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Effect of Smoking on Motor Recovery After Cervical American Spinal Injury Association Grade D Traumatic Spinal Cord Injury

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ABSTRACT

Background: Smoking is a known neurotoxin that has been shown to negatively impact neurological function and recovery in multiple animal studies. Patients who smoke have been shown to have decreased rates of motor improvement, fusion, and overall successful outcomes after elective spinal surgery, but the effect of smoking on outcomes after traumatic spinal cord injury (TSCI) has not been demonstrated in prior literature. This study aims to investigate how smoking effects motor recovery after TSCI.

Methods: Using the National Spinal Cord Injury Statistical Center database, patients who underwent surgical management of American Spinal Injury Association grade D cervical TSCI between 2009 and 2016 were included. Patients were grouped by smoking or nonsmoking status. Overall total motor score and change in motor scores at rehabilitation admission, rehabilitation discharge, and 1-year follow-up visits were compared between groups. Multiple linear regression analysis was completed, including any possible confounding demographic or injury variables.

Results: A total of 152 patients (121 smokers and 31 nonsmokers) completed their 1-year follow-up interview and physical examination and were included in the study. There were no differences in motor score between groups at rehabilitation admission or discharge. Smokers had worse improvement in motor score at 1 year (7.99 nonsmokers vs 4.61 smokers; $P = 0.019$ on multivariate analysis) and worse overall total motor score at 1 year (94.0 nonsmokers vs 90.0 smokers; $P = 0.018$ on multivariate analysis) after controlling for confounders.

Conclusions: These results indicate diminished motor recovery in patients who continue to smoke after TSCI. These patients should be targeted for aggressive smoking cessation and require intervention from providers and peers in order to maximize recovery after injury.

Clinical Relevance: This study demonstrates that smoking cessation may be beneficial for patients with cervical ASIA grade D spinal cord injury and may be a focus for providers of these patients.

Level of Evidence: 3.

Cervical Spine

Keywords: spinal cord injury, smoking, motor outcomes

INTRODUCTION

Motor recovery after traumatic spinal cord injury (TSCI) is dependent on a multitude of different variables, including initial level of injury and severity, age, social factors, comorbidities, surgical factors, and rehabilitation participation.[1–5] Cigarette smoking, a source of numerous neurotoxins, is very common in patients with TSCI. Some studies report rates of tobacco use of 24% to 48% in these patients.[6] This is despite the numerous documented negative effects of smoking after TSCI and spinal surgery, including increased pulmonary and cardiovascular complications, increased hospitalization, decreased rates of spinal fusion, and increased mortality.[6–13]

Smoking has been shown to negatively impact neurological function and recovery in multiple animal studies.[14,15] Additionally, multiple clinical investigations have demonstrated that smoking is associated with worse outcomes after surgical treatment of nontraumatic cervical myelopathy when measured by both the Nurick score[11,12] and the modified Japanese Orthopedic Association Scale.[13] This impact of smoking on motor outcome has not yet been described after surgical intervention for TSCI. The purpose of the present study is to investigate the impact of smoking on overall motor scores and motor improvement after TSCI. We hypothesized that patients who continue to smoke after TSCI show worse motor recovery than those who do not smoke after their injury.

MATERIALS AND METHODS

Data were collected through the spinal cord injury (SCI) model systems program and submitted to the National Spinal Cord Injury Statistical Center

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(NSCISC).[16] The NSCISC has had 29 SCI systems throughout the United States contribute to its database. For the purposes of inclusion in NSCISC, patients must have had an SCI defined as an "acute traumatic lesion of the neural elements of the spinal canal (spinal cord and cauda equina), results in temporary or permanent sensory and/or motor deficit." Briefly, inclusion criteria are (1) external event leading to SCI as defined above; (2) treatment within participating SCI system within 1 year of injury; (3) discharged either as deceased, to acute rehabilitation, or recovered with >1-week hospital stay; and (4) signed consent and Health Insurance Portability and Accountability Act authorization forms. Access to deidentified data, stripped of names, geographic identifiers, contact information, and dates other than years of treatment are available to providers for download and were accessed for this study. Deidentified data are available from the inception of the database (1972) through 1 October 2016. Overall, this database includes 32,159 patients with data from the index injury and 26,184 patients with at least 1 year of follow-up.

