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Adverse Effects of Smoking on Postoperative Outcomes in Cancer Patients

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ABSTRACT

Background. The possible negative effects of smoking on postoperative outcomes have not been well studied in cancer patients.

Methods. We used the VA Surgical Quality Improvement Program (VASQIP) database for the years 2002–2008, which assesses preoperative risk factors and postoperative outcomes for patients undergoing major surgery within the VA healthcare system.

Results. Compared with never smokers, prior smokers and current smokers with GI malignancies were significantly more likely to have surgical site infection (SSI) (odds ratio [OR], 1.25; 95% confidence interval [95% CI], 1.09–1.44) (OR, 1.20; 95% CI, 1.05–1.38), combined pulmonary complications (combined pulmonary outcome [CPO]: pneumonia, failure to wean from ventilator, reintubation) (OR, 1.60; 95% CI, 1.38–1.87) (OR, 1.96; 95% CI, 1.68–2.29), and return to the operating room (OR, 1.20; 95% CI, 1.03–1.39) (OR, 1.31; 95% CI, 1.13–1.53),

respectively. Both prior and current smokers had a significantly higher mortality at 30 days (OR, 1.50; 95% CI, 1.19–1.89) (OR, 1.41; 95% CI, 1.08–1.82) and 1 year (OR, 1.22; 95% CI, 1.08–1.38) (OR, 1.62; 95% CI, 1.43–1.85). Thoracic surgery patients who were current smokers were more likely to develop CPO (OR, 1.62; 95% CI, 1.25–2.11) and mortality within 1 year (OR, 1.50; 95% CI, 1.17–1.92) compared with nonsmokers, but SSI rates were not affected by smoking status. Current smokers had a significant increase in postsurgical length of stay (overall 4.3% [$P < .001$], GI 4.7% [$P = .003$], thoracic 9.0% [$P < .001$]) compared with prior smokers.

Conclusions. Prior and current smoking status is a significant risk factor for major postoperative complications and mortality following GI cancer and thoracic operations in veterans. Smoking cessation should be encouraged prior to all major cancer surgery in the VA population to decrease postoperative complications and length of stay.

In the United States, approximately half of adult men reported smoking cigarettes in 1965 and many of these individuals did so for more than 20 years.[1] The association between smoking and the increased risk of developing certain malignancies has been well established, and cigarette smoking accounts for approximately 30% of all cancer deaths in the general population.[2,3] There is also evidence that continued smoking after malignancy diagnosis may lead to a higher recurrence rate or second primary tumor compared with nonsmokers.[4,5]

There is conflicting evidence regarding the attributable risk of smoking on postoperative complications in patients undergoing major surgical procedures.[6–9] The risk of hospital death and pulmonary complications after lung cancer resection is increased by smoking.[10,11] This increased rate of complications in smokers may result in longer postoperative stay, increased health care costs, and postoperative mortality compared with nonsmokers.

Most solid organ based cancers are treated with surgical interventions. These are often complex procedures with associated morbidity and mortality. Cancer patients have higher prevalence of smoking and may be at higher incidence of smoking-related complications.[4]

Postoperative medical and surgical complications have been shown to result in an omission or significant delay in the initiation of adjuvant chemotherapy in colon and rectal cancer.[12,13] Delays in adjuvant chemotherapy were correlated with poorer disease-specific and overall survival in 1 of these studies.[12] Postoperative length of stay has also been shown to independently predict adjuvant chemotherapy delay in cancer patients.[12] Since smoking is a potentially modifiable preoperative risk factor for postoperative medical and surgical complications, smoking cessation interventions may decrease the risk of developing postoperative complications and length of stay and therefore improve the odds of smokers getting appropriate postoperative chemotherapy for their cancer.

Given that cancer operations are time sensitive, quantifying the potential benefit of smoking cessation intervention is necessary information to adopt this strategy. In addition, the negative effects of smoking may not be uniform across various disease sites. While there is evidence that smokers have an increased risk of postoperative complications and possibly death in general and thoracic surgery patients, this area has not been well studied for major gastrointestinal surgeries.

