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General

Smokeless Tobacco Use is Associated with Worse Outcomes Following Open Tibia Fracture

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Background

Smoking is a known risk factor for complications after open tibia fractures, but it is unclear if smokeless tobacco confers a similar risk.

Objective

The purpose of this study was to evaluate the rates of postoperative complications after surgical fixation of open tibia fractures in smokeless tobacco users as compared to matched tobacco naïve controls.

Methods

A retrospective cohort study was conducted using the national PearlDiver database. For patients who had a unilateral open tibia fracture, smokeless tobacco users (n=121) and tobacco-naïve controls (n=242) were matched at a 1:2 ratio. Rates of bone complications within 1 year were compared using multivariable logistic regression.

Results

Compared to controls, the smokeless tobacco user cohort demonstrated significantly higher rates of nonunion (OR: 3.42, 95% CI: 1.05 – 11.12), infection / inflammatory reaction of implant (OR: 12.45, 95% CI: 2.67 – 58.93), and osteomyelitis of the leg (OR: 6.15, 95% CI: 1.90 – 19.93) within 1 year of open tibia fracture. Compared to the most recent population figures, smokeless tobacco use was significantly under-reported in both males and females.

Conclusions

Smokeless tobacco use confers an increased risk of fracture nonunion, infection or inflammatory response to implant, and osteomyelitis of the leg in patients with open tibia fractures. Surgeons should consider this risk when counseling patients and deciding on treatment plans for patients with tibia fractures.

INTRODUCTION

Tibia fractures are one of the most common open long bone fractures, accounting for 10-15% of all open fractures.[1,2] These fractures often occur due to high energy mechanism injuries and are commonly associated with polytraumas.[3] Males are more often affected with a bimodal age distribution.[4] Management of open tibia fractures includes classification of the injury, early antibiotic coverage, debridement, possible soft tissue reconstruction, and skeletal stabilization.[3,5,6]

A vast array of complications can arise post-operatively including nonunion, infection, implant failure, and re-fracture, more often in open versus closed fractures.[1,7] Nonunion is a common complication of tibial fractures that occurs due to the long subcutaneous border of the tibia and its poor blood supply. Risk factors such as increased age, diabetes, opioid use, tobacco use, distal fracture, and high energy injury may predispose patients to unfavorable outcomes.[7] Smoking is one of the most prevalent risk factors that predisposes to orthopaedic surgery complications and as of 2021, 11.5 % of adults over the age of 18 reported cigarette use and 2.1% reported smokeless tobacco use.[8,9] Smoking is known to have a harmful effect on bone fusion during healing by disrupting bone turnover mechanisms.[8,10] Specifically, smoking history was found to be associated with an increased risk for osteomyelitis and time to union for open tibia fractures.[11] While previous studies have ex-

amined smoking as a risk factor for fracture healing, few studies have analyzed the effect of smokeless tobacco.

The purpose of this study was to evaluate the rates of postoperative complications after surgical fixation of open tibia fractures in smokeless tobacco users as compared to matched controls. It was hypothesized that smokeless tobacco users would exhibit significantly worse outcomes when compared to matched tobacco naïve controls.

MATERIALS AND METHODS

DATA SOURCE AND STUDY DESIGN

Patient records were queried from the PearlDiver Mariner Database (PearlDiver Inc., Colorado Springs, CO, USA), a commercially available administrative claims database which contains deidentified patient data from the inpatient and outpatient settings. The database contains the medical records of patients across the United States from 2010 through the third quarter of 2021 which are collected by an independent data abstractor. This study utilized the "M157Ortho" dataset within PearlDiver, which contains a random sample of 157 million patients. All health insurance payors are represented including commercial, private, and government plans. Researchers extract data using Current Procedural Technology (CPT) and International Classification of Diseases, Ninth and Tenth revision (ICD-9/ICD-10) diagnosis and procedural codes. Institutional Review Board exemption was granted as provided data was deidentified and compliant with the Health Insurance Portability and Accountability Act (IRB reference #2023-1083). No outside funding was received.

A retrospective cohort study was conducted to investigate the impact of smokeless tobacco use on fracture complications following open fracture of the tibia. Encounters for open fracture of the tibia were defined with ICD-10 diagnosis codes, as seen in Appendix A. To ensure all complications tied back to the open tibia fracture of correct laterality, patients with bilateral open tibia fractures and patients with concomitant contralateral closed tibia fractures were excluded. To limit potential transfer bias, only patients with continuous database enrollment for at least 1 year after the initial open tibia fracture diagnosis were included. Additionally, only patients aged 18 to 80 years old were included in the study.

