Association of Cigarette Use and Complication Rates and Outcomes Following Total Ankle Arthroplasty

Alexander Lampley, MD¹, Christopher E. Gross, MD², Cynthia L. Green, PhD³, James K. DeOrio, MD¹, Mark Easley, MD¹, Samuel Adams, MD¹, and James A. Nunley II, MD¹

Abstract

Background: Tobacco use is a known risk factor for increased perioperative complications and having worse functional outcomes in many orthopedic procedures. To date, no study has elucidated the effect of cigarette smoking on complications or functional outcome scores after total ankle replacement (TAR).

Methods: We retrospectively reviewed the records of 642 patients who had TAR between June 2007 and February 2014 with a known smoking status. These patients were separated into 3 groups based on their smoking status: 34 current smokers, 249 former smokers, and 359 nonsmokers. Outcome scores and perioperative complications, which included infection, wound complications, revision surgeries, and nonrevision surgeries were compared between the groups.

Results: When comparing perioperative complications in the active smokers to the nonsmokers, we found a statistically significant increased risk of wound breakdown (hazard ratio [HR] 3.08, P = .047). Although the active smokers had an increased rate of infection (HR 2.61, P = .392), revision surgery (HR 1.75, P = .470), and nonrevision surgery (HR 1.69, P = .172), these findings were not statistically significant. With regard to outcome scores, all groups demonstrated improvement at 1- and 2-year follow-up compared with their preoperative outcome scores. However, the active smokers had less improvement in their outcome scores than the nonsmokers at 1- and 2-year follow-up. Furthermore, there was no significant difference in the outcome scores when comparing the nonsmokers to the former smokers.

Conclusion: Active cigarette smokers undergoing TAR had a significantly higher risk of wound complications and worse outcome scores compared with nonsmokers and former smokers. Furthermore, tobacco cessation appeared to reverse the effects of smoking, which allowed TAR to be an effective and safe procedure for providing pain relief and improving function in former smokers as they had perioperative complication rates and outcomes similar to nonsmokers.

Level of Evidence: Level III, retrospective comparative series.

Keywords: total ankle arthroplasty, outcome studies, smoking

Introduction

While the prevalence of cigarette use has declined significantly over the past 30 years, cigarette smoking remains common among adults in the United States. The 2012 National Health Interview Survey reported that 18.1% of adults in the United States smoke cigarettes. Furthermore, cigarette smoking has been estimated to cost the USA $96 billion in medical expenses annually. With regard to operative procedures, cigarette use has been associated with an increase in postoperative complication rates, especially poor wound healing.

The harmful effects of cigarette smoking on postoperative complications have been confirmed in a multitude of orthopedic fields, including arthroplasty, hand surgery, spine surgery, fracture healing, and foot surgery. Furthermore, a recent meta-analysis demonstrated that patients undergoing both orthopedic and nonorthopedic surgeries had a dramatic decrease in perioperative complications when smoking cessation 4 weeks prior to the operation was performed.

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To date, no study has examined the effect of cigarette smoking on complications or functional outcome scores after total ankle replacement (TAR). The purpose of this study was to compare the rate of perioperative complications and outcome scores in nonsmokers, former smokers, and current smokers. We hypothesized that smokers would have worse functional outcome scores and a higher rate of perioperative complications compared with nonsmokers and former smokers after TAR.

Methods

Study Characteristics

After obtaining institutional review board approval, we retrospectively identified a consecutive series of 646 primary TARs performed between June 2007 and February 2014 in patients who had at least 3 months’ follow-up and a known smoking status. After review of the records, we found that 3 patients reported tobacco use in the form of chewing tobacco and 1 in the form of cigar smoking. However, documentation on the frequency of tobacco use was not available on these patients. Therefore, we excluded these patients so that the active smoking group only included cigarette smokers.

These 642 patients were then divided into a nonsmoker group (357 patients), an active smoker group (34 patients), and a former smoker group (247 patients).

Demographic information including age at surgery, sex, body mass index (BMI), indication for surgery, and comorbidities was collected. Comorbidities included hypertension, diabetes, coronary artery disease (CAD), anxiety, depression, peripheral vascular disease (PVD), congestive heart failure (CHF), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), and rheumatoid arthritis (RA).