Our study examined the effects of smoking on the rate of postoperative complications and mortality following major cancer surgery in the Veteran Affairs (VA) population, using a large national database, the VA Surgical Quality Improvement Program. Our objective was to examine whether smoking was associated with higher risk of postoperative complications and mortality after major surgery in patients with cancer, and whether this risk varies by the type of the primary tumor site.

METHODS

Data Source

Data for this study were obtained from the VA Surgical Quality Improvement Program (VASQIP), which assesses preoperative risk factors, operative data, and 30-day postoperative outcomes for patients undergoing major surgery within the VA system. The VASQIP started in 1991 to analyze risk-adjusted 30-day morbidity and mortality data within the Veterans Health Administration. Of the approximately 375,000 surgical procedures in the VA yearly, 150,000 are major surgeries. The VASQIP is a prospectively collected database for patients undergoing major surgery within all VA acute care facilities. A trained surgical clinical nurse collects the data from electronic charts. On the 30th postoperative day, the nurse obtains outcome information through chart review, reports from morbidity and mortality conferences, and communication with each patient by letter or by telephone.

The study protocol was reviewed and approved by the local VA Research and Development Committee and the Institutional Review Board at the institutions of each coauthor, as well as by the Surgical Quality Data Use Group of the Office of Patient Care Services, VA Central Office, Washington, D.C.

Patients

The original study population consisted of 502,647 patients undergoing elective surgery between years 2002 and 2008. Patients undergoing emergent surgery were excluded by using the emergency case variable in the data set, because the attributable risk of smoking on complications after emergent surgery would not be amendable to preoperative smoking cessation interventions to reduce them. For patients with multiple operations in the database, we used the patient's first operation for this study. The International Classification of Diseases (9th edition) code (ICD-9) was used to identify patients with gastrointestinal (GI), lung, and urinary tract malignancies (Supplemental Table 1A). The Current Procedure Terminology (CPT) codes (Supplemental Table 1B) were used to identify major surgical procedures related to the ICD-9 codes, resulting in 22,391 patients with available smoking status (current, prior, never smoker). Of these 22,391 patients, 1561 were found to have more than 1 cancer site possibly secondary to metastatic disease, and these patients were excluded from our study. This provided us with 20,830 subjects for analysis. After excluding all cases that were coded as emergencies, we were left with 20,413 cases. All gastrointestinal cancer patients were grouped into the GI group ($n = 12,432$), all lung cancer patients were grouped into the thoracic surgery group ($n = 4490$), and all urinary tract malignancies were grouped into the urology group ($n = 3491$).

Definitions of Outcomes of Interest

Postoperative outcomes of interest were complications occurring within 30 days of the index operation, return to OR within 30 days, postsurgical length of stay, 30-day and 1-year mortality. Postoperative complications included: surgical site infection (SSI) (including superficial and deep-wound infections); cardiovascular, pulmonary, urinary tract, and CNS complications; return to OR; and postoperative hospital length of stay. In addition, we also grouped complications into a composite pulmonary outcome (CPO) (pneumonia, failure to wean from ventilator >48 h or reintubation for cardiorespiratory failure). The following complications were grouped together and called vascular complications: venous thromboembolism, stroke/ cerebrovascular accident, myocardial infarction. A composite outcome was created by combining SSI, vascular, and pulmonary complications.

The VASQIP data collection includes 2 smoking variables: current smoker (patient has smoked cigarettes in the year prior to admission for surgery) and total number of pack years of smoking. For the purposes of this study, each patient was classified into current, prior, and never smoker. Current smoker was defined as a patient who was classified as "yes" for the current smoker variable, and had a value for pack years of >0 or missing. Prior smoker was defined as a patient who was classified as "no" for the current smoker variable and whose value for the pack-years variable was >0. Never smoker was defined as a patient who was classified as "no" for the current smoker variable and whose value for the pack-years variable was = 0 or missing. Patients who had a "yes" for current smoker, but who had pack years = 0 (an inconsistency), or who were missing the current smoker variable were excluded.