The American Spinal Injury Association (ASIA) Scale is a standardized and validated method of TSCI classification[17] and is included in the NSCISC database. This retrospective cohort study focuses on ASIA grade D TSCI, as prior studies have indicated that patients with ASIA grades A, B, or C TSCI may be unable to perform the act of cigarette smoking due to diminished recovery in the upper extremities over time compared with patients with ASIA grade D injuries.[4,18] Indeed, initial analysis of all patients with cervical TSCI in the utilized data set indicated that those patients with ASIA grades A through C injuries who smoked had higher baseline motor scores than those who did not (27.47 smokers vs 22.30 nonsmokers, $P = 0.002$). Additionally, smoking rates in patients with ASIA grades A through C injuries were lower than those with ASIA grade D injuries on initial analysis (13.3% vs 20.4%, $P < 0.001$).

Inclusion criteria for the present study were as follows: ASIA grade D cervical SCI, injury after 2009 with complete smoking status information (for which collection began at follow-up visits in 2011), and completion of 1-year follow-up interview and physical examination. Outcomes beyond 1 year were not investigated because the majority of neurological recovery occurs within 1 year of injury.[3] Patients were only considered for the analysis if they underwent surgery on the spinal column at the initial injury, including laminectomy, neural canal restoration, open reduction, spinal fusion, or internal fixation of the spine.

Variables considered in the analysis included positive smoking status, age at injury, sex, race, body mass index, diabetes diagnosis, presence of other injury, presence of traumatic brain injury (TBI), initial rehabilitation length of stay, number of rehospitalizations, and days of rehospitalization. These variables were considered to be possible confounders for total motor function at 1 year. Smoking status collection for the NSCISC database began in 2011 and is collected at the 1-year follow-up visit. Patients were coded as smokers if they answered yes to any amount of regular smoking. Due to patient deidentification, age was presented categorically in 15-year increments (15–29, 30–44, 45–59, 60–74, and 75+). No patients younger than 15 years had completed smoking data and thus were excluded from the analysis. Presence of other injury was documented if the patient suffered a TBI, extremity fracture requiring surgery, facial injury affecting sensory organ, chest injury requiring chest tube or ventilation, traumatic or surgical amputations, severe hemorrhage, or surgery for an internal organ.

The primary outcomes of the study were overall motor score at 1 year and improvement in total motor score between discharge from rehabilitation and 1-year follow-up. Total motor scores scaled 0 to 100 based on the ASIA examination were recorded at the time of rehabilitation admission, rehabilitation discharge, and 1-year follow-up. Using these data, change in total motor score was calculated between time of rehabilitation discharge and at 1 year. All statistical analyses were completed using IMB SPSS Version 27 (Armonk, NY: IBM Corp). Initial comparisons in demographic and injury data between the smoking and nonsmoking groups were completed using Pearson's χ^2 test for categorical variables and Student's t test for continuous variables. Multiple linear regression was used to determine whether there was an association between smoking and motor function at the time of rehabilitation discharge and at 1-year follow-up. To identify independent predictors of diminished motor scores, variables identified to have a P value less than 0.2 on univariate analysis were selected for inclusion in a multivariate linear regression model along with standard demographic factors (age, sex, and race) and smoking status. Significance was set at $P < 0.05$ for all results.

RESULTS

A total of 3462 patients in the NSCISC database had operative intervention with coded 1-year follow-up data after 2011. Of those patients, 2085 had cervical spine injuries, 603 of whom were initially classified as having ASIA

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Table 1. Demographic data for total study population and the smoking and nonsmoking groups.

