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The effects of smoking on perioperative outcomes and pseudarthrosis following anterior cervical corpectomy

Clinical article

Darryl Lau, M.D., Dean Chou, M.D., John E. Ziewacz, M.D., M.P.H., and Praveen V. Mummaneni, M.D.

Department of Neurological Surgery, University of San Francisco, California

Object. Smoking is one of the leading causes of preventable morbidity and death in the US and has been associated with perioperative complications. In this study, the authors examined the effects of smoking on perioperative outcomes and pseudarthrosis rates following anterior cervical corpectomy.

Methods. All adult patients from 2006 to 2011 who underwent anterior cervical corpectomy were identified. Patients were categorized into 3 groups: patients who never smoked (nonsmokers), patients who quit for at least 1 year (quitters), and patients who continue to smoke (current smokers). Demographic, medical, and surgical covariates were collected. Multivariate analysis was used to define the relationship between smoking and blood loss, 30-day complications, length of hospital stay, and pseudarthrosis.

Results. A total of 160 patients were included in the study. Of the 160 patients, 49.4% were nonsmokers, 25.6% were quitters, and 25.0% were current smokers. The overall 30-day complication rate was 20.0%, and pseudarthrosis occurred in 7.6% of patients. Mean blood loss was 368.3 ml and mean length of stay was 6.5 days. Current smoking status was significantly associated with higher complication rates ($p < 0.001$) and longer lengths of stay ($p < 0.001$); current smoking status remained an independent risk factor for both outcomes after multivariate logistic regression analysis. The complications that were experienced in current smokers were mostly infections (76.5%), and this proportion was significantly greater than in nonsmokers and quitters ($p = 0.013$). Current smoking status was also an independent risk factor for pseudarthrosis at 1-year follow-up ($p = 0.012$).

Conclusions. Smoking is independently associated with higher perioperative complications (especially infectious complications), longer lengths of stay, and higher rates of pseudarthrosis in patients undergoing anterior cervical corpectomy.

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Key Words • **cervical** • **complication** • **corpectomy** • **infection** • **pseudarthrosis** • **smoking**

Tobacco smoking is one of the leading causes of preventable morbidity and death in the US, and according to the Centers for Disease and Control and Prevention its use continues to rise.[2,27] Smoking is known to be highly detrimental to health and is linked with many serious diseases such as cancer,[9] heart disease,[3] chronic obstructive pulmonary disease (COPD),[22] stroke,[33] and birth defects.[10] But in addition to the chronic medical conditions associated with smoking, there is an expanding body of evidence suggesting that smoking is also an independent risk factor for perioperative complications.[14]

What is currently known about the effects of smoking on patient outcomes following spine surgery is almost entirely derived from long-term outcome measures. It has been shown that smoking is associated with poor bone quality,[30] lower fusion rates,[7] delayed fusion,[18] and increased likelihood of pseudarthrosis following spinal instrumentation and fusion.[34] There is only 1 recently published study assessing the relationship of smoking and perioperative outcomes following spine surgery.[29] In this study we assessed the effects of smoking on estimated blood loss (EBL), perioperative complications, length of hospital stay, and pseudarthrosis in patients undergoing anterior cervical corpectomy. This dual surgeon cohort and single procedure was chosen because it allowed the study to assess how smoking affects outcomes while minimizing heterogeneity and potential confounders.

Abbreviations used in this paper: BMI = body mass index; CI = confidence interval; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident; EBL = estimated blood loss; OR = odds ratio; TIA = transient ischemic attack.

Methods

Patient Population

A retrospective review of medical records from 2006 to 2011 was performed to identify all adult patients who underwent anterior cervical corpectomy by two spine neurosurgeons (D.C. and P.V.M) at the University of California, San Francisco. We included all patients over 18 years old treated for radiculopathy or myelopathy who underwent anterior cervical corpectomy with cage or structural allograft placement supplemented with an anterior plate. Patients who underwent additional posterior instrumentation and fusion were indicated and accounted for in the final analysis. The medical records were carefully reviewed by a single individual (D.L) and were then independently assessed a second time for accuracy and consistency by another coauthor (J.E.Z.).

Data Collection

Smoking status was based on a detailed review of medical records. The patients' smoking status was categorized as current smoker, quitter, and nonsmoker. In this study, the definition of quitter was smoking cessation for at least 1 year prior to surgery. Nonsmokers were patients who never smoked. The rest of the patients were current smokers. In addition, the following baseline demographic and clinical variables and comorbidities were collected: age, sex, body mass index (BMI), hypertension, diabetes mellitus, heart disease, hyperlipidemia, presence of cancer, kidney disease, liver disease, COPD, history of cerebrovascular accident (CVA)/transient ischemic attack (TIA), and alcohol use. Body mass index was calculated using the following formula: (weight in kg)/(height in meters).[2] Diagnosis-related and surgically related covariates (number of corpectomies performed) were also recorded. Diagnosis was categorized into 4 groups for statistical purposes: degenerative disease, trauma, tumor/metastasis, and osteomyelitis/infection. Preoperative neurological functional status was collected and measured with the use of Nurick grades.[26]

The primary outcomes of interest were EBL, 30-day postoperative complications, and length of hospital stay. EBL was obtained from operative reports. Complications were defined as any unforeseen or unexpected event that required additional medical or surgical treatment. Length of hospital stay was determined using the date of surgery until the date of hospital discharge. The secondary outcome of interest was radiographic pseudarthrosis at 1-year follow-up. All patients who were examined for pseudarthrosis were evaluated with dedicated 4-view radiographs of the cervical spine that include the lateral neutral, lateral flexion, lateral extension, and anterior-posterior neutral views. Pseudarthrosis was defined as any of the following features: 1) presence of radiolucent lines/area across the fusion site or around any of the screw sites; 2) absence of bridging trabeculae across the fusion site; 3) presence of motion between the spinous processes on flexion-extension radiographs; or 4) presence of motion between vertebral bodies on flexion-extension.[13,19] Therefore, if any of these were observed upon review, the patient was counted as having an abnormal finding.