Statistical Analyses

Baseline patient characteristics were compared among the 3 smoking groups (never, prior, and current) using Chi-square tests of association for categorical variables and the 1-factor analysis of variance for continuous variables. Unadjusted postoperative outcome rates were compared by smoking status using Pearson's Chi-square test of association.

For each of the dichotomous postoperative outcomes, the adjusted odds ratios for the current and prior smoking groups were compared with the never smokers as the reference group using multilevel multivariable logistic regression analysis. The association of pack years with postoperative outcomes was similarly performed for the most frequently occurring outcomes. Pack years was divided into quartiles and split by smoking status. A log-linear multilevel multivariable regression analysis modeled the association of smoking status and postsurgical length of stay. All regression analyses were adjusted for age, race/ ethnicity, work relative value unit (RVU), surgeon specialty, American Society of Anesthesiologists (ASA) classification, alcohol use, and year of surgery. SSI was additionally adjusted for wound classification. Clustering of patients within hospitals was accounted for with a random effect of hospital and included in the model when statistically appropriate. Reported odds ratios represent the ratio of the odds of a postoperative outcome in prior (or current) smokers to the odds of the same event in the nonsmoker group. A confidence interval that includes 1 implies no statistically significant difference in the odds of a given outcome between smoking groups. All analyses were performed using SAS software, Version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Patient characteristics of the study sample are presented in Table 1. Most of the baseline patient characteristics were statistically significantly different between the 3 smoking groups, although many of the differences were not clinically meaningful. Current smokers were younger, had higher pack years of smoking, had a lower prevalence of diabetes, but had higher rates of alcohol consumption, COPD, and >10% loss of body weight in the last 6 months.

All postoperative outcomes differed statistically significantly by smoking status (Table 2). The unadjusted rates of complications including postoperative pneumonia, failure to wean from the ventilator, reintubation, return to the OR, and combined pulmonary complications, and for the composite outcome were highest in the current smoker group. Prior smokers had the highest unadjusted rate of SSI, venous thromboembolism, stroke, myocardial infarction, renal failure, urinary tract infection, mortality rates at 30 days and 1 year as well as combined vascular complications. Mean postoperative surgical length of stay varied by almost 1 day between never smokers (9.8 days) and prior and current smokers (10.6–10.7 days; $P < .001$).

Table 3 presents adjusted odds ratios for selected postoperative outcomes comparing the current and prior smokers to the never smokers by cancer sites (GI, thoracic, and urologic), followed by direct comparison of current smokers to prior smokers, using prior smokers as a reference group (Table 4). Percent of patients who were current or prior smokers differed by cancer site: GI cancer (51%), thoracic cancer (84%), and urologic cancer (57%).

Compared with never smokers, prior smokers and current smokers with GI malignancies were significantly more likely to have surgical site infection (SSI), pneumonia, failure to wean from ventilator, reintubation, CPO, and

TABLE 1 Patient characteristics by smoking status in cancer patients, % (n) or mean (SD)