All surgeries were performed by 4 orthopedic foot and ankle surgeons with extensive TAR experience at a single institution. The indication for surgery was debilitating ankle pain with loss of function secondary to ankle arthritis that failed conservative treatment. Different types of third-generation ankle replacement systems were used including INBONE (Wright Medical, Arlington, TN), Salto-Talaris (Tornier, Bloomington, MN), and Scandinavian Total Ankle Replacement (STAR; Stryker, Kalamazoo, MI). All TARs were implanted using standard operative technique for each respective arthroplasty system. Additional procedures considered necessary by the operating surgeon to attain a balanced prosthesis and plantigrade foot were performed at the time of TAR.

Table 1. Patient Demographics for Each Group.

<table>
<thead>
<tr>
<th></th>
<th>Nonsmoker (n = 357)</th>
<th>Active Smoker (n = 34)</th>
<th>Former Smoker (n = 247)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y)</td>
<td>61.8 ± 11.2</td>
<td>52.9 ± 9.3</td>
<td>64.2 ± 9.1</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>29.2 ± 5.5</td>
<td>27.8 ± 4.6</td>
<td>30.1 ± 5.7</td>
<td>.023</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>40.9</td>
<td>47.1</td>
<td>54.7</td>
<td>.004*</td>
</tr>
<tr>
<td>Median follow-up (mo)</td>
<td>34.2 (range: 3.2-88.2)</td>
<td>36.2 (range: 7.3-84.6)</td>
<td>36.3 (range: 3.0-98.8)</td>
<td>.091</td>
</tr>
</tbody>
</table>

*Statistically significant.

Study Outcomes

Perioperative complications including infection, wound breakdown, revision surgery, and nonrevision surgery were collected. Infection was defined as a periprosthetic joint infection that required reoperation. Similarly, wound breakdown was defined as wound drainage or dehiscence requiring an additional procedure. Revision surgery included any subsequent procedure that required revision of the tibial or talar component while nonrevision surgery included any subsequent procedure that did involve revision of the tibial or talar component.

Preoperative, 1-year, and 2-year follow-up functional outcome scores were available for patients in each smoking group. Functional outcome scores included American Orthopaedic Foot & Ankle Society hindfoot-ankle (AOFAS-HF) scoring system,19 the Short Form-36 (SF-36), and the Short Musculoskeletal Function Assessment (SMFA).

Patient Demographics

The demographic information for each group are shown in Table 1. Overall, the smoker group was younger (P < .001) and had a smaller BMI (P = .023) when compared to the nonsmoker group and the former smoker group. The mean age of the active smoker group was 8.9 years younger than the nonsmoker group and 11.3 years younger than the former smoker group. The active smokers also had an average BMI 1.3 less than the nonsmoker group and 2.3 less than the former smoker group. Compared to the nonsmoker group, the active smokers had a higher proportion of males (40.9% vs 47.1%); however, the former smokers had the highest percentage of males (54.7%). The gender difference was statistically significant between smoking groups (P = .004). There was no statistical difference in the follow-up time across smoking groups (P = .091).

With regard to implants, the nonsmokers consisted of 173 (48.5%) INBONE, 53 (14.8%) Salto-Talaris, and 131 (36.7%)
The active smokers had 19 (55.9%) INBONE, 9 (26.4%) Salto-Talaris, and 6 (17.7%) STAR prostheses, and the former smokers had 173 (47.4%) INBONE, 53 (20.0%) Salto-Talaris, and 131 (32.6%) STAR prostheses.

Statistical Analysis

Continuous data were summarized using the mean, median, range, and standard deviation as appropriate for continuous variables and counts and percentages for categorical variables. Continuous data were checked for normality using the Kolmogorov-Smirnov test. An analysis of variance (ANOVA) was used to compare normally distributed data, whereas the Kruskal-Wallis test was used for nonnormally distributed data to determine if any differences existed across smoking groups with regard to age, body mass index (BMI), and follow-up time. To determine if differences existed between categorical variables, a chi-square test or Fisher exact test (expected cell counts <5) was completed. In addition, a series of generalized linear repeated measures models for correlated data predicting functional outcome status were completed to determine if any significant differences existed across time points (preoperative, 1- and 2-year postoperative) between the smoking groups, and between smoking groups over time (time by smoking group interaction). If significant main effects were found, pairwise differences were then compared using a simulated correction factor to determine which time points and smoking groups were significantly different. All statistical tests were 2-sided, and the significance level for all tests was $P < .05$. All statistical analyses were performed using SAS, version 9.4 (SAS, Cary, NC).

