1.01 (0.98-1.04) (n = 386)	.49

Abbreviations: OR, odds ratio; SSI, surgical site infection.

[a] All models are stratified logistic regression. An OR greater than 1 represents an increased risk of infection for smokers or recent smoking relative to nonsmokers or not recent smoking. For adjusted analyses, the model includes body mass index, duration of surgery, median intraoperative body temperature, and American Society of Anesthesiologists physical status.

[b] The reference category is individuals who are not current smokers.

[c] The reference category is individuals who did not smoke today.

episode; both were excluded from further consideration (Figure 1). Of the remaining cases, 48 followed emergency surgery, and at least 1 appropriate control could not be identified for 101; these cases were also excluded. Therefore, a total of 2452 SSI cases were included in the first analysis (evaluating the influence of current smoking status), with 437 cases matched to 1 control and 2015 cases matched to 2 controls. The second analysis (evaluating the influence of smoking on the day of surgery) attempted to match the 150 current smokers who developed SSI with at least 1 control (a current smoker who did not develop SSI). At least 1 appropriate control could not be identified for 13 cases, who were excluded from further analysis. Therefore, a total of 137 cases were included in the second analysis, with 19 matched to 1 control and 118 matched to 2 controls.

Current Smoking

As expected, cases and controls in the first analysis were well matched on age, sex, type of surgery, and duration of surgery (**Table 1**). Cases were more likely to be rated as ASA PS 3 or 4 compared with ASA PS 1 or 2 ($P < .001$, χ^2 test). The median intraoperative body temperature was identical in cases and controls. For all patients with smoking status information available (including those undergoing either type 1 or type 2 procedures), 7.5% of cases and 5.4% of controls self-reported being current smokers ($P = .001$, χ^2 test). For current smokers, daily cigarette consumption was similar between cases and controls. In multivariable analysis of cases and controls, those who reported current smoking were significantly more likely to develop SSI (**Table 2**). Odds ratios for both type 1 and type 2 surgical procedures were similar, and there was little effect of adjustment for potentially relevant covariates.

Smoking on the Day of Surgery

Cases and controls in the second analysis (which included only current smokers) were well matched on age, sex, type of surgery, and duration of surgery (**Table 3**). Cases were not significantly more likely to be rated as ASA PS 3 or 4 compared with ASA PS 1 or 2. Daily cigarette consumption was similar between cases and controls. In univariate analysis, cases were significantly more likely to have smoked on the day of surgery (67.9% [93 of 137] of cases vs 53.7% [137 of 255] of controls; $P = .007$, χ^2 test for all patients). In multivariable analysis of all cases and controls (undergoing either type 1 or type 2 procedures), those who smoked on the day of surgery were significantly more likely to develop SSI (Table 2). Similar trends were apparent when type 1 and type 2 surgical procedures were separately analyzed, but they did not always reach statistical significance.

In univariate analysis, preoperative exhaled carbon monoxide levels did not significantly differ between cases (median, 10 ppm; interquartile range [IQR], 5-16 ppm) and controls (median, 9 ppm; IQR, 5-15 ppm) ($P = .29$, rank sum test) (Table 2). In a multivariable model that included preoperative exhaled carbon monoxide levels (instead of whether patients smoked the day of surgery), preoperative exhaled carbon monoxide levels were not significantly associated with the frequency of SSI. Full model parameters for all multivariable analyses are included as supplemental materials (eTables 1, 2, and 3 in the Supplement).