	Overall (n = 20,413)	Never smoked (n = 8,375)	Prior smoker (n = 5,096)	Current smoker (n = 6,942)	P value
Patient demographics					
Male gender	97.8 (19,961)	97.6 (8,172)	98.6 (5,023)	97.5 (6,766)	<.001
Race					<.001
White, Hispanic	4.1 (842)	5.9 (497)	3.1 (156)	2.7 (189)	
Black	15.1 (3,089)	15.3 (1,282)	11.8 (601)	17.4 (1,206)	
White, not of Hispanic origin	63.8 (13,032)	61.9 (5,181)	68.0 (3,465)	63.2 (4,386)	
Unknown/other	16.9 (3,450)	16.9 (1,415)	17.2 (874)	16.7 (1,161)	
Age, mean (SD)	66.6 (10.2)	68.8 (10.4)	69.3 (9.3)	62.1 (9.0)	<.001
Pack years of smoking, mean (SD)	37.9 (39.0)	0.0 (0.0)	49.2 (36.3)	59.1 (34.7)	<.001
Preoperative status					
Diabetes	23.2 (4,733)	26.9 (2,249)	26.2 (1,333)	16.6 (1,151)	<.001
ETOH >2 drink a day 2 weeks. before admission	11.0 (2,231)	6.0 (497)	8.4 (429)	18.9 (1,305)	<.001
Chemotherapy for malignancy in last 30 days	1.7 (343)	1.4 (120)	1.6 (79)	2.1 (144)	.006
Congestive heart failure in 30 days before surgery	1.6 (325)	1.7 (139)	2.0 (101)	1.2 (85)	.004
History of severe COPD	20.5 (4,189)	9.7 (815)	24.9 (1,270)	30.3 (2,104)	<.001
Open wound/wound infection	1.0 (211)	1.0 (83)	1.0 (52)	1.1 (76)	.814
>10% loss of body weight in last 6 months	10.4 (2,114)	8.6 (722)	9.9 (505)	12.8 (887)	<.001
Functional health status (1–3)					<.001
Independent	94.7 (19,324)	93.9 (7,863)	94.5 (4,816)	95.7 (6,645)	
Partially dependent	4.8 (972)	5.4 (450)	5.0 (256)	3.8 (266)	
Totally dependent	0.6 (117)	0.7 (62)	0.5 (24)	0.4 (31)	
Preoperative serum albumin, mean (SD)	3.8 (0.6)	3.8 (0.6)	3.8 (0.5)	3.8 (0.6)	.004
Surgical profile					
ASA class					<.001
Healthy patient	0.4 (75)	0.6 (50)	0.2 (12)	0.2 (13)	
Mild systemic disease	16.9 (3,452)	20.5 (1,720)	13.3 (678)	15.2 (1,054)	
Severe systemic disease	71.7 (14,639)	68.5 (5,737)	73.5 (3,744)	74.3 (5,158)	
Constant threat to life	10.9 (2,234)	10.3 (863)	12.9 (656)	10.3 (715)	
Moribund patient	0.1 (13)	0.1 (5)	0.1 (6)	0.0 (2)	
Fiscal year (Oct 1–Sept 31)					<.001
2002	16.1 (3,295)	15.5 (1,297)	17.4 (886)	16.0 (1,112)	
2003	16.5 (3,359)	16.4 (1,370)	17.3 (884)	15.9 (1,105)	
2004	15.4 (3,153)	14.6 (1,223)	17.2 (874)	15.2 (1,056)	
2005	14.5 (2,964)	13.7 (1,144)	15.7 (798)	14.7 (1,022)	
2006	13.6 (2,778)	12.8 (1,076)	14.6 (743)	13.8 (959)	
2007	12.6 (2,569)	11.5 (964)	13.9 (707)	12.9 (898)	
2008	11.2 (2,295)	15.5 (1,301)	4.0 (204)	11.4 (790)	
Wound classification					<.001
Clean	23.7 (4,835)	20.8 (1,743)	24.1 (1,229)	26.8 (1,863)	
Clean/contaminated	73.3 (14,960)	75.7 (6,338)	73.1 (3,726)	70.5 (4,896)	
Contaminated	2.6 (534)	3.1 (260)	2.4 (123)	2.2 (151)	
Infected	0.4 (84)	0.4 (34)	0.4 (18)	0.5 (32)	
Work RVU, mean (SD)	23.8 (6.2)	23.4 (6.0)	23.7 (6.0)	24.5 (6.5)	<.001
Total operation time, mean (SD)	3.3 (1.8)	3.2 (1.7)	3.3 (1.7)	3.4 (1.9)	<.001

