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# The Influence of Smoking on Foot and Ankle Surgery: A Review of the Literature.

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## Abstract

The effect of tobacco smoking on foot and ankle procedures is likely to be more pronounced when compared to other orthopaedic surgery. This is due to the peripheral nature of the vasculature involved. This paper reviews the current clinical evidence on the effects of smoking foot and ankle surgery. In the trauma setting, the

evidence suggests that wound complications and non-unions are significantly higher in the smoking population. In the elective setting there is a significantly increased risk of non-union in ankle and hindfoot arthrodeses in smokers. In the setting of diabetes, ulceration rate in smokers is higher and there may be a higher risk of amputation.

**Keywords**

Smoking, foot and ankle, complications, cessation, e-cigarettes

## Introduction

Smoking is of particular concern in surgical patients. One recent systematic review by Theadom et al reported that in addition to increased perioperative complications, smokers are at higher risk of developing lung and heart complications, post-operative infection, impaired wound healing and longer hospital admission.(1) There is reasonable evidence to suggest a correlation between smoking and poor outcome in orthopaedic procedures.(2)(3) However, when considering foot and ankle operations in isolation the evidence base is relatively limited.

The annual cost of managing healthcare in smokers is significantly higher, and although somewhat offset by shorter life expectancy smoking has undoubtedly been shown to increase the burden on orthopaedic services.(4)(5) Health problems associated with smoking have been estimated to cost NHS £2.7 billion every year, excluding the cost of work days lost, sickness benefits and other indirect costs.(6) It

is estimated that up to £700 000 per million persons per year could be saved by supporting smoking cessation prior to surgery.(7)(8)

The aim of this review is to outline the current clinical evidence in the literature regarding the effects of smoking on outcomes following foot and ankle surgery.

**Methods**

In order to review the current evidence on smoking related outcomes in foot and ankle surgery. The PUBMED search engine was used to search the literature for English language articles. The literature review included individual searches using the following criteria; smoking and ankle fracture, smoking and calcaneal fracture, smoking and hindfoot fracture, smoking and midfoot fracture, smoking and lis franc, smoking and metatarsal fracture, smoking and forefoot fracture, smoking and toe fracture, smoking and total ankle arthroplasty, smoking and total ankle replacement, smoking and ankle arthrodesis, smoking and ankle fusion, smoking and hindfoot arthrodesis, smoking and hindfoot fusion, smoking and subtalar arthrodesis, smoking and subtalar fusion, smoking and midfoot arthrodesis, smoking and midfoot fusion, smoking and 1$^{st}$ metatarsal phalangeal joint arthrodesis, smoking and 1$^{st}$ metatarsal phalangeal joint fusion, smoking and forefoot surgery smoking and diabetes in foot surgery, smoking cessation and foot and ankle surgery.

This was a pragmatic search strategy, we understand that some papers may not report smoking related data in their abstract, however to maintain the search at a reasonable number for analysis we felt are search criteria to be appropriate. Each of the individual searches yielded at least 20 studies for interrogation. The Prisma flow

chart in figure 1 demonstrates our overall search. Papers initially accepted after abstract review were searched using the find function within the document for smoking. This allowed us to quickly search the study for data pertaining to smoking to see if it was appropriate for inclusion.

If not specifically stated in the manuscripts reviewed, then they were assigned a level of evidence using the criteria set out by the Oxford centre of evidence based medicine.(9) Table 1 summarises smoking related outcomes. Outcomes included relative risk (RR) and odd's ratio (OR) reported in the included manuscripts. Where not included, but sufficient raw data was reported then we performed a post hoc analysis to generate RR and OR. Statistical analysis was performed using SPSS Inc. 20.0 (IBM, New York 10504-1722).

## Foot and Ankle Trauma Surgery

### *Ankle Fractures*

Not only may smoking be associated with increased complications postoperatively, it may also increase the risk of developing an ankle fracture. Valtola et al performed a prospective review of 14, 220 women aged 47-56 in Finland, with over 5 years follow up. Smoking was found to have a dose dependent effect with smoking 1-19 cigarettes a day significantly increasing the rate of fracture over non-smokers (p value 0.05) and

smoking greater than 20 cigarettes a day having a further more significant effect (p value 0.012).(10)

Complications after ankle fracture are not uncommon, with rates reported of up to 30%. Smoking is often included in study analyses and reported in some to increase complications, however the type of complication is not often elaborated upon.(11)

Nasell et al reported results from a large prospective study of 906 operatively treated ankle fractures. They noted a higher rate of complications seen overall in smokers, with an odds ratio 1.7 (p value 0.0045), including an odds ratio of 1.7 with a superficial infection rate of 14.8% (p value < 0.05) and an odds ratio of 6.0 with a deep infection rate of 4.9% (p value < 0.001).(12) This was despite having significantly more diabetics in the non-operative group. There was no significant difference with regards to thromboembolism. They did not comment on non-union rates.