Subsequently, patients that use smokeless tobacco were identified by the presence of the ICD-10 diagnosis code "Nicotine dependence, chewing tobacco, uncomplicated" without codes for "nicotine dependence, smoking, uncomplicated" or "nicotine dependence, chewing tobacco, in remission" in their records. Controls for the smokeless tobacco cohort were defined as patients without any diagnosis codes related to tobacco use or nicotine dependence. Codes used to define tobacco use status are provided in Appendix B.

DEMOGRAPHIC DATA AND CLINICAL CHARACTERISTICS

Baseline demographic data was obtained for all patients. Clinical characteristics obtained included age, sex, Elixhauser comorbidity index (ECI), diabetes mellitus (DM), obesity, chronic kidney disease (CKD), alcoholism, and illicit drug use. Codes used to define clinical characteristics are provided in Appendix C. Demographics and clinical characteristics of the cohorts may be seen in Table 1.

FRACTURE PATTERNS

Differing open fracture patterns of the tibia were identified for each patient using ICD-10 diagnosis codes which delineated fractures based on location ("upper" versus "shaft" versus "lower") and the Gustilo-Anderson classification ("type I or II" versus "type III") yielding six distinct patterns of open tibia fractures.[12,13] Of note, in ICD-10, type I and type II fractures are grouped together while type III fractures are grouped independently. Codes used to define fracture patterns are provided in Appendix A. Fracture patterns of the cohorts may be seen in Table 2. Tibia fractures were not classified by the AO/OTA classification system, but rather the presence or absence of tibia fracture alone (JOT OTA Source).[14]

OUTCOMES

Rates of fracture complications within 1 year from open tibia fracture were captured, including delayed healing, malunion, nonunion, surgical repair of nonunion, infection / inflammatory reaction of implant, osteomyelitis of the leg, and amputation of the leg. Codes for these complications are provided in Appendix D.

STATISTICAL ANALYSIS

Statistical analyses were performed using R statistical software (Version 4.1.0; R Project for Statistical Computing, Vienna, Austria) integrated within the PearlDiver software with an α level set to 0.05. To reduce confounding bias, propensity score matching was performed at a caliper of 0.20 to generate patient cohorts. The smokeless tobacco user and control cohorts were propensity score matched at a 1:2 ratio with controls on the following clinical characteristics: age, sex, ECI, DM, obesity, and the six fracture patterns as described in *Demographic Data and Clinical Characteristics* and in *Fracture Patterns*. All clinical characteristics (Table 1) and fracture patterns (Table 2) that were significantly different between cohorts despite propensity score matching were controlled for in the appropriate multivariate logistic regressions to negate any potential confounding effects.

Categorical variables were compared with a chi-square test and continuous variables were compared with Welch's t test or the Mann Whitney U test. Rates of fracture complications after open tibia fracture were compared using multivariable logistic regressions. Observed versus theoretical categorical variables were compared using one-proportion z-test.

Table 1. Demographics and Clinical Characteristics of Smokeless Cohort of Patients with Open Tibia Fractures versus Matched Controls.

	Controls (n = 242)		Smokeless Tobacco Cohort (n = 121)		
Variable	*count*	*%*	*count*	*%*	*p*
Age (years), mean ± SD	44.9 ± 16.7	-	46.8 ± 14.3	-	0.27
Male	219	90.5%	117	96.7%	0.06
ECI, mean ± SD	2.7 ± 3.2	-	3.9 ± 3.3	-	< 0.001
Diabetes	66	27.3%	44	36.4%	0.10
Obesity	69	28.5%	48	39.7%	0.04
Chronic Kidney Disease	29	12.0%	16	13.2%	0.87
Alcoholism	16	6.6%	20	16.5%	< 0.001
Illicit Drug Use	*	-	*	-	0.03

ECI = Elixhauser comorbidity index
*To protect patient identities, the PearlDiver software only displays exact patient counts when defined buckets have at least 11 patients; however, all statistical tests performed in PearlDiver utilize exact patient numbers for said buckets with less than 11 patients.