TABLE 2 Postoperative outcomes by smoking status in cancer patients

	Overall (n = 20,413)	Never smoked (n = 8,375)	Prior smoker (n = 5,096)	Current smoker (n = 6,942)	P value
Surgical site infection	8.9 (1,824)	8.9 (744)	9.8 (498)	8.4 (582)	.030
Venous thromboembolism	1.3 (263)	1.3 (110)	1.7 (89)	0.9 (64)	<.001
Stroke/cerebrovascular accident	0.5 (106)	0.4 (37)	0.8 (39)	0.4 (30)	.019
Myocardial infarction	0.9 (178)	0.8 (68)	1.2 (63)	0.7 (47)	.004
Renal failure	2.1 (436)	2.0 (170)	2.8 (144)	1.8 (122)	<.001
Urinary tract infection	3.9 (799)	4.1 (340)	4.7 (238)	3.2 (221)	<.001
Pneumonia	7.3 (1,497)	4.9 (409)	8.2 (417)	9.7 (671)	<.001
Failure to wean	5.1 (1,048)	3.4 (282)	5.7 (293)	6.8 (473)	<.001
Reintubation	5.8 (1,183)	3.8 (322)	6.4 (328)	7.7 (533)	<.001
30-day mortality	3.4 (698)	2.9 (242)	4.6 (236)	3.2 (220)	<.001
1-year mortality*	16.1 (3,292)	13.5 (1,127)	18.5 (941)	17.7 (1,224)	<.001
Pulmonary complication (CPO)	11.1 (2,272)	7.8 (651)	12.5 (638)	14.2 (983)	<.001
Vascular complication	1.4 (277)	1.2 (103)	2.0 (100)	1.1 (74)	<.001
Composite outcome	19.1 (3,901)	16.0 (1,343)	21.2 (1,078)	21.3 (1,480)	<.001
Return to OR	9.4 (1,929)	8.1 (680)	9.8 (498)	10.8 (751)	<.001
Length of postoperative surgical stay, mean (SD)	10.3 (10.7)	9.8 (10.5)	10.7 (11.0)	10.6 (10.8)	<.001
Excluding those with 30-day mortality	10.3 (10.8)	9.8 (10.5)	10.7 (11.1)	10.6 (10.9)	<0.001

Results are presented as column-% (n) unless specified otherwise. For patients with 30-day mortality, it is unknown whether death occurred prior to hospital discharge

return to the OR. Both prior smokers and current smokers had a significantly higher mortality at 30 days and 1 year (Table 3). Direct comparison of current and prior smokers showed significantly higher risk of pneumonia, failure to wean from the ventilator, reintubation rates, CPO, and 1-year mortality for current smokers within the GI group (Table 4).

Compared with never smokers, current smokers in the thoracic group were more likely to develop pneumonia and experience failure to wean from ventilator, reintubation, and CPO. SSI rates did not differ by smoking status (Table 3). Current smokers also had significantly higher mortality risk at 1 year. Direct comparison of current to prior smokers showed a higher risk of pneumonia, failure to wean from the ventilator, reintubation rate, CPO, return to OR, and 1-year mortality for current smokers within the thoracic group (Table 4).

Compared with never smokers, urology cancer patients who were current smokers had increased risk of pneumonia, CPO, and return to OR. The risk of returning to OR was also elevated in prior smokers in the urology group (Table 3). Direct comparison of current to prior smokers showed no significant differences within the urology group (Table 4).

For all cancer sites combined, prior smokers did not show a significantly different length of stay compared with never smokers in the adjusted model. Current smokers had a

significant increase in their length of stay for combined cancer sites compared with never smokers (5.9%: P < .001) and for GI and thoracic individually (GI 7.5% [P < .001], thoracic 8.2% [P = .003]). Direct comparison of current to prior smokers showed similar findings of those between current and never smokers (overall 4.3% [P < .001], GI 4.7% [P = .003], thoracic 9.0% [P < .001]).

Table 5 presents postoperative complications analyzed by pack years of smoking in current and prior smokers. The number of pack years smoked showed no significant association with postoperative outcome in current or prior smokers.