Statistical Analysis

Patients were first stratified by smoking status. Descriptive and univariate statistics were used to compare the 3 groups to assess for baseline and comorbidity differences. The chi-square test and an ANOVA were used for categorical and continuous covariates, respectively. In a similar statistical manner, the outcomes of each group were compared.

We assessed whether smoking status was an independent risk factor for the outcomes measured in this study with the use of multivariate analysis models. First, descriptive and univariate statistics were used to determine associations between our covariates of interest and outcomes of interest. Chi-square analysis was used for categorical outcomes (complications and pseudarthrosis), and ANOVA was used for continuous outcomes (EBL and length of stay). Then, multivariate models of the outcomes of interest were constructed. The models adjusted for baseline differences among the 3 groups and potential confounders (covariates that had p values < 0.200 were included in the multivariate models). For the models of complications and pseudarthrosis, multivariate logistic regression was used; for the evaluation of EBL and length of stay, multivariate analysis of covariance was used; for the subgroup analysis comparing the proportion of infectious complications, the chi-square exact test was used; and p values < 0.050 were determined to be statistically significant. All statistical analysis was performed using SAS 9.3 (SAS Institute).

Results

A total of 166 patients were initially identified in the records. One of the patients was younger than 18 years and 5 did not have records available for review. This resulted in a total of 160 adult patients who underwent anterior cervical corpectomy and anterior plate placement and who were included in the study. Of the 160 patients, 79 (49.4%) were nonsmokers, 41 (25.6%) were quitters, and 40 (25.0%) were current smokers (Table 1). Preoperative Nurick Grade was 0 or 1 in 51.3% of the patients and the remainder had scores of 2 or greater. The cohort of patients consisted of 70.6% with degenerative disease, 8.1% with trauma, 8.1% with tumor/metastasis, and 13.1% with infection. A majority of the patients underwent 1-level corpectomy (69.4%); 18.8% and 11.9% underwent 2-level corpectomy and 3 or more level corpectomy, respectively. Supplemental posterior fusion was performed in 32.5% of patients.

Demographics, Baseline Variables, and Comorbidities

Table 1 compares demographic and baseline variables and comorbidities of the 3 smoking groups. Quitters (68.3%) and current smokers (72.5%) had significantly more males compared with nonsmokers (45.6%; p = 0.001). As expected, the current smoker group had significantly more patients with COPD (17.5%) than the nonsmokers (3.8%) and quitters (4.9%; p = 0.021). There were no significant differences in age and the rest of the comorbidities. Among the 3 groups, there was a significant

TABLE 1: Demographic and baseline characteristics of patients who underwent cervical corpectomy stratified by preoperative smoking status*

Risk Factor	Preop Smoking Status†			p Value‡
	Never	Quit	Current	
no. of patients	79 (49.4)	41 (25.6)	40 (25)	
mean age ± SD (yrs)	52.2 ± 11.3	55.0 ± 11.7	52.0 ± 12.0	0.400
males	36 (45.6)	28 (68.3)	29 (72.5)	**0.001**
mean BMI ± SD (kg/m^2)	28.5 ± 6.1	28.6 ± 6.7	28.3 ± 5.7	0.981
hypertension	31 (39.2)	22 (53.7)	16 (40.0)	0.287
diabetes	12 (15.2)	7 (17.1)	7 (17.5)	0.936
heart disease	12 (15.2)	8 (19.5)	3 (7.5)	0.293
hyperlipidemia	17 (21.5)	13 (31.7)	7 (17.5)	0.283
cancer	5 (6.3)	4 (9.8)	5 (12.5)	0.513
kidney disease	4 (5.1)	3 (7.3)	3 (7.5)	0.829
liver disease	6 (7.6)	4 (9.8)	7 (17.5)	0.248
COPD	3 (3.8)	2 (4.9)	7 (17.5)	**0.021**
CVA/TIA	2 (2.5)	1 (2.4)	2 (5.0)	0.733
alcohol use	29 (36.7)	22 (53.7)	16 (40.0)	0.196
preop Nurick Grade				**0.041**
0 or 1	47 (59.5)	21 (51.2)	14 (35.0)	
2 or greater	32 (40.5)	20 (48.8)	26 (65.0)	
diagnosis				**0.005**
degenerative	60 (76.0)	34 (82.9)	19 (47.5)	
trauma	6 (7.6)	3 (7.3)	4 (10.0)	
tumor/metastasis	5 (6.3)	3 (7.3)	5 (12.5)	
infection	8 (10.1)	1 (2.4)	12 (30.0)	
no. of levels (corpectomies)				**0.004**
1	61 (77.2)	30 (73.2)	20 (50.0)	
2	12 (15.2)	9 (22.0)	9 (22.5)	
3 or more	6 (7.6)	2 (4.9)	11 (27.5)	
fusion				**0.022**
anterior	59 (74.7)	29 (70.7)	20 (50.0)	
anterior & posterior	20 (25.3)	12 (29.3)	20 (50.0)	

* Among the 3 groups, there were significant differences in sex, COPD, preoperative Nurick grade, diagnosis, number of levels, and fusion. These differences were accounted for in the multivariate analysis when assessing the relation between smoking and the outcomes of interest.

