



OPEN

Tobacco smoking is associated with more pain and worse functional outcomes after torsional ankle fracture

Megan A. Audet, MD, Alex Benedick, MD, Heather A. Vallier, MD*

Abstract

Objective: The purpose of this study was to assess the impact of current and remote tobacco smoking on clinical and functional outcomes after torsional ankle fracture.

Methods: Nine hundred thirty-five patients treated surgically for torsional ankle fracture over 9 years were reviewed. Tobacco smoking status at the time of injury was defined as current (48.3%), former (11.7%), and nonsmoker (40.0%). Complications, unplanned secondary procedures, pain medication use, and functional outcome scores, as measured by Foot Function Index and Short Musculoskeletal Function Assessment (SMFA) surveys.

Results: Mean age was 44.8 years, with 50.3% male. More than 6 months following injury current smokers were more likely than former smokers and nonsmokers to report ankle pain (67.8% vs 45.8% vs 47.5%) and to use prescription pain medicines (23.0% vs 10.4% vs 6.3%), all P < .05. Multiple logistic regression found current tobacco use to be an independent predictor for prescription pain medication use, and worse scores for the Foot Function Index, SMFA Dysfunction, and SMFA Bothersome scores, all P < .05. Complications occurred in 15.5% of all patients, and 10.7% underwent unplanned secondary operations. Tobacco smoking was not associated with more complications or secondary procedures.

Conclusion: Current smokers are more likely to use prescription pain medications several months after injury and have worse patient-reported functional outcome scores after surgical treatment of torsional ankle fractures than former smokers and nonsmokers.

Keywords: ankle fracture, complications, functional outcomes, opioids, pain, SMFA, tobacco

1. Introduction

The United States has 42.1 million cigarette smokers, and tobacco use is considered the leading cause of preventable death.^[1,2] Perioperative tobacco use is associated with serious adverse effects including greater risk of infection, longer length of stay, and prolonged healing times following orthopaedic

OTAI (2022) e175

Received: 9 July 2021 / Accepted: 18 December 2021

Published online 19 January 2022

http://dx.doi.org/10.1097/OI9.00000000000175

surgery.^[3–9] Furthermore, tobacco use is more prevalent in the orthopaedic trauma population than the general public.^[10–13]

Although tobacco smoking has been associated with poor soft tissue and bone healing, prior work to our knowledge has not comprehensively characterized the impact of tobacco use on outcomes following ankle fracture. Additionally, many studies fail to differentiate between active and former smokers. This study will examine the impact of current and former cigarette smoking on clinical and functional outcomes following torsional ankle fracture. We hypothesize that tobacco use will be associated with more infectious and healing complications and will have a negative impact on functional outcomes.

2. Methods

Institutional Review Board approval was obtained for this project. The records of 935 skeletally mature patients who underwent fixation for torsional ankle fracture (OTA/AO 44) at a single Level-I urban trauma center between 2006 and 2015 were reviewed. Tobacco smoking history at the time of the injury was categorized as current (n=452), former (n=109), and nonsmoker (n=374). Patients with >6 months abstinence from tobacco use were categorized as former smokers. Alcohol and recreational drug use was similarly defined by use within 6 months of injury. Patients without tobacco smoking or recreational substance utilization data were not included in this study. Specific types of recreational drugs and other forms of tobacco use were not studied. Fractures were classified according to the OTA/AO system.^[14]

This study was IRB-approved.

No funds were received in support of this study. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. All of the devices in this manuscript are FDA-approved.

The authors have no conflicts of interest to disclose.

MetroHealth Medical Center, Cleveland, Ohio, affiliated with Case Western Reserve University.

^{*} Corresponding author. Address: Department of Orthopaedic Surgery, 2500 MetroHealth Drive, Cleveland, OH 44109. Tel: +216 778 7476; fax: +216 778 4690. E-mail: address: hvallier@metrohealth.org (H. A. Vallier).

Copyright © 2022 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of the Orthopaedic Trauma Association.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Definitive treatment consisted of open reduction and internal fixation of displaced malleoli and syndesmotic structures, using conventional techniques and small fragment implants at the discretion of treating orthopaedic surgeons. Open injuries were urgently debrided and irrigated in the operating room, and intravenous antibiotics were administered upon arrival and for 24 hours postoperatively. Timing of treatment for closed injuries was at the discretion of treating surgeons, depending on the status of the injured soft tissues. Nonweightbearing was recommended for all patients postoperatively for a period of 6 to 12 weeks, depending on patient and injury factors and clinician judgment.