DISCUSSION

To our knowledge, this is the largest study to date examining smoking-related postoperative complications in patients with cancer. We analyzed postoperative complications and mortality in 3 common cancer groups (GI, thoracic, and urologic) undergoing cancer surgeries stratified by smoking status (current, prior, never) in more than 20,000 VA patients. GI cancer patients had elevated risk of SSI, pneumonia, failure to wean from ventilator, reintubation, CPO, return to OR, postoperative length of stay, 30-day and 1-year mortality in both current and prior smokers when these groups were compared with never smokers. Direct comparison of current to prior smokers

TABLE 3 Comparison of current and prior smokers, using never smokers as a reference group

Cancer site/smoking status	Odds ratio (95% confidence interval)							
	Surgical site infection	Pneumonia	Failure to wean	Reintubation	Combined pulmonary outcome	Return to OR	30-day mortality	1-year mortality
GI, n = 12,432								
Never (49%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Prior (25%)	1.25 (1.09–1.44)	1.52 (1.26–1.84)	1.58 (1.28–1.97)	1.66 (1.35–2.04)	1.60 (1.38–1.87)	1.20 (1.03–1.39)	1.50 (1.19–1.89)	1.22 (1.08–1.38)
Current (26%)	1.20 (1.05–1.38)	1.98 (1.64–2.40)	2.21 (1.79–2.73)	2.15 (1.75–2.65)	1.96 (1.68–2.29)	1.31 (1.13–1.53)	1.41 (1.08–1.82)	1.62 (1.43–1.85)
Thoracic, n = 4,490								
Never (16%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Prior (29%)	0.69 (0.38–1.26)	1.05 (0.76–1.44)	1.15 (0.76–1.74)	1.11 (0.77–1.60)	1.08 (0.81–1.42)	0.97 (0.68–1.39)	1.43 (0.88–2.34)	1.19 (0.92–1.54)
Current (55%)	0.93 (0.54–1.60)	1.51 (1.12–2.03)	1.64 (1.11–2.40)	1.72 (1.22–2.42)	1.62 (1.25–2.11)	1.30 (0.94–1.81)	1.30 (0.79–2.13)	1.50 (1.17–1.92)
Urology, n = 3,491								
Never (43%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Prior (21%)	1.18 (0.70–1.99)	1.48 (0.90–2.45)	1.48 (0.81–2.71)	1.09 (0.63–1.86)	1.26 (0.85–1.86)	1.69 (1.15–2.49)	1.26 (0.68–2.34)	1.04 (0.77–1.41)
Current (36%)	1.23 (0.78–1.93)	1.97 (1.23–3.15)	1.37 (0.75–2.48)	1.27 (0.77–2.10)	1.57 (1.09–2.27)	1.44 (1.00–2.07)	1.16 (0.62–2.17)	1.19 (0.90–1.58)

Current current smoker within 1 year, *Prior* noncurrent smoker with > 0 recorded pack-years of smoking, *Never* noncurrent smoker with 0 or missing recorded pack-years of smoking

Adjusted for fixed effects of age, race/ethnicity, work RVU, surgeon specialty, ASA classification, alcohol use, and year. SSI additionally adjusted for wound class. Models include a random effect for hospital when possible

TABLE 4 Direct comparison of current smokers to prior smokers, using prior smokers as a reference group