Demographic Data	Total (N = 152)	Nonsmoker (n = 121)	Smoker (n = 31)	P Value
Age at injury, y				0.078[a]
15–29	17 (11.1%)	12 (9.9%)	5 (16.1%)	
30–44	18 (11.8%)	11 (9.1%)	7 (22.6%)	
45–59	67 (44.1%)	53 (43.8%)	14 (45.2%)	
60–74	38 (25%)	35 (28.9%)	3 (9.7%)	
>75	12 (7.9%)	10 (8.3%)	2 (6.5%)	
Sex				0.173[a]
Men	113 (74.3%)	87 (71.9%)	26 (83.9%)	
Women	39 (25.7%)	34 (28.1%)	5 (16.1%)	
Race (N = 151)				0.435[a]
White	106 (70.2%)	86 (71.7%)	20 (64.5%)	
Black	37 (24.5%)	27 (22.5%)	10 (32.3%)	
Asian	5 (3.3%)	5 (4.2%)	0 (0.0%)	
Other	3 (2.0%)	2 (1.7%)	1 (3.2%)	
Body mass index	27.4 ± 5.7	27.6 ± 5.8	27.1 ± 5.5	0.730[b]
Diabetes (N = 134)				0.323[a]
No	110 (82.1%)	88 (72.7%)	22 (71.0%)	
Yes	24 (17.9%)	17 (26.3%)	7 (29.0%)	
Other injury				0.402[a]
No	121 (79.6%)	98 (70.3%)	23 (71.0%)	
Yes	31 (20.4%)	23 (29.7%)	8 (29.0%)	
Traumatic brain injury (N = 125)				0.229[a]
No	107 (85.6%)	85 (70.3%)	22 (71.0%)	
Yes	18 (14.4%)	12 (29.7%)	6 (29.0%)	
Rehabilitation length of stay, d	31.0 ± 20.1	31.8 ± 21.4	27.9 ± 13.9	0.350[b]
No. of rehospitalizations	0.3 ± 0.7	0.3 ± 0.6	0.5 ± 1.2	0.180[b]
Days of rehospitalization	2.3 ± 11.9	2.2 ± 12.5	2.7 ± 9.3	0.830[b]

Note: Values presented as n (column %) or mean ± SD.
[a]Pearson's χ^2 test.
[b]Student's t test.

grade D injuries by their provider. Three hundred twenty patients had complete follow-up interviews, but only 152 patients completed both their 1-year follow-up interview and physical examination and could be included in the study.

Patients were stratified by smoking status: 121 patients in the nonsmoking group and 31 in the smoking group (20.4%). Demographic and posthospitalization data are shown in Table 1. Median age range was 45 to 59 years, and there were a total of 113 men and 39 women. There were no differences between the 2 groups in any of the collected demographic variables (Table 1). The mean total motor scores at initial rehabilitation admission (P = 0.737) and rehabilitation discharge (P = 0.915) did not differ between groups (Table 2).

Stepwise linear regression analysis was used to study the relationship between the primary outcomes and smoking, correcting for possible confounders. Standard demographic factors (age, sex, and race) and factors with P values <0.2 when analyzed for univariate impact on the dependent variables (TBI, rehabilitation length of stay, total rehospitalizations, and rehospitalization days) were included in the analysis along with smoking status.

Results of the multivariate regression for change in total motor score are shown in Table 3. There was a significantly worse improvement in total motor score at 1 year in the smoking group compared with the nonsmoking group after controlling for confounders (7.99 vs 4.61, multivariate P = 0.019). Other factors influencing change in motor score were age (P = 0.024) and initial rehabilitation length of stay (P = 0.048), though smoking was still a significant predictor even with these variables included (Table 3).

Results of the multivariate regression for overall total motor score are shown in Table 4. Patients in the smoking

Table 2. Total motor score at 3 separate timepoints, as well as change in total motor score from time of discharge from rehabilitation to 1-y follow-up visit.