Table 2. Fracture Patterns of Smokeless Cohort of Patients with Open Tibia Fractures versus Matched Controls

	Controls (n = 242)		Smokeless Tobacco Cohort (n = 121)		
Fracture Pattern	*count*	*%*	*count*	*%*	*p*
Type I & II Fractures, Upper	17	7.0%	*	-	1.00
Type III Fractures, Upper	*	-	*	-	1.00
Type I & II Fractures, Shaft	137	56.6%	59	48.8%	0.19
Type III Fractures, Shaft	51	21.1%	29	24.0%	0.62
Type I & II Fractures, Lower	30	12.4%	20	16.5%	0.36
Type III Fractures, Lower	*	-	*	-	1.00

*To protect patient identities, the PearlDiver software only displays exact patient counts when defined buckets have at least 11 patients; however, all statistical tests performed in PearlDiver utilize exact patient numbers for said buckets with less than 11 patients.

To assess whether rates of smokeless tobacco use were under reported in the medical records of the patients with unilateral open tibia fracture with one year of follow-up within the database, one-proportion z-tests were calculated using the most recent U.S. Census Bureau data from 2020 which shows that there were 258.3 million persons 18 years and older in the United States with 50.5% of persons being female.[15,16]

RESULTS

STUDY POPULATIONS

A total of 17,511 patients with ICD-10 diagnosis codes for unilateral open tibial fractures with at least 1 year of subsequent, continuous enrollment in the database were identified. These 17,511 patients included 123 patients who use smokeless tobacco (defined by having the ICD-10-D code for “nicotine dependence, chewing tobacco, uncomplicated” in their charts without codes for “nicotine dependence, smoking, uncomplicated” or “nicotine dependence, chewing tobacco, in remission” in their charts) and 9,150 without a history of tobacco use. After 1:2 propensity score matching, 121 smokeless tobacco users were matched with 242 tobacco-naïve controls (Table 1).

Of the 17,511 patients identified in the database with unilateral open tibial fracture and at least 1 year of follow-up, 10,512 (60.0%) were male and 6,999 (40.0%) were female. Of those 10,512 male patients, 175 (1.6%) had any one of multiple codes that denote smokeless tobacco use. Of the 6,999 female patients, 10 (0.1%) had any one of multiple codes that denote smokeless tobacco use. These 175 male smokeless tobacco users and 10 female smokeless tobacco users may have also had codes for “nicotine dependence, smoking, uncomplicated” in their charts, in addition to codes for “nicotine dependence, chewing tobacco, uncomplicated”.

COHORT DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

Compared to controls, the smokeless tobacco user cohort had a significantly higher mean ECI ($p < 0.001$) and higher rates of obesity ($p = 0.04$), alcoholism ($p < 0.001$), and illicit drug use ($p = 0.03$). The variables that were significantly different between cohorts despite propensity score matching were subsequently controlled for in the multivariate lo-

Table 3. Complication Rates of Smokeless Tobacco Cohort versus Matched Controls within 1 Year of Open Tibia Fracture.

	Controls (n = 242)		Smokeless Tobacco Cohort (n = 121)		
Complication	*count*	*%*	*count*	*%*	*OR*
Delayed Healing	*	-	*	-	1.87 (0.66 - 5.27)
Malunion	*	-	0	0.0%	-
Nonunion	*	-	*	-	3.42 (1.05 - 11.12)
Surgical Repair Nonunion	*	-	*	-	3.46 (0.79 - 15.17)
Infection / Inflammatory Reaction of Implant	*	-	12	9.9%	12.45 (2.67 - 57.93)
Leg Osteomyelitis	*	-	12	9.9%	6.15 (1.90 - 19.93)
Leg Amputation	*	-	*	-	1.15 (0.20 - 6.63)

Highlighted odds ratios (OR) represent statistically signficant results
*To protect patient identities, the PearlDiver software only displays exact patient counts when defined buckets have at least 11 patients; however, all statistical tests performed in PearlDiver utilize exact patient numbers for said buckets with less than 11 patients.

gistic regressions to negate any potential confounding effects.

FRACTURE PATTERNS

Compared to controls, the smokeless tobacco user cohort had similar rates of all fracture patterns.