Discussion

There are 2 main findings of this study. First, patients who report current smoking are more likely to develop SSI in an analy-

Table 3. Demographics and Surgical Characteristics of Surgical Site Infection (SSI) Cases and Matched Controls With Matching Performed in Current Smokers (Second Analysis)

Variable	Type 1 Surgical Procedures (Clean)		Type 2 Surgical Procedures (Clean-Contaminated)		Overall	
	Controls (n = 124)	SSI Cases (n = 66)	Controls (n = 131)	SSI Cases (n = 71)	Controls (n = 255)	SSI Cases (n = 137)
Age, median (IQR), y	51 (41-58)	49 (41-55)	54 (48-61)	54 (48-61)	53 (45-59)	51 (45-60)
Sex, No. (%)						
Male	68 (54.8)	36 (54.5)	50 (38.2)	28 (39.4)	118 (46.3)	64 (46.7)
Female	56 (45.2)	30 (45.5)	81 (61.8)	43 (60.6)	137 (53.7)	73 (53.3)
BMI, median (IQR) (n = 390)	28.3 (24.4-33.6)	29.2 (24.5-34.7)	26.7 (23.3-30.3)	25.9 (22.5-28.9)	27.5 (24.0-31.3)	26.8 (23.7-32.0)
Cigarettes per day, No. (%)						
Unknown	30 (24.2)	16 (24.2)	25 (19.1)	10 (14.1)	55 (21.6)	26 (19.0)
1-10	53 (42.7)	33 (50.0)	67 (51.1)	37 (52.1)	120 (47.1)	70 (51.1)
11-20	39 (31.5)	15 (22.7)	36 (27.5)	23 (32.4)	75 (29.4)	38 (27.7)
≥21	2 (1.6)	2 (3.0)	3 (2.3)	1 (1.4)	5 (2.0)	3 (2.2)
Smoked today, No. (%)[a]	71 (57.3)	47 (71.2)	66 (50.4)	46 (64.8)	137 (53.7)	93 (67.9)[b]
Preoperative exhaled carbon monoxide level, median (IQR), ppm	9 (5-15)	9 (5-15)	8 (4-15)	10 (5-18)	9 (5-15)	10 (5-16)
ASA physical status, No. (%)						
1-2	84 (67.7)	38 (57.6)	86 (65.6)	41 (57.7)	170 (66.7)	79 (57.7)
3-4	40 (32.3)	28 (42.4)	45 (34.4)	30 (42.3)	85 (33.3)	58 (42.3)
Type of surgery, No. (%)						
Breast or chest	2 (1.6)	1 (1.5)	0	0	2 (0.8)	1 (0.7)
Cardiac	8 (6.5)	4 (6.1)	0	0	8 (3.1)	4 (2.9)
General	13 (10.5)	7 (10.6)	86 (65.6)	47 (66.2)	99 (38.8)	54 (39.4)
Gynecologic	0	0	26 (19.8)	14 (19.7)	26 (10.2)	14 (10.2)
Miscellaneous	8 (6.5)	5 (7.6)	2 (1.5)	1 (1.4)	10 (3.9)	6 (4.4)
Multiple types	2 (1.6)	1 (1.5)	2 (1.5)	1 (1.4)	4 (1.6)	2 (1.5)
Neurologic	15 (12.1)	8 (12.1)	0	0	15 (5.9)	8 (5.8)
Orthopedic	61 (49.2)	32 (48.5)	0	0	61 (23.9)	32 (23.4)
Plastics	2 (1.6)	1 (1.5)	0	0	2 (0.8)	1 (0.7)
Thoracic	0	0	11 (8.4)	6 (8.5)	11 (4.3)	6 (4.4)
Urologic	0	0	4 (3.1)	2 (2.8)	4 (1.6)	2 (1.5)
Vascular	13 (10.5)	7 (10.6)	0	0	13 (5.1)	7 (5.1)
Duration of surgery, median (IQR), h	2.2 (1.5-3.2)	2.2 (1.5-3.6)	4.1 (2.8-5.8)	4.1 (2.8-6.5)	3.0 (1.9-5.0)	3.3 (2.0-5.4)
Intraoperative body temperature, median (IQR), °C (n = 388)	36.2 (35.7-36.6)	36.4 (36.1-36.7)	36.1 (35.6-36.7)	36.1 (35.6-36.5)	36.1 (35.7-36.6)	36.3 (35.8-36.6)

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

[a] Patients were classified as having smoked on the day of surgery if they self-reported smoking or if their preoperative exhaled carbon monoxide level was 10 ppm or higher.