Cancer site/Smoking status	Surgical site infection	Pneumonia	Failure to wean	Reintubation	Combined pulmonary outcome	Return to OR	30-day mortality	1-year mortality
GI, n = 12,432								
Never (49%)	0.80 (0.70–0.91)	0.66 (0.54–0.79)	0.63 (0.51–0.78)	0.60 (0.49–0.74)	0.62 (0.53–0.73)	0.84 (0.72–0.97)	0.67 (0.53–0.84)	0.82 (0.72–0.93)
Prior (25%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Current (26%)	0.96 (0.82–1.11)	1.30 (1.07–1.59)	1.40 (1.12–1.74)	1.30 (1.05–1.60)	1.22 (1.04–1.44)	1.10 (0.93–1.30)	0.94 (0.72–1.23)	1.33 (1.16–1.53)
Thoracic, n = 4,490								
Never (16%)	1.44 (0.79–2.62)	0.95 (0.69–1.31)	0.87 (0.57–1.31)	0.90 (0.62–1.30)	0.93 (0.70–1.23)	1.03 (0.72–1.47)	0.70 (0.43–1.14)	0.84 (0.65–1.09)
Prior (29%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Current (55%)	1.34 (0.83–2.18)	1.44 (1.15–1.81)	1.42 (1.06–1.90)	1.55 (1.19–2.01)	1.51 (1.23–1.85)	1.34 (1.03–1.74)	0.91 (0.64–1.30)	1.26 (1.05–1.52)
Urology, n = 3,491								
Never (43%)	0.85 (0.50–1.43)	0.67 (0.41–1.12)	0.68 (0.37–1.24)	0.92 (0.54–1.58)	0.79 (0.54–1.17)	0.59 (0.40–0.87)	0.79 (0.43–1.47)	0.96 (0.71–1.30)
Prior (21%)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Current (36%)	1.04 (0.62–1.75)	1.33 (0.80–2.20)	0.92 (0.50–1.71)	1.17 (0.67–2.04)	1.25 (0.84–1.86)	0.85 (0.58–1.25)	0.92 (0.46–1.81)	1.14 (0.83–1.57)

Current current smoker within 1 year, *Prior* noncurrent smoker with > 0 recorded pack years of smoking, *Never* noncurrent smoker with > 0 or missing recorded pack-years of smoking

Adjusted for fixed effects of age, race/ethnicity, work RVU, surgeon specialty, ASA classification, alcohol use, and year. SSI additionally adjusted for wound class. Models include a random effect for hospital when possible

TABLE 5 Effect of pack years on postoperative outcomes

Postoperative outcome	Never smoked	Prior smokers (pack years)				Current smokers (pack years)			
		1–20	21–40	41–60	>60	1–20	21–40	41–60	>60
Surgical site infection	1.00	1.22 (0.43–3.50)	1.18 (0.41–3.39)	1.63 (0.56–4.73)	1.04 (0.36–2.96)	0.72 (0.31–1.68)	1.27 (0.29–5.64)	0.28 (0.04–2.07)	1.07 (0.32–3.53)
Combined pulmonary outcome	1.00	0.90 (0.21–3.79)	1.24 (0.37–4.12)	1.38 (0.41–4.63)	1.17 (0.40–3.47)	1.12 (0.51–2.47)	0.77 (0.10–6.10)	1.61 (0.54–4.74)	1.76 (0.65–4.76)
1-year mortality	1.00	2.07 (0.92–4.68)	1.15 (0.44–3.03)	0.60 (0.18–2.00)	0.26 (0.06–1.10)	1.14 (0.64–2.06)	0.77 (0.17–3.47)	1.39 (0.56–3.47)	0.95 (0.36–2.53)

showed that current smokers had a higher risk of pneumonia, failure to wean from the ventilator, reintubation rate, CPO, and 1-year mortality. The thoracic cancer group had an elevated risk of pulmonary complications, length of stay, and 1-year mortality for current smokers only. Direct comparison of current to prior smokers showed a persistently higher risk of pneumonia, failure to wean, reintubation, CPO, return to OR, and 1-year mortality. Urology cancer patients had higher risk of pneumonia, CPO, and return to OR in current smokers. Direct comparison of current to prior smokers showed no significant differences in risk of postoperative complications in this group of patients.

These findings support the need for considering smoking cessation interventions even in "time-sensitive" operations for GI cancers and thoracic cases, where current smoking status was shown to have significantly elevated risk for complications complication rates and mortality, following major cancer operations in the VA population. Since current smokers had a persistently elevated risk of pulmonary complications compared with never smokers as well as prior smokers, even short-term smoking cessation programs may improve cancer surgery outcomes and could lower medical costs by decreasing postoperative complications and length of postsurgical hospital stay. In addition, decreasing postoperative complications, return to OR, and postsurgical length of stay, via smoking cessation interventions may decrease the risk of delaying or completely omitting appropriate postoperative chemotherapy in selected patients.