COMPLICATIONS

Compared to controls, the smokeless tobacco user cohort demonstrated significantly higher rates of nonunion (OR: 3.42, 95% CI: 1.05 – 11.12), infection / inflammatory reaction of implant (OR: 12.45, 95% CI: 2.67 – 58.93), and osteomyelitis of the leg (OR: 6.15, 95% CI: 1.90 – 19.93) within 1 year of open tibia fracture (Table 3).

SMOKELESS TOBACCO USE REPORTING

Compared to the most recent population figures for current smokeless tobacco use among United States adult males (4.5%), smokeless tobacco use was significantly under-reported in the sample of adult males 18 to 80 years with a unilateral open tibia fracture with one year of follow-up within the database (175 of 10,512, 1.7%) (z-statistic = -12.98, one-tailed p-value < 0.001).[9]

Compared to the most recent population figures for current smokeless tobacco use among United States adult females (0.3%), smokeless tobacco use was significantly under-reported in the sample of adult females 18 to 80 years with a unilateral open tibia fracture with one year of follow-up within the database (10 of 6,999, 0.1%) (z-statistic = -2.41, one-tailed p-value = 0.01).[9]

DISCUSSION

The present study demonstrated significantly higher rates of nonunion, infection or inflammatory response to implant, and osteomyelitis of the leg in smokeless tobacco users compared to matched tobacco-naïve controls. The increased rates of nonunion may be due to the negative impacts of nicotine on bone healing and remodeling. Nicotine induces oxidative stress, which has been demonstrated to inhibit bone growth and induce bone resorption.[17-19] Additionally, nicotine decreases peripheral circulation through vasoconstriction, and smokeless tobacco users have been found to reach an even higher plasma blood level of nicotine than smokers.[20,21] Relative to other long bones, the tibia has a poor blood supply and is at higher risk of nonunion.[7] Impaired peripheral blood flow to the tibia due to nicotine may further contribute to the increase in rates of nonunion seen in this study. Similarly, the increased rates of infection and osteomyelitis seen in this study may also be due to nicotine's impact on peripheral blood flow, which is associated with increased rates of infection.[22] Nicotine has also been demonstrated to negatively affect the immune system by reducing the response of antibodies and impairing neutrophil function.[22]

Interestingly, despite the impact of nicotine on bone growth and peripheral blood flow, this study did not find a significant increase in rates of surgical repair of nonunion or delayed healing. Surgical repair of nonunion trended towards but did not reach statistical significance with the available number of smokeless tobacco users in the study. One possible reason that surgical repair of nonunion did not reach significance despite a significant increase in nonunion among smokeless tobacco users could be the use of other, non-surgical modalities to treat nonunion. Bone growth stimulators and injections, for example, have been established as treatment options for fracture nonunion.[23-25] Nail dynamization is another established method used to promote fracture healing in non-union and was not included in procedure codes used to define surgical repair of nonunion in the present study.[26]

A Swedish study by W-Dahl et al. demonstrated no delayed bone healing in oral tobacco users compared to smokers.[27] However, it is important to note that there are numerous varieties of smokeless tobacco, with varying composition worldwide.[28,29] The composition of smokeless tobacco is not standardized, so it is difficult to generalize the impact it has on bone healing as a whole. Snuff is the most common type of smokeless tobacco used in the United

States, so it can be inferred that this is the likely variety of smokeless tobacco used by patients in the present study.[28] There is a paucity of evidence evaluating the impact of snuff use on bone and tissue, so further research is needed to understand the mechanism behind the increased rates of nonunion and infection seen in this study.

The present study also demonstrated significantly higher mean ECI, and significantly higher rates of obesity, alcoholism, and illicit drug use in the smokeless tobacco cohort. These results are unsurprising, given previous evidence that smokeless tobacco is associated with higher body weight, alcohol use, and illicit drug use.[30-32] The high prevalence of these comorbidities in patients using tobacco is important for physicians to consider, because the presence of comorbid conditions is known to make smoking or nicotine cessation treatment more challenging.[33]

Smokeless tobacco use was significantly underreported in this study population. Among males with open tibia fracture, 1.7% were reported to use smokeless tobacco, compared to 4.5% of men in the United States as reported by the CDC.[9] Among females with open tibia fracture, 0.1% were reported to use smokeless tobacco, compared to 0.3% reported in the general population.[9] This discrepancy suggests that smokeless tobacco use is underreported in clinical practice, however the reason for underreporting is not examined in the present study. One possible reason may be that patients are not being asked about smokeless tobacco use by orthopaedic surgeons. Also, the specific type of tobacco usage may not be captured or input into the formal medical record. Previous studies evaluating the risk of smokeless tobacco on complications following total joint replacement and scaphoid fracture recommend implementing more thorough intake forms to capture smokeless tobacco use for orthopaedic patients.[34-36] As patients with open tibia fractures are more likely to be seen in the emergency department than clinic, it may be beneficial for surgeons to ask all patients presenting with tibia fractures about smokeless use during initial evaluation.