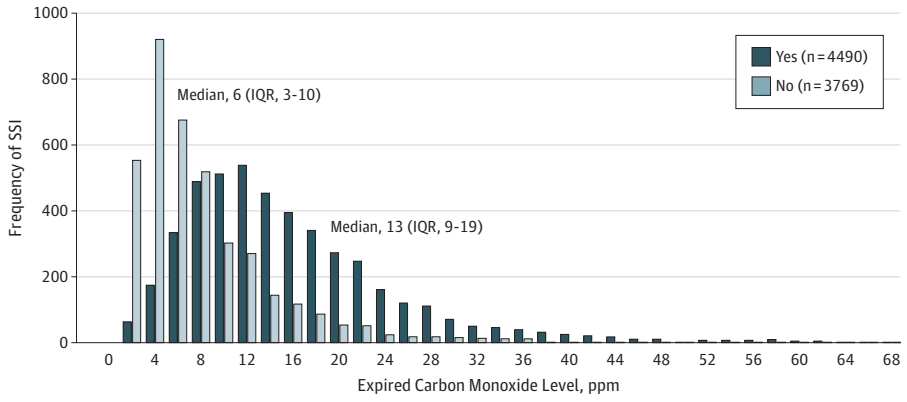
[b] Significant difference from controls ($P < .05$).

sis that uses systematic ascertainment of smoking status at the time of surgery and adjustment for relevant covariates. Second, among current smokers, abstaining from smoking on the day of surgery is associated with a decreased frequency of SSI, an association that does not appear to be related to preoperative exhaled carbon monoxide levels.

Prior studies have consistently found that being a current smoker increases the risk of SSI. A recent meta-analysis[3] of 107 studies found an overall relative risk (RR) of wound complications in current smokers compared with nonsmokers of 2.15 (95% CI, 1.87-2.49). This finding ranged from an RR of 1.99 (95% CI, 1.58-2.48) in former smokers to an RR of 3.70 (95% CI, 1.60-8.58) in current smokers with a 20 to 25 pack-year history of smoking. A study perhaps most directly comparable to the present study was performed by Turan et al,[20] who used the American College of Surgeons National Surgical Quality Improvement Program data set to examine the association between smoking status and postoperative wound-related complications within 30 days. Compared with never smokers, current smokers (defined as a self-report of smoking within 1 year of surgery) had significantly higher odds of having superficial (OR, 1.30; 95% CI, 1.20-1.42) and deep (OR, 1.42; 95% CI, 1.21-1.68) incisional infections.[20] Our data are consistent with these findings and have the further advantage of ascertaining smoking status immediately before surgery in every patient (ensuring that current smokers are indeed current) and controlling for some other potentially relevant covariates shown in prior work to modify risk.[1]

Evaluation of the primary hypothesis (that the frequency of SSI is reduced in smokers who abstain from smoking on the day

Figure 2. Distribution of Preoperative Exhaled Carbon Monoxide Levels for Smokers Who Reported Smoking on the Day of Surgery (Yes) and Those Who Reported Abstaining (No)



Data are from all smokers evaluated in the preoperative holding areas between December 18, 2009, and June 24, 2014. IQR indicates interquartile range; SSI, surgical site infection.