Results

The active smokers had an average daily cigarette use of $0.9 \pm 0.4$ (standard deviation [SD]) packs per day. The active smoker group had an average history of cigarette use of $25.6 \pm 11.8$ (SD) years at the time of surgery. This amounted to an average cumulative smoking history of $25.1 \pm 11.3$ (SD) pack years for the active smoker group. The former smokers had an average history of cigarette use of $20 \pm 10.5$ (SD) pack-years. The former smokers quit smoking on average 23.4 (range, 0.1-54.6) years prior to surgery.

With regard to comorbidities in each group (Table 2), the active smoker group had a statistically significant ($P = .002^*$) higher rate of COPD (8.8%) when compared to the nonsmokers (0.3%) and former smokers (2.0%). The active smokers had a higher rate of CAD (8.8%) than the nonsmokers (5.6%); however, the former smokers had the highest rate of CAD (11.7%). The indications for TAR were similarly distributed ($P = .130$) in all 3 groups (Table 3), with the majority of patients undergoing TAR for posttraumatic arthritis in each group.

When comparing the perioperative complications between the active smoker group and the nonsmoker group (Table 4), the active smokers had a greater rate of each complication. Although the active smokers had a higher rate of infection (hazard ratio [HR] 2.61, 95% confidence interval [CI] 0.29-23.33, $P = .392$), revision surgery (HR 1.75, 95% CI 0.38-8.01, $P = .470$) and nonrevision surgery (HR 1.69, 95% CI 0.80-3.59, $P = .172$), these findings did not reach statistical significance. The increased rate of wound
breakdown in the active smoker group (HR 3.08, 95% CI 1.01-9.38, P = .047) was statistically significant. For the active smoker group, the majority of wound breakdowns were treated with wound debridement without flap reconstruction (Table 5).

Meanwhile, when comparing the complications between the former smokers and nonsmoker groups, the former smokers had a lower rate of each complication. Although the former smokers had lower rate of infection (HR 0.36, 95% CI 0.04-3.25, P = .364), wound breakdown (HR 0.81, 95% CI 0.34-1.92, P = .628), revision surgery (HR 0.94, 95% CI 0.37-2.40, P = .899), and nonrevision surgery (HR 0.97, 95% CI 0.62-1.52, P = .900), these findings were not statistically significant (Table 6).

Ten patients in the nonsmoker group, 2 patients in the active smoker group, and 8 patients in the former smoker group required revision surgery, which was defined as a subsequent procedure that required revision of the tibial or talar component. Indications for revision surgery included infection, aseptic loosening, and talar subsidence and are summarized in Table 7.

On the other hand, nonrevision surgeries included arthroscopic gutter debridement, open gutter debridement, subtalar fusion, bone cyst bone grafting, wound debridement with rotational flap, free flap, or primary closure. The majority of nonrevision surgeries in the nonsmokers and former smokers group were arthroscopic or open gutter debridement. The types of nonrevision surgeries for each group are summarized in Table 5.
With regard to functional outcome scores, all groups demonstrated an improvement in functional outcome scores when comparing preoperative scores to 1- and 2-year follow-up. Furthermore, all changes in the SF-36, AOFAS-HF, and SMFA from preoperative assessment to 1-year follow-up in the nonsmoker, active smoker, and former smoker groups were statistically significant (P < .001). Similarly, all changes in the aforementioned outcome scores from preoperative assessment to the 2-year follow-up in all 3 groups were statistically significant (P < .001). The changes in the outcome scores from the 1-year follow-up to the 2-year follow-up were not statistically significant in the nonsmoker group (SF-36 P = .661, SMFA P = .999, AOFAS-HF P = 1.000), active smoker group (SF-36 P = .998, SMFA P = 1.000, AOFAS-HF P = .999), and the former smoker group (SF-36 P = .874, SMFA P = .945, AOFAS-HF P = .680).

When comparing the nonsmoker group to the active smoker group (Table 8), the active smokers had worse outcome scores at preoperative assessment. This was statistically significant for the SF-36 (P = .028) only. Notably, the magnitude of improvement in the SF-36, SMFA, and AOFAS-HF was greater in the nonsmoker group. This was statistically significant for the SF-36 at 1-year postoperative follow-up (P < .001) and 2-year postoperative follow-up (P = .002) as well as the SMFA at 1-year postoperative follow-up (P = .004) and 2-year postoperative follow-up (P = .005). The differences in AOFAS-HF score among the 2 groups were not statistically significant at preoperative evaluation (P = .846), 1-year postoperative follow-up (P = .056), or 2-year postoperative follow-up (P = .272).