† All data given as value (%) unless otherwise indicated.

‡ Significance indicated in bold.

difference in preoperative Nurick score ($p = 0.041$), diagnosis ($p = 0.005$), number of levels operated ($p = 0.004$), and use of posterior spinal fusion ($p = 0.022$). Nonsmokers and quitters tended to undergo 1-level corpectomy for degenerative diseases, while current smokers underwent surgery for a greater variety of diagnoses.

Complications

Table 2 shows the association between the covariates of interest and postoperative complications. The overall complication rate was 20.0%. Smoking status was significantly associated with perioperative complications ($p < 0.001$). More specifically, current smokers had a higher complication rate (42.5%) than both quitters (19.5%) and patients who never smoked (8.9%). Hypertension ($p = 0.013$), diabetes ($p = 0.042$), COPD ($p < 0.001$), CVA/TIA ($p < 0.001$), diagnosis ($p < 0.001$), number of levels ($p < 0.001$), and posterior fusion ($p < 0.001$) were significantly associated with complication rate.

Table 3 shows the results of multivariate logistic regression analysis for smoking status and its relationship to perioperative complications adjusted for age, hypertension, diabetes, COPD, CVA/TIA, preoperative Nurick grade, diagnosis, number of levels, and posterior fusion. Current smoking status was an independent risk factor for complications. Relative to nonsmokers, current smokers had significantly higher odds of experiencing a complication (odds ratio [OR] 2.87, 95% confidence interval [CI] 1.15–3.04; $p = 0.012$). Quitters did not experience increased odds

TABLE 2: Univariate analysis of covariates with complications and pseudarthrosis in patients who underwent anterior cervical corpectomy*

	Complications			Pseudarthrosis		
	Overall	With Complications		Overall	With Pseudarthrosis	
Variable	Value (%)	Value (%)	p Value†	Value (%)	Value (%)	p Value†
total	160	32 (20.0)		132	10 (7.6)	
smoking status			**<0.001**			0.163
never	79 (49.4)	7 (8.9)		70 (53.0)	3 (4.3)	
quit	41 (25.6)	8 (19.5)		37 (28.0)	3 (8.1)	
current	40 (25.0)	17 (42.5)		25 (18.9)	4 (16.0)	
age (yrs)			0.111			0.406
<45	31 (19.4)	4 (12.9)		27 (20.5)	3 (11.1)	
45–65	110 (68.8)	21 (19.1)		89 (67.4)	7 (7.9)	
>65	19 (11.9)	7 (36.8)		16 (12.1)	0 (0.0)	
sex			0.522			0.059
male	93 (58.1)	17 (18.3)		77 (58.3)	3 (3.9)	
female	67 (41.9)	15 (22.4)		55 (41.7)	7 (12.7)	
BMI (kg/m^2)‡			0.337			0.961
<18.5	3 (2.6)	0 (0.0)		2 (1.9)	0 (0.0)	
18.5–24.9	28 (24.3)	5 (17.9)		24 (23.3)	2 (8.3)	
25.0–29.9	42 (36.5)	3 (7.1)		37 (35.9)	3 (8.1)	
≥30	42 (36.5)	8 (19.0)		40 (38.8)	4 (10.0)	
hypertension			**0.013**			0.381
yes	69 (43.1)	20 (29.0)		57 (43.2)	3 (5.3)	
no	91 (56.9)	12 (13.2)		75 (56.8)	7 (9.3)	
diabetes			**0.042**			0.823
yes	26 (16.3)	9 (34.6)		23 (17.4)	2 (8.7)	
no	134 (83.8)	23 (17.2)		109 (82.6)	8 (7.3)	
heart disease			0.430			0.727
yes	23 (14.4)	6 (26.1)		18 (13.6)	1 (5.6)	
no	137 (85.6)	26 (19.0)		114 (86.4)	9 (7.9)	
hyperlipidemia			0.851			0.613
yes	37 (23.1)	7 (18.9)		31 (23.5)	3 (9.7)	
no	123 (76.9)	25 (20.3)		101 (76.5)	7 (6.9)	
cancer			0.576			0.843
yes	14 (8.8)	2 (14.3)		11 (8.3)	1 (9.1)	
no	146 (91.3)	30 (20.5)		121 (91.7)	9 (7.4)	
kidney disease			0.414			0.436
yes	10 (6.3)	3 (30.0)		7 (5.3)	0 (0.0)	
no	150 (93.8)	29 (19.3)		125 (94.7)	10 (8.0)	
liver disease			0.700			0.374
yes	17 (10.6)	4 (23.5)		9 (6.8)	0 (0.0)	
no	143 (89.4)	28 (19.6)		123 (93.2)	10 (8.1)	
COPD			**<0.001**			0.678
yes	12 (7.5)	8 (66.7)		9 (6.8)	0 (0.0)	
no	148 (92.5)	24 (16.2)		123 (93.2)	10 (8.1)	
CVA/TIA			**<0.001**			0.181
yes	5 (3.1)	4 (80.0)		4 (3.0)	1 (25.0)	
no	155 (96.9)	28 (18.1)		128 (97.0)	9 (7.0)	

(continued)

TABLE 2: Univariate analysis of covariates with complications and pseudarthrosis in patients who underwent anterior cervical corpectomy* *(continued)*