Secondary operations and complications throughout treatment course were noted. Wound infection was considered superficial, requiring oral antibiotics and wound care, or deep, requiring surgical debridement, and intravenous antibiotics. Patients with at least 6 weeks of clinical follow-up were included in assessment of these early complications. Failure to achieve radiographic union 6 months after treatment was defined as nonunion, which was subclassified as symptomatic or asymptomatic. Malunions were defined as more than 5 degrees of angulation in any plane in a healed fracture. All unplanned secondary operations following initial fracture fixation were documented and included implant removal, revision fixation, total ankle arthroplasty, or arthrodesis, and amputation.

In patients with clinical follow-up greater than 6 months (n = 307, 32.8%), reports of continued ankle pain or use of any pain medications for the ankle were documented. Patients with any reports of pain in the injured ankle more than 6 months following injury were defined as having chronic pain in that ankle. Type of pain medication was described as non-prescription, prescription narcotics, and other prescription pain medications. Return to work in previously employed individuals and new permanent use of ambulatory aids including walker or cane were also recorded.

Functional outcomes were assessed using Short Musculoskeletal Function Assessment (SMFA) and Foot Function Index (FFI) surveys. Patients were contacted via telephone or mail after minimum 12 months postinjury for survey completion and for additional assessment of ankle pain and related medications. The FFI is a lower extremity-specific score which consists of subscores for pain, disability, and activity,^[15] which are normalized by the number of questions answered by the patient. The FFI total score is an average of these 3 subscores. Higher scores indicate worse function. The SMFA is a generalized musculoskeletal outcomes questionnaire consisting of 46 questions scored by the patient using a 5-point Likert scale. The 6 SMFA subscores include daily activity, emotional status, arm and hand function, mobility, dysfunction, and bothersome, each with a maximum of 100 points, with worse outcomes indicated by a higher score.^[16] Both the FFI and the SMFA have been consistently shown to be valid, reliable, and reproducible.^[15,17–20]

Independent samples student *t* tests and one-way analysis of variance were performed to compare means of continuous variables. Pearson chi-square tests and Fisher exact tests were performed to compare frequencies of categorical variables. Multiple logistic regression analysis was performed to identify significant independent predictors of wound infection and chronic pain medication use >6 months following fracture. All analyses were 2-tailed and significance was defined as P < .05.

3. Results

Mean age was 44.8 years and mean body mass index was 31.2. Half of all patients were male (n = 470). One hundred forty-eight patients (15.8%) had open fractures, and 374 had dislocations (40%). Mean ages for current, former, and nonsmokers were 40.9, 57.0, and 45.9 years, respectively (P < .001) and mean body mass index was lowest for current tobacco smokers: 29.6 vs 34.4 and 32.2 for former and nonsmokers (P < .001, Table 1). Diabetes mellitus was less common among current smokers (9.1%, vs 24.8% and 14.7%, P < .001). However, current smokers were more likely to report concomitant alcohol abuse (9.5% vs 3.2%, P < .001) and recreational drug use, including marijuana (19.1% vs 4.1%, P < .001) when compared with nonsmokers.

One hundred forty-five patients (15.5%) experienced 153 complications. Superficial infection was the most common complication (4.9%, Table 2). Nonunions occurred in 5.3% of all patients. Infectious complications and nonunions were no more frequent in current or former smokers (Table 3). On multiple logistic regression analysis, open fracture (odds ratio (OR): 3.14, P=.001) and recreational drug use (OR: 2.42, P=.013) were independent predictors for any wound infection, and diabetes mellitus was associated with deep wound infection (OR: 6.87, P=.025) (Table 4). One hundred patients (10.7%) had 127 unplanned secondary operations, with no differences in rates based on smoking history.