Cheung et al. examined the etiology of delays in the initiation of adjuvant chemotherapy and their impact on outcomes for stage II and III rectal cancer using the SEER database.[12] They found that while advanced age and African-American race contribute to adjuvant chemotherapy delays, postoperative recovery is the most important factor. In addition, increase in the length of postoperative hospital stay independently predicted delay in adjuvant chemotherapy as well. Hendren et al. also examined surgical complications and their association with omission of chemotherapy for Stage III colorectal cancer.[13] Adjuvant chemotherapy was omitted in 46% of patient with complications, compared with 31% of patients without complications (P < .001). Having a complication was independently associated with omission of chemotherapy in multivariable analysis in their study. They concluded that implementation of quality improvement measures that effectively reduce perioperative complications may also provide a long-term cancer survival benefit. Delay in initiation of adjuvant chemotherapy was shown to be associated with inferior survival in patients with early-stage breast cancer as well.[14]

The negative effects of smoking on perioperative outcomes have been studied in the thoracic surgery

literature.[10,11] Smoking is a predictor of prolonged length of stay after lobectomy for lung cancer. Wright et al. conducted a large study using the Society of Thoracic Surgeons database showing that smoking significantly and independently contributed to adverse postoperative events in lung cancer patients. These adverse perioperative events impair quality of life, delay return to work and other regular everyday activities, increase cost of health care, and raise the risk of death. Sorensen et al. performed a large study examining risk factors for tissue and wound complications in GI surgery.[8] Independent predictors of perioperative complications were smoking, comorbidities, and perioperative blood loss. However, the overwhelming majority of patients in this study had benign disease (85%) with more than 40% of these operations having been performed for hernias.

There are several difficulties in trying to implement smoking cessation prior to major cancer operations. The optimal time for smoking cessation is debatable.[15–18] Smoking cessation for more than 4 weeks has been reported to demonstrate benefits, at least in wound healing.[15] Most cancer cases need to be done within a few weeks after diagnosis for fears of disease spreading and lesions becoming inoperable. Notable exceptions could be locally advanced esophageal and rectal tumors, where the current standard of care is neoadjuvant chemoradiation. However, these patients make up only a small minority of most general surgery/surgical oncology practices. In addition, coordinating a smoking cessation program with neoadjuvant chemotherapy could be challenging, especially in a patient population with significant social issues. On the other hand, an accurate staging and preoperative medical clearance following cancer diagnosis in mostly middle-aged or elderly patients usually takes some time, giving a window of opportunity to intervene. Furthermore, preoperative smoking cessation interventions may indirectly improve cancer surgery outcomes, including time to adjuvant therapy via decreasing postsurgical complications, return to OR, and surgical length of stay. Future studies should examine the relationship between smoking-related complications and delay of adjuvant chemotherapy.

Our study has several limitations. This is a retrospective review of a prospectively collected multi-institutional database from multiple VA medical centers across the United States. The majority of our patients are upper middle-age or elderly males, so our results may not be directly applicable to the private sector with younger patients and more females. We also had a higher than average rate of smokers; for instance, only 17% of our patients were never smokers in the thoracic surgery group. There might be the chance for some misclassification in our smoking status groups, due to missing data for number of pack years of smoking. In addition, there is evidence from prior studies that there is a poor correlation between self-reporting and actual smoking status, further contributing to the chance of misclassification of actual smoking status in our study.[4]

In summary, we found that smoking has significantly increased the risk of postoperative complications in patients undergoing major cancer surgery in the VA. In addition to showing significantly elevated risk of postoperative complications and mortality when comparing current and prior smokers to nonsmokers, undergoing elective GI and thoracic operations, we also showed a significantly elevated risk of postoperative complications and death when directly comparing current to prior smokers with GI cancers and thoracic malignancies. Based on these results, we recommend considering smoking cessation interventions prior to all major cancer operations in the VA population to decrease risk of postoperative complication, mortality, and prolonged surgical length of stay.

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