	Complications			Pseudarthrosis		
	Overall	With Complications		Overall	With Pseudarthrosis	
Variable	Value (%)	Value (%)	p Value†	Value (%)	Value (%)	p Value†
alcohol use			0.810			0.952
yes	67 (41.9)	14 (20.9)		54 (40.9)	4 (7.4)	
no	93 (58.1)	18 (19.4)		78 (59.1)	6 (7.7)	
preop Nurick grade			0.082			0.206
0 or 1	82 (51.3)	12 (14.6)		67 (50.8)	7 (10.4)	
2 or greater	78 (48.8)	20 (25.6)		65 (49.2)	3 (4.6)	
diagnosis			**<0.001**			0.659
degenerative	113 (70.6)	13 (11.5)		101 (76.5)	8 (7.9)	
trauma	13 (8.1)	5 (38.5)		9 (6.8)	1 (11.1)	
tumor/metastasis	13 (8.1)	4 (30.8)		8 (6.1)	1 (12.5)	
infection	21 (13.1)	10 (47.6)		14 (10.6)	0 (0.0)	
no. of levels (corpectomies)			**<0.001**			0.813
1	111 (69.4)	11 (9.9)		97 (73.5)	8 (8.2)	
2	30 (18.8)	11 (36.7)		23 (17.4)	1 (4.3)	
3 or more	19 (11.9)	10 (52.6)		12 (9.1)	1 (8.3)	
fusion			**<0.001**			0.315
anterior	108 (67.5)	8 (7.4)		97 (73.5)	6 (6.2)	
anterior & posterior	52 (32.5)	24 (46.2)		35 (26.5)	4 (11.4)	

* Smoking status was significantly associated with complications. Current smokers had the highest rate of complications compared with both nonsmokers and quitters. Current smokers also had the highest rate of pseudarthrosis.

† Significance indicated in bold.

‡ Not all data points were available for all patients.

of complications (OR 1.71, 95% CI 0.64–11.45; p = 0.174); this may represent the effectiveness of preoperative smoking cessation in reducing complication risk.

Table 4 shows the specific complications encountered in this cohort stratified by smoking status. Figure 1 demonstrates a comparison of the proportion of infectious complications among the smoking subgroups. Of the complications that were experienced by the patients, current smokers experienced a larger proportion of infectious complications compared with both quitters and nonsmokers (p = 0.013). In nonsmokers, 14.3% of the complications were infectious, as were 37.5% in quitters, and 76.5% in current smokers.

Pseudarthrosis

Table 2 shows the association between the covariates of interest and pseudarthrosis rates. Of the 160 patients, 132 underwent follow-up and sufficient imaging to evaluate the fusion at 1 year. Of the patients lost to follow-up, 6 died prior to follow-up. Pseudarthrosis was detected in 7.6% of patients at the 1-year follow-up evaluation. An example of solid fusion can be observed in Fig. 2A, and conversely, examples of evidence of lucent bone, nonunion, and pseudarthrosis can be observed in Fig. 2B–D, respectively. Current smokers had higher rates of pseudarthrosis (16.0%) compared with quitters (8.1%) and nonsmokers (4.3%); however, this difference was not statistically significant (p = 0.163). Males had lower rates of pseudarthrosis compared with females (3.9% vs 12.7%, respectively; p = 0.059).

A multivariate logistic regression model of pseudarthrosis is shown in Table 3. The model included smoking status, sex, and CVA/TIA. Current smoking status was independently associated with higher odds of pseudarthrosis compared with nonsmokers (OR 1.72, 95% CI 1.13–2.63, p = 0.012). Being male was an independent factor associated with lower odds of pseudarthrosis (OR 0.19, 95% CI 0.04–0.84, p = 0.029).

Estimated Blood Loss

Table 5 shows the univariate association between covariates and EBL. Overall mean EBL was 368.3 ml. There was a trend for current smokers having the highest mean EBL of 518.9 ml; quitters had intermediate with a mean EBL of 462.1 ml, and nonsmokers had the lowest mean EBL of 249.6 ml (p = 0.065). Hypertension (p = 0.024), diabetes (p = 0.001), diagnosis (p = 0.014), number of levels (p < 0.001), and posterior fusion (p = 0.001) were all significantly associated with EBL. Upon multivariate analysis, smoking status was no longer significantly associated with blood loss, but hypertension (p = 0.026), diabetes (p = 0.014), diagnosis of infection (p = 0.007), and 3 or more levels (p = 0.005) were independently associated with higher EBL (Table 6).

TABLE 3: Independent predictors of complications and pseudarthrosis in patients who underwent anterior cervical corpectomy*

Variable	Complications			Pseudarthrosis		
	OR	95% CI	p Value†	OR	95% CI	p Value†
smoking status						
never	reference	reference	reference	reference	reference	reference
quit	1.71	0.64–11.45	0.174	1.64	0.51–5.31	0.411
current	2.87	1.15–3.04	**0.012**	1.72	1.13–2.63	**0.012**
age (yrs)						
<45	reference	reference	reference			
45–65	0.29	0.05–1.60	0.156			
>65	0.49	0.06–4.36	0.524			
sex						
male				0.19	0.04–0.84	**0.029**
female				reference	reference	reference
hypertension						
yes	3.10	0.75–12.83	0.119			
no	reference	reference	reference			
diabetes						
yes	2.42	0.53–11.03	0.254			
no	reference	reference	reference			
COPD						
yes	10.45	1.89–57.84	**0.007**			
no	reference	reference	reference			
CVA/TIA						
yes	35.16	1.66–745.61	**0.022**	5.61	0.35–90.55	0.225
no	reference	reference	reference	reference	reference	reference
preop Nurick grade						
0 or 1	reference	reference	reference			
2 or greater	1.31	0.39–4.38	0.657			
diagnosis						
degenerative	reference	reference	reference			
trauma	4.76	0.77–29.36	0.093			
tumor/metastasis	1.07	0.57–2.02	0.836			
infection	0.72	0.11–4.58	0.724			
no. of levels (corpectomies)						
1	reference	reference	reference			
2	1.92	0.38–9.59	0.429			
3 or more	1.15	0.66–2.01	0.620			
fusion						
anterior	reference	reference	reference			
anterior & posterior	15.48	3.08–77.90	**0.001**			

* Current smoking status remained an independent risk factor for higher odds of postoperative complications and pseudarthrosis on multivariate analysis after adjusting for potential confounder and baseline differences.
† Significance indicated in bold.