Meanwhile, the former smoker group demonstrated similar outcome scores to the nonsmoker group with no statistical differences at preoperative evaluation, 1-year postoperative follow-up, and 2-year postoperative follow-up (Table 9). The former smoker group also had a similar magnitude of improvement to the nonsmoker group in all outcome scores.

**Discussion**

Tobacco use has been associated with an increased risk of complications in a multitude of orthopedic procedures; however, the effect of cigarette use in TAR has not been reported. In our study, we found that active smokers had a significantly higher rate of wound complications requiring additional procedures when compared to the nonsmokers. The active smoker group did not have an increased rate of comorbidities that would increase their risk of wound complications such as diabetes mellitus, peripheral vascular disease, or rheumatoid arthritis, when compared to the nonsmoker group. Therefore, the statistically significant increased rate of wound complications in the active smoker group is most likely explained by cigarette use. This link between tobacco use and a higher risk of wound complications is well defined in the orthopedic and general surgery literature. In a systematic review and meta-analysis comparing preoperative smoking status and perioperative complications in patients undergoing general surgery, head/neck surgery, orthopedic surgery, plastic surgery, and oral surgery, Grønkjær et al found that patients who were active smokers

### Table 8. Comparison of Outcome Scores Between Nonsmokers and Active Smokers.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Preoperative</th>
<th>1 Year Postoperative</th>
<th>2 Year Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nonsmokers</td>
<td>Active Smokers</td>
<td>P Value</td>
</tr>
<tr>
<td>SF-36</td>
<td>49.3 ± 18.3</td>
<td>38.6 ± 16.2</td>
<td>.028*</td>
</tr>
<tr>
<td>AOFAS-HF</td>
<td>40.6 ± 16.0</td>
<td>37.8 ± 15.3</td>
<td>.846</td>
</tr>
<tr>
<td>SMFA</td>
<td>82.7 ± 18.5</td>
<td>91.2 ± 14.7</td>
<td>.162</td>
</tr>
</tbody>
</table>

Abbreviations: AOFAS-HF, American Orthopaedic Foot & Ankle Society hindfoot-ankle; SF-36, Short Form-36; SMFA, Short Musculoskeletal Function Assessment.

*Statistically significant.

### Table 9. Comparison of Outcome Scores between Nonsmokers and Former Smokers.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Preoperative</th>
<th>1 Year Postoperative</th>
<th>2 Year Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nonsmokers</td>
<td>Former Smokers</td>
<td>P Value</td>
</tr>
<tr>
<td>SF-36</td>
<td>49.3 ± 18.3</td>
<td>47.7 ± 16.0</td>
<td>0.720</td>
</tr>
<tr>
<td>AOFAS-HF</td>
<td>40.6 ± 16.0</td>
<td>41.8 ± 15.0</td>
<td>0.914</td>
</tr>
<tr>
<td>SMFA</td>
<td>82.7 ± 18.5</td>
<td>83.9 ± 17.5</td>
<td>0.958</td>
</tr>
</tbody>
</table>

Abbreviations: AOFAS-HF, American Orthopaedic Foot & Ankle Society hindfoot-ankle; SF-36, Short Form-36; SMFA, Short Musculoskeletal Function Assessment.
compared to nonsmokers had a statistically significant higher rate of wound complications (relative risk [RR] 2.15) and infection (RR 1.54), and our study confirms this correlation between cigarette use and wound complications in patients undergoing TAR.

The association between cigarette smoking and perioperative wound complications is likely caused by the negative effects of the toxic components absorbed systemically when using tobacco. Although cigarette smoke contains greater than 4000 toxic components, nicotine, carbon monoxide, and hydrogen cyanide are most attributed to the deleterious effects of smoking in the postoperative period. Nicotine has been shown to increase platelet adhesiveness, which leads to microvascular occlusion and decreased microperfusion. In addition, nicotine also causes vasoconstriction, which, when combined with microvascular occlusion, can eventually lead to tissue ischemia. Carbon monoxide also decreases the oxygen available to the healing tissue by competitively inhibiting the binding of oxygen to hemoglobin, thereby reducing the oxygen-carrying capacity of red blood cells. Hydrogen cyanide potentiates tissue ischemia induced by nicotine and carbon monoxide by inhibiting cellular enzymes involved in oxidative metabolism. The combined action of these 3 chemicals creates an environment detrimental to bone and soft tissue healing. In addition to these direct soft tissue effects, smoking also increases a patient’s risk of developing COPD and/or atherosclerosis. Both of these conditions may worsen the already decreased soft tissue oxygen tension.