There has been an abundance of research dedicated to determining the optimal time to recommend smoking cessation prior to elective orthopaedic surgery.[37] A meta-analysis by Mills et al. found that while a minimum of 24 hours of smoking cessation is recommended, longer periods of time were associated with increasing improvements in postoperative outcomes.[38] There is a paucity of evidence regarding smokeless tobacco use and cessation prior to orthopaedic surgery, however the results of this study indicate cessation of smokeless tobacco use may be beneficial in decreasing rates of tibia fracture nonunion and infection. Treatment for open tibia fracture involves emergent debridement and antibiotics within 24 hours, followed by either external fixation, intramedullary nail fixation, or open reduction internal fixation.[1,39] More extensive skin and soft tissue injury may require joint orthopaedic and plastic surgery management with free flap reconstruction coverage.[6,40] Unlike elective orthopaedic procedures, open tibia fractures require more emergent surgery and prolonged smoking cessation is not possible preoperatively. Surgeons should understand the risks of smokeless tobacco use on fracture nonunion, infection, and osteomyelitis, and use this information to inform clinical decision making and recommendations to patients. Further research is needed to investigate the potential benefit of smokeless tobacco cessation at the time of tibia fracture and operative management.

LIMITATIONS

There are several limitations to this study. Complications were only evaluated within 1 year following open tibia fracture. Therefore, the analysis is limited to short-term outcomes. Furthermore, continuous database enrollment for 1 year following open tibia fracture was required for inclusion, so patients who died within 1 year after surgery were excluded. Consequently, the results may not be applicable to patients with high postinjury mortality risk. The possibility of coding errors is inherent with analysis of administrative claims data. However, coding errors are rare and made up only 0.7% of Medicare and Medicaid payments in 2021.[41] It is possible that some patients using smokeless tobacco were not included in the study, due to the nonspecific ICD-10-D-F17.200 diagnosis code, "nicotine dependence, other tobacco product, uncomplicated", which was not included in the smokeless tobacco use cohort in this study. Additionally, due to the use of diagnosis codes to determine smokeless tobacco usage, this study was not able to determine the type of smokeless tobacco or amount used. There also may be overlap between patients using cigarettes and smokeless tobacco, which may not be accurately reflected in diagnosis codes. Under-reporting of smokeless tobacco use was demonstrated in this study population as well as in several other orthopaedic patient populations.[34-36] Thus, patients who use smokeless tobacco but do not have the associated diagnosis codes may be present within the control cohort. If so, the higher rates of nonunion, infection or inflammatory response to implant, and osteomyelitis of the leg in smokeless tobacco users demonstrated in this study could be an underestimate. Another limitation of the study is that the fixation technique, implant utilized, and soft tissue procedures to treat each tibia fracture is unknown. It is possible that differences in technique, implant, and timing may have contributed to differences seen between the study cohort and control population.

CONCLUSION

Smokeless tobacco use confers an increased risk of fracture nonunion, infection or inflammatory response to implant, and osteomyelitis of the leg in patients with open tibia fractures. Surgeons should consider this risk when counseling patients and deciding on treatment plans for patients with open tibia fractures.

AUTHORSHIP CONTRIBUTION

Timothy L. Waters: Formal analysis, Methodology, Writing original draft.
Julianna E. Winter: Writing original draft & editing.
Bela P. Delvadia: Writing original draft & editing.
William F. Sherman: Conceptualization, Writing review & editing.
Olivia C. Lee: Conceptualization, Writing review & editing

SUMMARY POTENTIAL CONFLICT OF INTEREST

Timothy L. Waters: None
Julianna E. Winter: None
Bela P. Delvadia: None
William F. Sherman: Editorial board member for arthroplasty today, American Academy of Orthopaedic Surgery knee committee member, Paid consultant for Stryker, Associate editor for Orthopedic Reviews
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