Length of Hospital Stay

Table 5 shows the associations between the covariates of interest and length of stay. Mean length of stay for this cohort was 6.5 days. Smoking status was significantly associated with length of hospital stay ($p < 0.001$). Current smokers experienced mean stays of 9.5 days, quitters 6.8 days, and nonsmokers 4.8 days. Age ($p = 0.005$), hypertension ($p = 0.014$), kidney disease ($p = 0.022$), liver disease ($p = 0.028$), diagnosis ($p < 0.001$), number of levels ($p < 0.001$), and fusion ($p < 0.001$) were all significantly associated with length of stay. After adjusting for potential confounders, current smoking status remained an independent risk factor for longer hospital stay ($p < 0.001$; Table 6). Other independent risk factors for in-

TABLE 4: Specific complications stratified by smoking status*

Never (n = 79)		Quit (n = 41)		Current (n = 40)	
Complication	No.	Complication	No.	Complication	No.
wound infection ± requiring reoperation	2	urinary tract infection, pneumonia	1	pneumonia	4
C-5 palsy	2	epidural hematoma requiring reoperation, bacteremia	1	wound infection ± requiring reoperation	3
seroma requiring reoperation	1	airway obstruction requiring tracheotomy	1	hardware failure, infection	1
implant failure requiring reoperation	1	MI, pneumonia	1	new rt upper-extremity weakness	1
CSF leak requiring reoperation, DVT	1	pulmonary edema	1	airway obstruction requiring intubation	1
total	7	seizure	1	sepsis	1
		hepatic encephalopathy	1	pneumonia, wound infection	1
		acute renal failure	1	urinary tract infection	1
		total	8	meningitis	1
				pericardial effusion	1
				septic joint	1
				pleural effusion	1
				total	17

* DVT = deep venous thrombosis; MI = myocardial infarction.

creased length of stay on multivariate analysis included age greater than 65 years ($p < 0.001$), BMI of 25.0–29.9 kg/m^2 ($p < 0.001$), BMI of 30 kg/m^2 or greater ($p = 0.001$), kidney disease ($p = 0.041$), liver disease ($p = 0.047$), diagnosis of tumor/metastasis ($p < 0.001$), diagnosis of infection ($p < 0.001$), 3 or more levels ($p < 0.001$), and posterior fusion ($p < 0.001$).

Discussion

There is a growing body of evidence that smoking is associated with higher perioperative complications and morbidity following surgery.[14,16,17] A recent systematic review of 12 general surgery cohort studies showed that patients who continued to smoke before surgery experienced more complications than nonsmokers.[31] In a retrospective study of 164,608 patients, smokers not only had higher odds of complications, but they also had significantly higher odds of death after surgery.[32] Similar to these findings, our results suggest that current smoking status is associated higher perioperative complications, longer lengths of stay, and higher rates of pseudarthrosis. In addition, current smoking status remained an independent risk factor for all 3 outcomes after multivariate logistic regression analysis. A finding from this study that was not as distinct was that quitters did not have the same risk for poor outcome as current smokers, indicating that preoperative smoking cessation is likely beneficial.

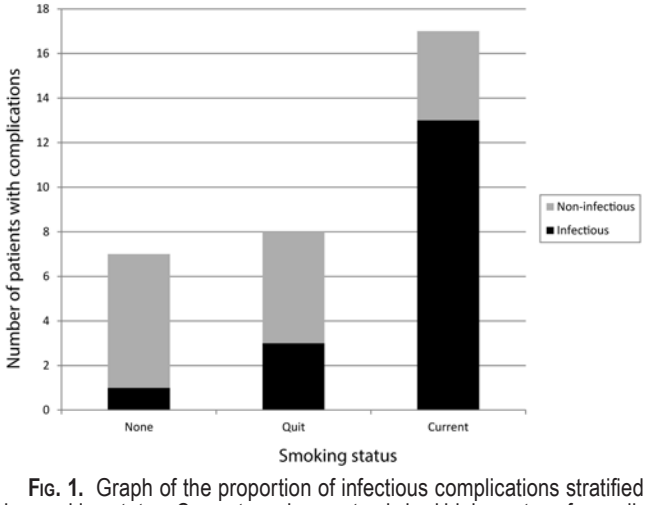

Fig. 1. Graph of the proportion of infectious complications stratified by smoking status. Current smokers not only had higher rates of complications, but the proportion of complications that were infectious in origin was significantly higher compared with the other 2 groups ($p = 0.013$). In nonsmokers and quitters, 14.3% and 37.5% of complications were secondary to infections, respectively, and 76.5% of complications were infectious in current smokers. The most common infectious complication was pneumonia.