	Current smoker (N $=$ 452)	Former smoker (N=109)	Nonsmoker (N $=$ 374)	P value
Demographics				
0 1	262 (FE 80()	EQ (47 70/)	166 (44 40/)	D 004
Male sex	252 (55.8%)	52 (47.7%)	166 (44.4%)	P=.004
Age, years, mean (SD)	40.9 (13.15)	57.0 (15.9)	45.9 (18.0)	P<.001
BMI, mean (SD)	29.6 (7.23)	34.4 (8.0)	32.2 (8.4)	P<.001
Comorbidities				
Alcohol abuse	43 (9.5%)	4 (3.7%)	12 (3.2%)	P<.001
Recreational drug use	83 (19.1%)	5 (4.7%)	15 (4.1%)	P<.001
Diabetes mellitus	41 (9.1%)	27 (24.8%)	55 (14.7%)	P<.001
Injury characteristics				
Weber A	6 (1.3%)	0 (0.0%)	5 (1.3%)	P = .70
Weber B	309 (68.7%)	80 (74.1%)	248 (66.3%)	P = .31
Weber C	135 (30.0%)	28 (25.9%)	121 (32.4%)	P = .42
Open fracture	65 (14.4%)	16 (14.7%)	67 (17.9%)	P = .36
Dislocation	162 (35.8%)	45 (41.3%)	167 (44.7%)	P=.035

BMI = body mass index; SD = standard deviation.

Table 2

Clinical outcomes including complication rates, secondary operations, and use of pain medications more than 6 months after injury based on tobacco smoking status

	Current smoker	Former smoker	Nonsmoker	P value
All Complications	71 (15.7%)	24 (22.0%)	50 (13.4%)	P=.09
Superficial infection	24 (5.3%)	7 (6.4%)	15 (4.0%)	P = .50
Wound healing	16 (3.5%)	10 (9.2%)	16 (4.3%)	P=.04
Deep infection	10 (2.2%)	3 (2.8%)	6 (1.6%)	P=.70
Malunion	2 (0.4%)	1 (0.9%)	4 (1.1%)	P=.46
Nonunion	24 (5.3%)	4 (3.7%)	11 (2.9%)	P=.25
Secondary Operations	46 (10.2%)	17 (15.6%)	37 (9.9%)	P = .21
Implant removal	32 (7.1%)	11 (10.1%)	24 (6.4%)	P=.42
Arthrodesis/TAA	5 (1.1%)	0	6 (1.6%)	P = .42
Amputation	2 (0.8%)	0	2 (1.8%)	P=.02
Revision fixation	10 (2.2%)	3 (2.8%)	6 (1.6%)	P = .70
Pain >6 mo	101 (67.8%)	22 (45.8%)	56 (47.5%)	P=.001
Any pain medications	59 (39.9%)	9 (18.8%)	22 (19.8%)	P<.001
Prescription medications	34 (23.0%)	5 (10.4%)	7 (6.3%)	P=.001
Opioids	11 (7.4%)	2 (4.2%)	3 (2.7%)	P=.22

TAA = total ankle arthroplasty.

149 current smokers, 48 former smokers, and 118 nonsmokers had clinical follow-up for more than 6 months (n=315, 33.7%). Within this group, current smokers were significantly more likely than former smokers and nonsmokers to report chronic ankle pain (67.8% vs 45.8% vs 47.5%, P=.001). Eighty-seven (27.6%) patients used any pain medication for their ankle for longer than 6 months after their injury, and 16 patients had long-term opioid prescriptions (5.1%). Current smokers were most likely to use any pain medications for their ankle, longer than 6 months after their injury (39.9% vs 18.8% vs 19.8%, P < .001)

Table 3

Multiple logistic regression using patient demographics, medical history, social history, and injury characteristics to predict infectious complications

	All wound infections (N=65)		Superficial wound infection (N=45)		Deep wound infection (N $=$ 19)	
	OR	Р	OR	Р	OR	Р
Age	1.00	.83	1.01	.61	0.99	.59
Sex (female)	0.61	.08	0.43	.012	1.51	.44
Obesity	1.20	.53	1.02	.96	1.90	.26
Comorbidities	0.99	.97	1.08	.85	0.71	.68
Diabetes mellitus	2.17	.07	1.22	.69	6.87	.025
Current smoker	1.17	.61	1.12	.76	1.32	.63
Former smoker	1.12	.81	1.43	.48	0.52	.56
Alcohol abuse	1.35	.52	1.32	.61	1.23	.81
Drug use	2.42	.013	1.98	.10	3.35	.06
Open fracture	3.14	.001	2.53	.015	4.24	.015
Dislocation	0.83	.53	0.86	.65	0.84	.75

OR = odds ratio.