Outcome Variable	Total (N = 152)	Nonsmoker (n = 121)	Smoker (n = 31)
Total motor score—rehabilitation admission	74.1 ± 15.4	74.5 ± 15.4	73.3 ± 14.3
Total motor score—rehabilitation discharge	85.6 ± 11.2	86.0 ± 10.4	85.4 ± 10.1
Total motor score—1-y follow-up	92.8 ± 9.7	94.0 ± 7.9	90.0 ± 9.0
Change in motor score—rehabilitation discharge to 1-y follow-up	7.3 ± 8.0	8.0 ± 7.6	4.6 ± 8.7

Note: Values presented as mean ± SD.

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Table 3. Results of multiple linear regression with dependent variable of change in total motor score.

Change in Motor Score—Rehabilitation Discharge to 1-y Follow-Up	Effect Size	95% CI	Standardized β	*P* Value
Smoking	−3.80	(−6.98, −0.63)	−0.192	**0.019**
Age	−1.40	(−2.61, −0.19)	−0.186	**0.024**
Sex	−1.98	(−4.87, 0.90)	−0.109	0.117
Race	0.56	(−0.96, 2.07)	0.057	0.470
Rehabilitation length of stay	0.06	(0.00, 0.13)	0.159	**0.048**
No. of rehospitalizations	−0.62	(−2.60, 1.37)	−0.059	0.541
Days of rehospitalization	−0.06	(−0.18, 0.07)	−0.083	0.385

Note: Boldface indicates statistical significance.

group also had decreased overall motor scores at 1 year compared with the nonsmoking group after controlling for confounders. (93.95 vs 90.00, multivariate $P = 0.018$). Sex ($P = 0.04$) and initial rehabilitation length of stay ($P < 0.001$) also significantly impacted total motor score at 1 year (Table 4).

DISCUSSION

Cigarette smoke is a well-established neurotoxin and has multiple documented detrimental effects on the spinal cord and neurological recovery. Spinal cord ischemia is likely potentiated by the vasoconstrictive effects of nicotine, decreased oxygen-carrying capacity due to carboxyhemoglobin formation, and diminished neovascularization.[11,19,20] Smoking greatly increases formation of reactive oxygen species, which is detrimental to tissue healing, especially early in the SCI recovery process.[15,21] Animal studies have indicated that cotinine, the metabolite of nicotine, inhibits spinal cord regeneration and myelin reformation after TSCI in rats.[14] These findings correlate with results of human studies that have found worse recovery after decompression of cervical myelopathy in smokers compared with nonsmokers.[11–13]

This present study suggests that cigarette smoke may have a direct toxic effect on spinal cord recovery after TSCI as indicated by lower total motor scores and motor improvement 1 year after injury. This association holds true after accounting for demographic and surgical factors that also independently impact motor function. On average, nonsmokers improved an average of 8 points from the time of rehabilitation discharge to 1 year. These data in nonsmokers are similar to an average of 8.6 points of recovery after ASIA grade D SCI shown to occur within 9 months after rehabilitation discharge (from 3 to 12 months after SCI) as reported by Fawcett et al in patients from the Sygen database. Smokers, however, improved only 4.6 points during this time, which, according to Fawcett, is the expected improvement from 6 to 12 months after SCI.[22]

The prevalence of cigarette smoking before injury in TSCI patients was documented in 1 study to be 37.9%, much higher than the rate in the general population.[23] Post-TSCI data show continuation of this trend, with rates at SCI onset reported from 24% to 48%.[18] The smoking rate in the present study was on the low end of the reported ranges, at 20.4%. This is likely because smoking data in the NSCISC database are collected at the 1-year timepoint. The rates of smoking drop to near that of the normal population after 16 months, and this reduction in smoking likely occurs after the majority of motor recovery has occurred. Continued smoking in TSCI patients occurs despite the known negative impact on overall health outcomes and TSCI complications.[24] In a survey of 1076 SCI patients, Saunders et al, found that 77.2% of smokers had tried to quit, though only 29.9% had help from professional resources.[18] Limited smoking cessation assistance has been noted by Weaver et al as well.[25] Noted barriers to quitting in SCI patients include alcohol use, limited

Table 4. Results of multiple linear regression with dependent variable of total motor score.