Most of the current literature and studies pertaining to smoking following spine surgery evaluated long-term outcomes and fusion rates, and only a few studies evaluated perioperative outcomes.[7,11,18,23,28,34] Dean et al. performed a retrospective study of 500 patients who underwent lumbar spine surgery and demonstrated with linear regression that smokers had significantly greater mean EBL per decompressed level (97 vs 137 ml) and mean EBL per fused level (162 vs 221 ml).[5] A similar phenomenon was also observed among smokers who underwent craniotomy for tumor resection.[17] Although we did not demonstrate statistically significant differences in EBL, there was a robust trend for greater EBL in smokers. The mechanisms underlying this phenomenon are not well defined. However, there is evidence that smoking can lead to acute hyperemia secondary to buildup of transient vasodilating metabolites in blood vessels,[1,8] and smoking can result in permanent structural changes of vessels leading to dysfunction/inhibition of vessel accommodation during bleeding.[15]

Currently, there is only 1 large retrospective study by Seicean et al. that has evaluated the association of

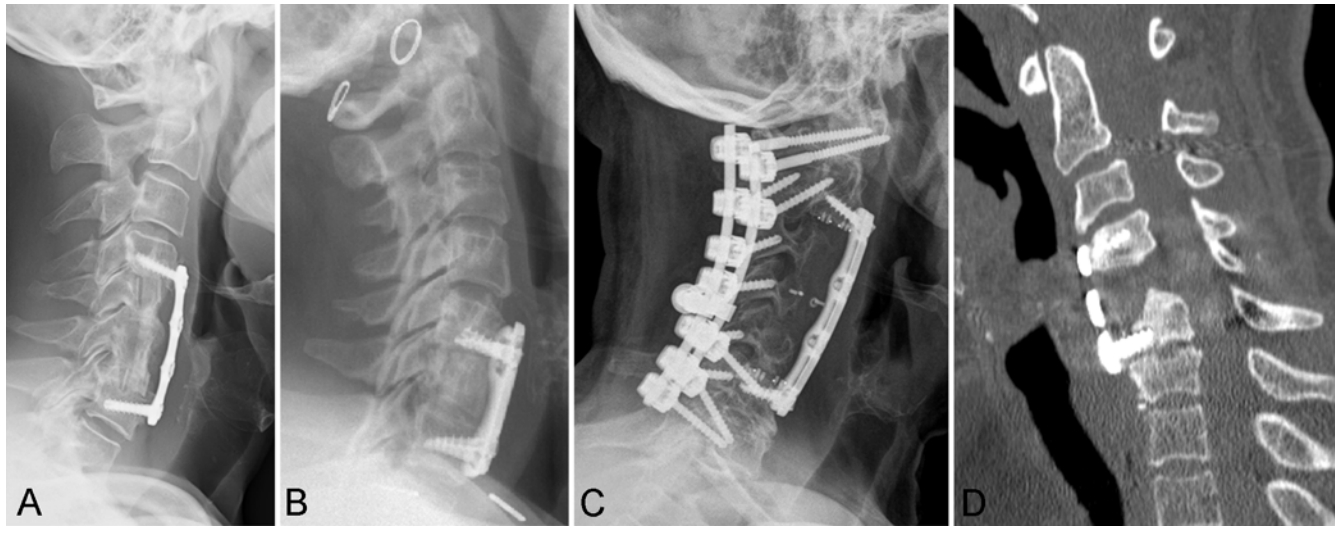

Fig. 2. Images showing examples of solid fusion (A), lucent bone (B), nonunion (C), and pseudarthrosis (D). **A:** Lateral plain radiograph of the cervical spine demonstrating solid bone fusion in between C-4 and C-7 following a 2-level corpectomy and anterior plate supplementation. **B:** Lateral plain radiograph of the cervical spine demonstrating pseudarthrosis with evidence of lucency within the corpectomy site between C-5 and C-7. **C:** Lateral plain radiograph of the cervical spine showing complete absence of bone fusion in the corpectomy sites between C-2 and C-6 in a current smoker with pseudarthrosis. **D:** Follow-up sagittal CT scan of the cervical spine showing absence of fusion at the prior C-5 corpectomy site in a current smoker with pseudarthrosis.

smoking status with perioperative complications following spine surgery.[29] Their study used the multicenter American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database to generate a cohort of 14,500 patients who underwent elective spine surgery. Using propensity score matching and logistic regression, they found that smoking itself was not found to be associated with poorer operative or 30-day outcomes in patients undergoing elective spine surgery. Their findings are valuable given the statistical power in the study. However, because most large prospectively collected databases are not developed to answer a specific question, there are underlying confounders that cannot be controlled when utilizing such a database. Examples of potential confounders that were unable to be sufficiently addressed in their analysis included exact procedure performed, number of spinal levels surgically addressed, preoperative neurological status, severity of disease, diagnosis, and extent of instrumentation. In fact, in our analysis, these covariates were significantly associated with outcome, and likely alter the postoperative course. There still remains a need of additional studies that control for such potential confounders mentioned.

In our study, we concentrated on a single procedure to allow homogeneity, and we accounted for comorbidities, preoperative neurological status, and extent of surgery in our multivariate models. Current smokers experienced an approximately 5-times higher complication rate compared with nonsmokers (42.5% vs 8.9%) and more than 2 times the complication rate compared with quitters (42.5% vs 19.5%). In fact, in this cohort, current smoking status was an independent factor that was associated with a 3-times increase in odds to experience a complication compared with nonsmokers. For a potentially modifiable behavior, this increase is extremely high. Interesting and important is the observation that quitting status was not independently associated with greater odds of complications, suggesting that preoperative smoking cessation may be effective in mitigating the detrimental effects of smoking on perioperative complications.