Table 4

Multiple logistic regression using patient demographics, comorbidities, and injury characteristics to predict pain medication use 6 months after fixation

	Any pain medication		Prescription pain medication		Opioids	
	OR	Р	OR	Р	OR	Р
Age	0.96	<.001	0.97	.023	0.97	.19
Sex (female)	1.20	.54	0.71	.33	0.81	.72
Obesity	1.46	.19	0.86	.68	1.01	.98
Diabetes mellitus	0.50	.17	0.55	.38	0.44	.48
Current smoker	2.61	.004	4.58	.002	3.85	.10
Former smoker	1.54	.38	3.47	.07	4.52	.17
Alcohol use	2.01	.26	4.04	.03	12.12	.002
Drug use	1.63	.21	1.00	1.0	0.51	.42
Open fracture	0.85	.66	1.57	.31	1.59	.51
Dislocation	1.35	.31	1.02	.96	1.42	.56

OR = odds ratio.

	FFI total		SMFA dysfunction		SMFA bothersome	
Smoking history (n=219)	37.3		31.2		31.6	
Nonsmoker (n = 175)	30.4	P=.014	25.0	P=.009	24.5	P=.009
Current smoker $(n = 171)$	38.9		32.8		33.3	
Former smoker ($n = 48$)	31.6		25.3		25.6	
Nonsmoker (n=175)	30.4	P=.014	25.0	P=.005	24.5	P=.007

Table 5

Mean patient-reported functional outcomes scores based on tobacco smoking status

FFI = foot function index; SMFA = Short Musculoskeletal Function Assessment.

and to use any prescription pain medication (23.0% vs 10.4% vs 6.3%, P=.001). However, there were no differences in long-term opioid use among tobacco smoking groups. Multiple logistic regression found current tobacco use to be an independent predictor for long-term pain medication use and prescription pain medication use (Table 4). There were no differences in ability to return to work or long-term use of supportive devices, such as a walker or cane, between these groups.

After mean of 5.9 years following injury (range: 1.7 - 13.2 years), 394 patients (42.1%) completed the FFI and SMFA, including 171 current smokers (37.8%), 48 former smokers (44.0%), and 175 non-smokers (46.8%). Patients with lifetime smoking history had worse FFI (37.3 vs 30.4, P=.014), SMFA Dysfunction (31.2 vs 25.0, P=.009), and SMFA Bothersome (31.6 vs 24.5, P=.009) scores than non-smokers (Table 5). Current tobacco smokers had the highest FFI (38.9 vs 31.6 vs 30.4, P=.01), SMFA Dysfunction (32.8 vs 25.3 vs 25.0, P=.005), and SMFA Bothersome (33.3 vs 25.6 vs 24.5, P=.007) scores compared to former smokers and nonsmokers, respectively. Multiple linear regression found current tobacco use to be an independent predictor of worse scores for FFI (P=.04), SMFA Dysfunction (P=.024), and SMFA Bothersome (P=.041) tests.

4. Discussion

Tobacco smoking is a major cause of morbidity and mortality. However, the impact of tobacco use on recovery after ankle fracture has not been well characterized. The goal of our study was to assess potential impact of tobacco use on clinical and functional outcomes following ankle fracture. Patients with >6months abstinence from tobacco use were categorized as former smokers. We developed this definition for this project. Current smokers were more likely to report chronic pain (more than 6 months after injury) and to be prescribed pain medications more than 6 months following injury. Lifetime smokers also had significantly worse patient-reported functional outcomes scores using the FFI and SMFA, highlighting the need for attention to tobacco smoking cessation initiatives. Our institution now has a referral program for smoking cessation, which includes individual and group counseling strategies and medications. Our practice is to offer referral to the program and to offer medication potentially helpful for cessation to mitigate some of these concerns.

Nicotine decreases blood flow, reduces collagen production, and causes tissue hypoxia, resulting in poor bone and wound healing.^[9,21–29] Tobacco smoking has been associated with higher rates of overall complications and wound complications following spine, knee, hip, tibia, and clavicle fractures, as well as total hip arthroplasty.^[9,21,23,24,27,30–33] Smoking has also been associated with more nonunions following fractures of the tibia, hip, cervical spine, and lumbar spine.^[27,34–37] Other work has shown tobacco use to be associated with a significant increase in time to fracture union.^[38,39] Our results were limited by loss of patients to follow-up. It is likely that the majority of those patients experienced fracture union, as nonunion is very uncommon following ankle fracture, even in the setting of tobacco usage. Our study may be underpowered for this outcome.