Total Motor Score—1-y Follow-Up	Effect Size	95% CI	Standardized β	*P* Value
Smoking	−4.53	(−8.27, −0.79)	−0.195	**0.018**
Age	−0.62	(−2.07, 0.84)	−0.067	0.404
Sex	−3.73	(−7.29, −1.68)	−0.166	**0.040**
Race	0.25	(−1.46, 1.97)	0.023	0.770
Traumatic brain injury	−2.13	(−6.52, 2.26)	−0.077	0.338
Rehabilitation length of stay	−0.19	(−0.27, −0.11)	−0.363	**<0.01**
No. of rehospitalizations	1.62	(−3.45, 6.67)	0.120	0.528
Days of rehospitalization	−0.62	(−1.33, 0.08)	−0.334	0.084

Note: Boldface indicates statistical significance

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social interaction, and environments that encourage smoking.[25]

Limited professional help to quitting continues to occur is despite evidence that the use of clinical practice guidelines by providers doubled the rate of smoking cessation in SCI patients.[7] The results of the present study indicate the importance of provider focus on smoking cessation as soon as possible after TSCI. Cessation efforts must continue after discharge from rehabilitation to permanent residence to maximize motor outcomes as well as other well-reported health outcomes. Health care provider and social support are 2 of the largest facilitators to smoking cessation and should be encouraged by all providers interacting with SCI patients.[26] This may be aided by the use of specific smoking cessation counseling, medications, and behavioral interventions as noted by Lane et al, Saunders et al, and others.[7,24–26]

There are multiple limitations to this study. The retrospective nature of the data leads to inherent biases based on design and limits the variables that can be collected, primarily information about surgical and hospital management. By utilizing a national database, access to a large and broad patient population was available, but this limits analysis to only the data points collected by the NSCISC. Collection of radiographic biomarkers is an important predictor of outcomes that was unavailable in this data set. Smoking data did not include information on packs per day or duration of smoking; therefore, a possible dose-response relationship may have been missed. Data regarding preinjury smoking status were also not available, so this study is unable to determine its impact on outcomes. However, the poor outcomes noted in patients who continue to smoke at 1 year do identify the need for aggressive smoking cessation in this TSCI population. The 50% 1-year loss to follow-up rate is similar to those reported in other studies from the NSCISC as well the National Spinal Cord Injury Model Systems and Sygen database.[27,28] Because of regional or other limitations, many patients who completed 1-year follow-up interviews were unable to present for an in-person examination and had to be excluded. This may have led to increased selection bias due to higher loss to follow-up compared with similar studies. Despite this limitation, overall smoking rates within the study match similar rates reported in prior literature, and there were no demographic or injury differences between the smoking and nonsmoking groups. The inclusion of only ASIA grade D patients may have introduced a ceiling effect for motor recovery due to higher initial motor scores, limiting differences in improvement between the 2 groups.[3] It also limits the generalizability of the study. Inclusion of patients with ASIA grades A through C injuries may have slighted this impact, but their exclusion was necessary because patients with more complete injuries who are functionally able to smoke have greater baseline motor function than those who cannot. This is indicated by both our initial analysis of all cervical TSCI patients, as mentioned in the Methods section and in reports from prior literature.[6]

CONCLUSION

To our knowledge, this study is the first to demonstrate the negative association between smoking and both overall motor scores and motor score improvement 1 year after incomplete traumatic cervical SCI independent of other confounding variables. These results highlight the potentially direct toxic effect that cigarette smoking has on TSCI recovery. It is critical that providers caring for TSCI patients stress the importance of smoking cessation early and often not only to improve overall health outcomes and mortality but also to maximize motor outcomes as well.

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