The types of postoperative complications that patients experience can be specific and highly dependent on the type of surgery the patient has undergone. But studies from many of the surgical subspecialties have shown that smokers experience a wide array of complications and adverse events following surgery: cardiac arrest, myocardial infarction, stroke, superficial and deep wound infections, sepsis, and shock.[32] Despite this wide range of complications, there is a trend for smokers to have higher rates of infectious complications, especially wound infections and pneumonia.[12,14,17,32] In addition, smokers are at increased risk for unplanned intubation and mechanical ventilation.[32] In our study, we performed a separate analysis to assess for differences in the proportion of infectious complications among the groups, and accordingly a significantly greater proportion of the complications (76.5%) experienced by current smokers were in fact infectious (pneumonia being the most common).[14,17] This finding is especially important because a common expected impediment following anterior approaches to the cervical spine is dysphagia, and dysphagia itself is a risk for aspiration pneumonia. Therefore, smoking cessation may be even more critical in patients undergoing anterior approaches to the cervical spine.

In this study, smokers stayed in the hospital twice as long as nonsmokers and 1.5 times as long as quitters. This finding is most likely secondary to the fact that smokers experienced more complications. Interestingly, patients who quit smoking also had longer hospital stays than nonsmokers. The exact reason for this observation is unclear.

TABLE 5: Univariate association of covariates with EBL and length of stay in patients who underwent anterior cervical corpectomy*

	EBL		Length of Stay	
Variable	ml ± SD	p Value†	Days ± SD	p Value†
total	368.3 ± 606.4		6.5 ± 5.6	
smoking status		0.065		**<0.001**
never	249.6 ± 199.6		4.8 ± 3.6	
quit	462.1 ± 556.5		6.8 ± 6.3	
current	518.9 ± 1035.9		9.5 ± 6.9	
age (yrs)		0.263		**0.005**
<45	228.4 ± 168.7		4.6 ± 4.3	
45–65	385.7 ± 704.6		6.4 ± 5.4	
>65	525.0 ± 478.9		9.9 ± 7.2	
sex		0.070		0.671
male	445.1 ± 756.2		6.2 ± 5.6	
female	250.9 ± 194.0		6.6 ± 5.7	
BMI (kg/m^2)		0.199		0.138
<18.5	350.0 ± 132.3		7.0 ± 4.4	
18.5–24.9	206.0 ± 127.7		4.8 ± 3.7	
25.0–29.9	251.4 ± 195.3		3.6 ± 2.4	
≥30	375.7 ± 494.4		5.9 ± 6.6	
hypertension		**0.024**		**0.014**
yes	507.1 ± 866.6		7.7 ± 6.4	
no	268.6 ± 273.4		5.5 ± 4.8	
diabetes		**0.001**		0.272
yes	739.1 ± 1309.1		7.6 ± 6.2	
no	291.4 ± 259.3		6.2 ± 5.5	
heart disease		0.399		0.541
yes	255.6 ± 165.3		7.1 ± 6.4	
no	385.8 ± 647.3		6.4 ± 5.5	
hyperlipidemia		0.799		0.484
yes	392.7 ± 550.3		5.9 ± 5.9	
no	360.9 ± 624.7		6.6 ± 5.6	
cancer		0.757		0.310
yes	422.7 ± 381.0		7.9 ± 5.9	
no	363.4 ± 623.5		6.3 ± 5.6	
kidney disease		0.589		**0.022**
yes	481.3 ± 264.5		10.4 ± 8.5	
no	361.1 ± 621.7		6.2 ± 5.3	
liver disease		0.474		**0.028**
yes	478.6 ± 479.9		9.3 ± 5.3	
no	355.4 ± 619.9		6.1 ± 5.6	
COPD		0.260		0.075
yes	588.9 ± 588.8		9.3 ± 5.2	
no	352.4 ± 606.9		6.2 ± 5.6	
CVA/TIA		0.876		0.155
yes	410.0 ± 332.4		10.0 ± 7.7	
no	366.7 ± 615.3		6.3 ± 5.6	

(continued)

TABLE 5: Univariate association of covariates with EBL and length of stay in patients who underwent anterior cervical corpectomy* *(continued)*

Variable	EBL		Length of Stay	
	ml ± SD	p Value†	Days ± SD	p Value†
alcohol use		0.696		0.248
yes	391.8 ± 831.4		5.7 ± 4.7	
no	350.3 ± 355.1		7.0 ± 6.2	
preop Nurick grade		0.061		0.104
0 or 1	271.7 ± 260.8		5.8 ± 5.4	
2 or greater	467.8 ± 814.0		7.2 ± 5.8	
diagnosis		**0.014**		**<0.001**
degenerative	294.7 ± 331.6		4.5 ± 3.8	
trauma	259.1 ± 189.5		8.7 ± 6.7	
tumor/metastasis	600.0 ± 478.8		12.0 ± 7.5	
infection	782.8 ± 1468.1		12.2 ± 5.7	
no. of levels (corpectomies)		**<0.001**		**<0.001**
1	274.7 ± 355.8		4.7 ± 3.9	
2	348.1 ± 245.5		8.5 ± 6.1	
3 or more	1028.6 ± 1487.7		13.5 ± 7.1	
fusion		**0.001**		**<0.001**
anterior	258.7 ± 322.7		3.9 ± 3.3	
anterior & posterior	635.3 ± 962.5		11.8 ± 5.9	

* Current smokers had the highest mean EBL among the 3 groups, which was close to being statistically significant. Smoking status was also significantly associated with length of stay. There was a trend for quitters to stay longer in the hospital than nonsmokers, and current smokers to stay the longest.

† Significance indicated in bold.