Multiple studies have demonstrated higher pain intensity scores among smokers.^[40–46] Flanagan et al^[47] reported that tobacco users required significantly more opioid pain medication while inpatient following orthopaedic injury. Furthermore, the endogenous opioid system is involved in the reward system of nicotine, and smokers appear to have upregulation of μ opioid receptors when compared with nonsmokers.^[48–52] Current tobacco use was an independent predictor for prolonged prescription pain medication use. This adds to the existing body of literature suggesting perception of pain and recovery after traumatic injury is altered in tobacco users.

Variable findings have been reported regarding potential impact of tobacco on functional outcomes following ankle fracture. Bhanderi et al found that smoking was associated with worse SF-36 scores 3 months after operative ankle fracture, but Dean et al found no association with smoking and physical function (PF) and pain interference (PI) PROMIS scores after a minimum of 2 years.^[53,54] Although our current smokers had the worst FFI and SMFA scores, former smokers also had worse scores than nonsmokers. Differences in SMFA between current smokers and nonsmokers coincide with the minimally important clinical difference previously published for the SMFA.^[55] It may be that smokers and former smokers have less functional capacity prior to their injury, resulting in more difficulty with physical functions reflected in worse generalized and extremity-specific functional outcome scores. Both of the surveys we used also indicate pain, and both are consistent with current and former smokers experiencing a greater level of pain for a longer period of time following ankle fracture.

Limitations of this study largely stem from its retrospective nature. Pack years were not reliably reported, which limits our ability to examine the relationship between quantity of tobacco use and patient outcomes. Furthermore, reporting bias may influence the validity of patient's self-reported tobacco use history at the time of their ankle injury. Other forms of tobacco use and vaping habits were also not included in this study, which is another limitation. The largest limitation of this study was the loss of patients to follow-up and unavailable for later clinical assessment or outcomes surveys. A prospective study design in the future would be a useful addition to the current body of literature regarding the impact of tobacco use on clinical and functional outcomes and ankle fracture. Another limitation of our outcomes assessment is the possibility of a ceiling effect for FFI scores, in other words, limited ability to distinguish between various higher functioning patients. Despite this, the current study presents one of the largest series of torsional ankle fractures to date, and our findings may benefit the orthopaedic community caring for patients with these common injuries.

In conclusion, current tobacco smokers had a higher frequency of alcohol abuse and recreational drug use than nonsmokers. Although no differences were identified in rates of complications and secondary operations, current or former tobacco smoking was associated with more chronic pain and with worse FFI and SMFA scores following torsional ankle fracture. Provider awareness of this may improve our ability to counsel and treat patients more effectively.

Acknowledgment

The authors gratefully acknowledge the assistance of Chang-Yeon Kim, MD, with data analysis.