The active smoker group also had a higher rate of revision surgery and infection. Although these findings were not statistically significant, they do agree with the total knee arthroplasty (TKA) and hip arthroplasty (THA) literature. Duchman et al systematically reviewed 78,191 patients who underwent primary THA or TKA and found active smokers to have not only a higher risk of wound complications but also an increased rate of deep infection. Likewise, active smokers have been shown to have higher rates of revision surgery and lower implant survivorship after THA and TKA when compared to nonsmokers.

Another major finding of our study was that although cigarette smokers can expect an improvement in their preoperative functional outcome scores after TAR at the 1- and 2-year follow-up, their outcome scores will have a smaller magnitude of improvement when compared to nonsmokers undergoing TAR. The difference in outcome scores was especially noteworthy as the active smoker group, with a mean age of 52.9 years old, was significantly younger than the nonsmoker group. Patients younger than 55 years old have been shown to have greater improvement in their Oswestry Disability Index, EuroQol, and SF-36 when compared to nonsmokers.

Several mechanisms can be proposed to explain the link between active smokers and worse outcome scores. Cigarette use increases blood levels of pro-inflammatory cytokines, which have been shown to be potent signalers of pain in the central nervous system. Tobacco use has also been linked with osteoporosis. Active smokers may have worse pain at the bone-prosthesis interface because of their decreased bone mineral density. Although these suggested mechanisms could explain the poorer results, the exact etiology between smoking and inferior outcome scores after TAR is likely multifactorial and largely speculative.

Although the functional outcome scores for active smokers were inferior, it should be noted that former smokers experienced similar complication rates and outcome scores equivalent to the nonsmoker group. Therefore, this study should be used as another argument for the importance of preoperative smoking cessation. Our findings of similar outcomes in the former smokers and nonsmokers agree with 2 randomized controlled trials, showing that a perioperative smoking cessation program reduced the risk of postoperative complications.

Our study is not without limitations. Although smoking status ideally would be determined by measuring serum cotinine levels, our retrospective study design relied on patient-reported smoking status. This creates concern that some patients may not have accurately reported their smoking status. However, Bender et al found that patient-reported smoking status is reliable as validated by serum cotinine measurements in an orthopedic patient population. Although our study demonstrated that former smokers had outcomes similar to nonsmokers, these findings may not be generalizable for patients stopping cigarette use near the time of surgery. The wide range of time between quitting smoking and surgery (0.1-54.6 years) precluded us from calculating a “minimum” time needed for former smokers to reverse the increased risk of wound breakdown and poorer functional outcomes. Additionally, although the smokers had a higher risk of all complications, all of these findings except for wound breakdown were not statistically significant, which suggests that our study was underpowered or that adding patients to the active smoking group may reverse these findings.
these limitations, we feel that the major conclusions from our study are valid.

 Conclusion

Overall, our study highlights the importance of preoperative smoking cessation as cigarette smokers have a statistically significant increased risk of wound complications requiring reoperation and less improvement in their patient-reported outcomes after TAR. Meanwhile, there was no significant difference in the complication rates or outcome scores when comparing the nonsmokers to the former smokers. While some orthopedic surgeons feel that primary care providers are best suited to provide smoking cessation counseling, a study of 3041 spine patients who were active smokers showed that when the surgeon placed a “high priority” on smoking cessation, the quit rate was 35.6% compared with a quit rate of 19.5% when the surgeon placed a “low priority” on smoking cessation.25 Before TAR, smokers showed that when the surgeon placed a “high priority” on smoking cessation, the quit rate was 35.6% compared with a quit rate of 19.5% when the surgeon placed a “low priority” on smoking cessation.25 Before TAR, surgeons should educate active smokers of their increased risk of wound complications and poorer functional outcomes, and TAR should ideally be delayed until smoking cessation is obtained.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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