However, it is possible that patients who have a history of smoking have already accumulated comorbid conditions (such as heart disease, hypertension, diabetes, COPD, and others), and therefore quitters stayed longer in the hospital because of the extra time required in managing their comorbidities prior to discharge. Evidence for this is the fact that our patients with hypertension, diabetes, kidney disease, and liver disease had longer hospital stays. Hospital stay is not only a good indicator for time to recovery, but longer hospital stays have intrinsic risks of their own such as nosocomial infections[6] and can be an economic burden to the health care system.[21]

Most of the data pertaining to smoking and long-term outcomes evaluate fusion rates. There is a general consensus that smoking is detrimental to fusion, such as delayed spinal fusion,[18] poor spinal fusion rates,[7,11,23,28] and higher rates of pseudarthrosis following spinal instrumentation.[34] Similarly, in our study, current smoking status was independently associated with higher rates of radiographic pseudarthrosis. The mechanism behind poor fusion in smokers is related to poor bone quality secondary to tobacco smoking sequelae. Nicotine exposure is associated with delayed vascularization and smaller areas of revascularization, which lead to reduced levels of osteogenesis and hypocellular fusion mass.[4] Given that quitters had lower pseudarthrosis rates than current smokers, this may suggest that smoking cessation can lower pseudarthrosis risk.

The results from this study, in conjunction with the growing evidence in the current literature, suggest that current smoking status is associated with poorer perioperative outcomes and higher rates of pseudarthrosis. Importantly, this study also suggests that smoking cessation may possibly mitigate these risks. There are a few large randomized clinical trials that demonstrate that smoking cessation before surgery was able to decrease complications rates and improve outcomes.[20,24,25] Patient education regarding the benefits of preoperative smoking cessation needs to be implemented.

There are a few limitations to this study. The most pertinent limitations are related to the innate drawbacks associated with a retrospective design. First, the validity of the medical records is difficult to assess and can vary for multiple reasons, such as poor patient recall and unintentional inaccuracies of documentation of the care provider. This is an unfortunate drawback that cannot be avoided when performing a retrospective clinical study utilizing the medical records. Nonetheless, the methodology of data gathering was consistent and accurate to minimize error. Second, as the goal of the study was to assess whether smoking itself is a risk factor for complications, there are potential confounders that we were not able to measure and adjust for in our models. We did, however, use a 2-surgeon experience and a single procedure to minimize confounders. In addition, we analyzed and adjusted for variables that were suspected to be associated with outcomes. A second limitation is the definition of smoking cessation. In this study, 1 year was the

TABLE 6: Independent predictors of EBL and length of stay in patients who underwent anterior cervical corpectomy*

Variable	EBL	Length of Stay
smoking status		
never	reference	reference
quit	0.255	0.466
current	0.121	**<0.001**
age (yrs)		
<45		reference
45–65		0.980
>65		**<0.001**
sex		
male	0.219	
female	ref	
BMI (kg/m^2)		
<18.5	NA	NA
18.5–24.9	reference	reference
25.0–29.9	0.338	**<0.001**
≥30	0.725	**0.001**
hypertension		
yes	**0.026**	0.092
no	reference	reference
diabetes		
yes	**0.014**	
no	reference	
kidney disease		
yes		**0.041**
no		reference
liver disease		
yes		**0.047**
no		reference
COPD		
yes		0.913
no		reference
CVA/TIA		
yes		0.668
no		reference
preop Nurick grade		
0 or 1	reference	reference
2 or greater	0.524	0.394
diagnosis		
degenerative	reference	reference
trauma	0.174	0.322
tumor/metastasis	0.436	**<0.001**
infection	**0.007**	**<0.001**
no. of levels (corpectomies)		
1	reference	reference
2	0.184	0.903
3 or more	**0.005**	**<0.001**
fusion		
anterior	reference	reference
anterior & posterior	0.293	**<0.001**

* Current smoking status was an independent predictor of longer hospital stay, but not EBL on multivariate analysis after adjusting for potential confounders and baseline differences. Values in bold are statistically significant p values. NA = not applicable.

definition for smoking cessation because this was what was available in the medical records. Therefore, it is unclear exactly how long smoking cessation needs to occur before the benefits are observed (likely less than 1 year). In addition, it is not always realistic for patients to quit smoking for 1 year before surgery. A prospective study design would be necessary to better address this issue.

Conclusions

There remains a paucity of spine literature regarding the effects of smoking and perioperative outcomes. Following anterior cervical corpectomy and fusion, current smoking status was an independent risk factor for higher odds of complications, longer hospital stay, and higher odds of pseudarthrosis. The proportions of infectious complications were highest in smokers. Patients who quit smoking experienced better outcomes than smokers and quitting status was not an independent risk factor for poor outcome. Therefore, preoperative smoking cessation appears to be an effective way to mitigate perioperative morbidity and allow the best possible outcomes following surgery. While additional studies are needed to verify and supplement the findings from this study, encouragement of smoking cessation prior to spinal fusion should be encouraged.

Disclosure

Dr. Mummaneni has received royalties from DePuy Spine, Quality Medical Publishers, and Thieme Publishers; honoraria from Globus and Depuy Spine; and has purchased stock in Spinicity. Dr. Chou has received honoraria from Globus, Medtronic, Depuy, and Orthofix for teaching.

Author contributions to the study and manuscript preparation include the following. Conception and design: Lau. Acquisition of data: Lau. Analysis and interpretation of data: Lau, Chou. Drafting the article: Lau. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Mummaneni. Statistical analysis: Lau. Study supervision: Mummaneni, Ziewacz.

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Address correspondence to: Praveen V. Mummaneni, M.D., University of California, San Francisco, Department of Neurological Surgery, 505 Parnassus Ave., Rm. M779, San Francisco, CA 94143-0112. email: vmum@aol.com.