References

- U.S. Department of Health and Human ServicesSmoking Cessation: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.
- Jamal A, King B, Neff L, et al. Current cigarette smoking among adults -United States, 2005–2015. MMWR Morb Mortal Wkly Rep. 2016;65:1205–1211.
- Hawn MT, Houston TK, Campagna EJ, et al. The attributable risk of smoking on surgical complications. Ann Surg. 2011;254:914–920.
- 4. Lu C, Saless N, Wang X, et al. The role of oxygen during fracture healing. Bone. 2013;52:220–229.
- Patel RA, Patel PA. The effect of smoking on bone healing. Arch Surg. 2012;147:373–383.
- 6. Sorenson L. Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. Ann Surg. 2012;255:1069–1079.
- Duchman KR, Gao Y, Pugely AJ, et al. The effect of smoking on shortterm complications following total hip and knee arthroplasty. J Bone Joint Surg Am. 2015;97:1049–1058.
- Kapadia BH, Johnson AJ, Naziri Q, et al. Increased revision rates after total knee arthroplasty in patients who smoke. J Arthroplasty. 2012;27: 1690–1695.e1.
- Kapadia BH, Issa K, Pivec R, et al. Tobacco use may be associated with increased revision and complication rates following total hip arthroplasty. J Arthroplasty. 2014;29:777–780.
- MacKenzie E, Bosse M, Kellam J, et al. Characterization of patients with high-energy lower extremity trauma. J Orthop Trauma. 2000;14:455–466.
- Vitesnikova J, Dinh M, Leonard E, et al. Use of AUDIT-C as a tool to identify hazardous alcohol consumption in admitted trauma patients. Injury. 2014;45:1440–1444.
- Levy R, Hebert C, Munn B, et al. Drug and alcohol use in orthopedic trauma patients: a prospective study. J Orthop Trauma. 1996;10:21–27.
- 13. Koleszar JC, Childs BR, Vallier HA. Frequency of recidivism in patients with orthopedic trauma. Orthopedics. 2016;39:300–306.
- Meinberg E, Agel J, Roberts C, et al. Fracture and dislocation classification compendium–2018. J Orthop Trauma. 2018;32 (Supplement 1):S1–S170.
- Budiman-Mak E, Conrad KJ, Roach KE. The Foot Function Index: a measure of foot pain and disability. J Clin Epidemiol. 1991;44:561–570.
- Bouffard J, Bertrand-Charette M, Roy J-S. Psychometric properties of the Musculoskeletal Function Assessment and the Short Musculoskeletal Function Assessment: a systematic review. Clin Rehabil. 2016;30: 393–409.
- Agel J, Obremsky W, Kregor P, et al. Administration of the Short Musculoskeletal Function Assessment: impact on office routine and physician-patient interaction. Orthopedics. 2003;26:783–788.
- Barei DP, Agel J, Swiontkowski MF. Current utilization, interpretation, and recommendations: the Musculoskeletal Function Assessments (MFA/SMFA). J Orthop Trauma. 2007;21:738–742.
- Engelberg R, Martin D, Agel J, et al. Muscloskeletal Function Assessment instrument: criterion and construct validity. J Orthop Res. 1996;14:182– 192.

- Martin D, Engelberg R, Agel J, et al. Development of a musculoskeletal extremity health status instrument: the Musculoskeletal Function Assessment instrument. J Orthop Res. 1996;14:173–181.
- 21. Sadr Azodi O, Bellocco R, Eriksson K, et al. The impact of tobacco use and body mass index on the length of stay in hospital and the risk of postoperative complications among patients undergoing total hip replacement. J Bone Joint Surg Br. 2006;88:1316–1320.
- Møller AM, Pedersen T, Villebro N, et al. Effect of smoking on early complications after elective orthopaedic surgery. J Bone Joint Surg Br. 2003;85:178–181.
- 23. Singh JA. Smoking and outcomes after knee and hip arthroplasty: a systematic review. J Rheumatol. 2014;38:1824–1834.
- 24. Singh JA, Houston TK, Ponce BA, et al. Smoking as a risk factor for short-term outcomes following primary total hip and total knee replacement in veterans. Arthritis Care Res (Hoboken). 2011;63: 1365–1374.
- Jorgensen LN, Kallehave F, Christensen E, et al. Less collagen production in smokers. Surgery. 1998;123:450–455.
- Sørensen LT, Jørgensen S, Petersen LJ, et al. Acute effects of nicotine and smoking on blood flow, tissue oxygen, and aerobe metabolism of the skin and subcutis. J Surg Res. 2009;152:224–230.
- Castillo RC, Bosse MJ, MacKenzie EJ, et al. Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures. J Orthop Trauma. 2005;19:151–157.
- Sorensen LT, Karlsmark T, Gottrup F. Abstinence from smoking reduces incisional wound infection. Ann Surg. 2003;238:1–5.
- 29. Porter SE, Hanley EN. The musculoskeletal effects of smoking. J Am Acad Orthop Surg. 2013;9:9–17.
- Fini M, Giavaresi G, Salamanna F. Harmful lifestyles on orthopedic implantation surgery: a descriptive review on alcohol and tobacco use. J Bone Miner Metab. 2011;29:633–644.
- Bedard N, DeMik D, Owens J, et al. Tobacco use and risk of wound complications and periprosthetic joint infection: a systematic review and meta-analysis of primary total joint arthroplasty procedures. J Arthroplast. 2019;34:385–396.
- Mulligan R, McCarthy K, Grear B, et al. Preoperative risk factors for complications in electie ankle and hindfoot reconstruction. Foot Ankle Spec. 2018;11:54–60.
- Scolaro J, Schenker M, Yannascoli S, et al. Cigarette smoking increases complications following fracture: a systematic review. J Bone Joint Surg Am. 2014;96:674–681.
- Jackson KL2nd, Devine JG. The effects of smoking and smoking cessation on spine surgery: a systematic review of the Literature. Global Spine J. 2016;6:695–701.
- Nauth A, Creek AT, Zellar A, et al. Fracture fixation in the operative management of hip fractures (FAITH): an international, multicentre, randomised controlled trial. Lancet. 2017;389:1519–1527.
- 36. Westgeest J, Weber D, Dulai S, et al. Factors associated with development of nonunion or delayed healing after an open long bone fracture: a prospective cohort study of 736 subjects. J Orthop Trauma. 2016;30: 149–155.
- Pearson R, Clement R, Edwards K, et al. Do smokers have greater risk of delayed and non-union after fracture, osteotomy and arthrodesis? A systematic review with meta-analysis. BMJ Open. 2016;6:e010303.
- Hu J, Zhang C, Zhu K, et al. Adverse radiographic outcomes following operative treatment of medial malleolar fractures. Foot Ankle Int. 2018;39:1301–1311.
- Matson A, Hamid K, Adams S. Predictors of time to union after operative fixation of closed ankle fractures. Foot Ankle Spec. 2017;10:308–314.
- 40. John U, Hanke M, Meyer C, et al. Tobacco smoking in relation to pain in a national general population survey. Prev Med. 2006;43:477–481.
- Vogt M, Hanscom B, Lauerman W, et al. Influence of smoking on the health status of spinal patients: the National Spine Network database. Spine (Phila Pa 1976). 2002;27:313–319.
- 42. Hooten W, Townsend C, Bruce B, et al. Effects of smoking status on immediate treatment outcomes of multidisciplinary pain rehabilitation. Pain Med. 2009;10:347–355.
- 43. Weingarten T, Moeschler S, Ptaszynski A, et al. An assessment of the association between smoking status, pain intensity, and functional interference in patients with chronic pain. Pain Physician. 2008;11: 643–653.
- 44. Weingarten T, Podduturu V, Hooten W, et al. Impact of tobacco use in patients presenting to a multidisciplinary outpatient treatment program for fibromyalgia. Clin J Pain. 2009;25:39–43.
- 45. Ditre J, Zale E, Heckman B, et al. A measure of perceived pain and tobacco smoking interrelations: pilot validation of the pain and smoking inventory. Cogn Behav Ther. 2017;46:339–351.