of elective surgery) required accurate ascertainment of whether patients smoked the day of surgery. Prior work in our practice found self-reported abstinence rates on the day of surgery of 40% to 74%.[21-24] Self-report is known to overestimate true abstinence in many settings; therefore, we used preoperative exhaled carbon monoxide levels as biochemical confirmation of recent smoking status, choosing the most conservative value within the recommended threshold range of 8 to 10 ppm.[15] Because preoperative exhaled carbon monoxide levels and self-reported smoking abstinence were available for all patients anesthetized after December 2009 (not just those analyzed in this study), we also examined the association between these values in the population of current smokers undergoing surgery at Mayo Clinic, Rochester. During the study period (2009-2014), data were available for 8259 patients who reported being a current smoker; 4490 (54.4%) of these self-reported abstinence on the day of surgery. Among those reporting abstinence, the median preoperative exhaled carbon monoxide level was 6 (IQR, 3-10) ppm compared with a median of 13 (IQR, 9-19) ppm in those not reporting abstinence (**Figure 2**). In a receiver operating characteristic curve of exhaled preoperative carbon monoxide levels by self-reported abstinence, sensitivity and specificity were maximized at a carbon monoxide threshold of greater than 9 ppm (area under the curve, 0.80). This finding provides further support for using a threshold of 10 ppm or higher in this population, recognizing that several factors may influence exhaled preoperative carbon monoxide levels in this setting, including the time of surgery (eg, morning vs afternoon procedures), prior cigarette consumption, and exposure to environmental tobacco smoke.

Our results support the primary hypothesis but do not provide insight about the potential mechanisms underlying the association of recent smoking and SSI. In particular, we found no evidence that the frequency of SSI is related to exhaled preoperative carbon monoxide levels per se. This result could be due to the fact that a variable amount of time elapses between the exhaled preoperative carbon monoxide level measurement and commencement of surgery (such that the association between carbon monoxide levels measured in the preoperative holding area and intraoperative and postoperative exhaled carbon monoxide levels is inconsistent). Other constituents of cigarette smoke may be responsible for the increased risk, or that a patient's inability to maintain morning abstinence may be a marker for other factors that independently increase the risk of SSI, such as greater nicotine dependence, less intent to maintain postoperative abstinence, or higher cigarette consumption. However, comparison of perioperative cigarette consumption in this study showed no difference between cases and controls. It is also possible that an inability to maintain abstinence the day of surgery is associated with more frequent or severe smoking-related disease: increasing numbers of comorbid conditions appear to increase the risk of SSI.[1] Distinguishing between whether abstinence on the day of surgery is causal or confounding in reducing SSI risk has practical importance; our data do not permit this distinction. If smoking on the day of surgery carries with it a significantly increased risk of the development of SSI, advising patients to abstain the day of surgery regardless of their long-term quit plans has new importance. However, if morning smoking serves as a marker for other systemic factors responsible for risk, promotion of abstinence may not reduce the risk of SSI. For this reason, further studies are needed, although they may be difficult to conduct given the low absolute rates of SSI and the practical difficulties of such a trial.

Limitations

This study has several other limitations. Despite the consistent query for smoking status by clinical personnel on the day of surgery, there is the potential for misclassification. Preoperative exhaled carbon monoxide levels were only measured in those patients who admitted to being current smokers at the preoperative assessment. If patients were not truthful or viewed themselves as no longer being current smokers (eg, they made the commitment to quit that morning), they would be classified for study purposes as nonsmokers and would not have had preoperative exhaled carbon monoxide levels measured. Such misclassification would bias against finding differences based on smoking status. In addition, nonsmokers in this analysis included both never and former smokers, and former smokers may also be at risk for SSI because of smoking-related disease.[4] Finally, the accuracy of carbon monoxide measurements in this clinical environment must be considered. Although carbon

monoxide analyzers are easy to use, it is possible that because of the large number of personnel performing these measurements in a clinical practice setting the accuracy of these measurements was diminished compared with measurements performed in strictly research settings.

Conclusions

This study adds to existing evidence that current smoking is associated with more frequent SSI in patients undergoing elective surgery and finds that smokers who abstain from smoking on the day of surgery are less likely to develop SSI. These data cannot distinguish whether abstinence per se reduces risk or whether it is associated with other factors that may be causative; further study will be needed to make this distinction. However, just as clinicians routinely request that patients consume nothing by mouth on the day of surgery, they should also consider recommending at least morning abstinence from smoking in those patients otherwise not willing to make a more prolonged preoperative quit attempt.[25]

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Study concept and design: Nolan, Martin, Warner.
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Drafting of the manuscript: Nolan, Thompson, Warner.
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