- Mulligan RP, Mccarthy KJ, Grear BJ, et al. Psychosocial risk factors for postoperative pain in ankle and hindfoot reconstruction. Foot Ankle Int. 2016;37:1065–1070.
- 47. Flanagan C, Wysong E, Ramey J, et al. Traumatic orthopaedic injury is not an independent risk factor for high postdischarge opioid consumption. J Am Acad Orthop Surg Glob Res Rev. 2017;1:e058.
- Kuwabara H, Heishman S, Brasic J, et al. Mu opioid receptor binding correlates with nicotine dependence and reward in smokers. PLoS One. 2014;9:e113694.
- 49. Walters C, Cleck J, Kuo Y, et al. Mu-opioid receptor and CREB activation are required for nicotine reward. Neuron. 2005;46:933–943.
- 50. Shi Y, Weingarten T, Mantilla C, et al. Smoking and pain: pathophysiology and clinical implications. Anesthesiology. 2010;113: 977–992.

- 51. Weerts E, Wand G, Kuwabara H, et al. Association of smoking with muopioid receptor availability before and during naltrexone blockade in alcohol-dependent subjects. Addict Biol. 2014;19:733–742.
- 52. Talka R, Tuominen R, Salminen O. Methadone's effect on nAChRs—a link between methadone use and smoking? Biochem Pharmacol. 2015;97:542–549.
- Dean DM, Ho BS, Lin A, et al. Predictors of patient-reported function and pain outcomes in operative ankle fractures. Foot Ankle Int. 2017;38:496–501.
- Bhandari M, Sprague S, Hanson B, et al. Health-related quality of life following operative treatment of unstable ankle fractures: a prospective observational study. J Orthop Trauma. 2004;18:338–345.
- 55. McCreary DL, Cunningham BP. Minimum clinically important difference in Short Musculoskeletal Function Assessment: what change matters in ankle fractures. Foot Ankle Spec. 2020;online ahead of print.