Increased complications, namely surgical site infections in smokers was also reported in a large retrospective review from three level 1 trauma centres in China. After adjustment for confounders smoking was found to be significantly associated with increased infection, having an odds ratio 2.7 and p value 0.032. Moreover they reported that smoking was the single most predictor for surgical site infection.(13) In contrast, one retrospective study of 478 patients was unable to demonstrate smoking as an independent risk factor for wound complications.(14) They only reported 4 minor wound complications out of 76 ( 5.3%) in smokers, compared to 10 minor wound complications out of 402 (2.5%) non-smokers, there was no statistical

difference (p value 0.19). They defined minor complication as one requiring outpatient wound care and or oral antibiotics. The authors did however suggest that their departments standard pre, peri and post-operative smoking counsel and smoking cessation program may well have influenced that outcome.

The elderly ankle fracture population have particularly vulnerable soft tissues. One retrospective review of 110 patients over 80-years managed operatively reported a relative risk of 3.3 for wound complications in smokers (p value < 0.05).(15) Three non-unions were reported in this study, however distinctions between smoking status was not made.

In addition to increasing wound complications smoking has also been linked to significantly poorer physical function following ankle fracture fixation. Bhandari et al performed a prospective observational study of 30 patients. Even up to 24 months a significantly reduced SF-36 physical function score was noted (p value 0.009). Interestingly the same group also reported no wound issues, deep infection or non-union. (16) In fact smoking has been reported to have sustained adverse effects on patient reported outcomes for several years following fracture. Utvag et al performed a retrospective review of 959 patients unstable closed ankle fractures managed surgically. Follow up was between 3-6 years (median 4.2 years) and outcomes were evaluated using OMAS, LEFS and SEFAS scores. Subgroups were matched for fracture classification and the use of syndesmosis fixation was not found to be significant. All three outcome scores were significantly lower in smokers (p value < 0.05).(17)

These findings were corroborated by William et al in their retrospective review 43 patients whom underwent implant removal. Using a short musculoskeletal function assessment, smoking 10 or pack years correlated with a poorer improvement in outcomes postoperatively.(18)

With regards to fracture union Matson et al performed a large retrospective review of 112 patients managed surgically in a tertiary academic centre. Overall time to union was 15.9 weeks (union defined as resolved fracture lines on radiograph and painless weight bearing) and those who smoked were significantly more likely to be united at 12 weeks when compared to non-smokers (p value 0.035). Interestingly, the union rate was not significantly different between smoking and non-smoking groups. Age, gender, BMI and presence of Diabetes were not found to influence overall union rate. However it was unclear from their manuscript whether these variables were matched in the smoking and non-smoking groups.(19)

Dodson et al performed a retrospective study of 58 patients and demonstrated that smokers are more likely to require prolonged immobilization secondary to delayed union.(20) This was also reported by Krannitz et al, they reported performed a retrospective review of 52 patients, 26 managed operatively and 26 non-operatively for supination-external rotation II fractures. In their non-operative treatment arm they reported a time to union of 97 days in smoking group and 81 days in non-smoking group (p value 0.034). In the operative treatment arm those that smoked had a time to radiological union of 56 days and in the non-smoking subgroup a time

to union of 45 days (p value 0.006). (21)

In summary there is level 2 evidence for significantly higher wound healing problems, level 2 evidence for significantly poorer physical function in smokers and there is level 4 evidence for increased rate of delayed union in smokers.

***Calcaneal Fractures***

The literature typically describes extensile lateral or sinus tarsi approaches to calcaneal fracture fixation.(22) There is limited evidence comparing both approaches in both smoking and non-smoking patient groups. The largest single series on calcaneal fracture fixation outcomes was a retrospective review of 4481 patients and due to limitations in data collection they could not comment on smoking status.(23) One study by Kwon et al compared smokers to non-smokers in both an extensile lateral and a combined percutaneous or sinus tarsi group. This was a retrospective study of 405 patients, wound complications included; superficial infections, deep infections, superficial wound dehiscence and deep wound dehiscence. Independent of surgical approach smoking significantly associated with wound complications, with an odds ratio of 1.9 and p value of 0.028. The extensile lateral group in isolation was more strongly associated with wound complications with an odds ratio of 2.2 and a p value of 0.015. There was no significant association between smokers and increased wound complications in the percutaneous and sinus tarsi group (p value > 0.05), however interestingly a delay to surgery of greater than 2 weeks significantly increased wound complications in the percutaneous and sinus tarsi group (p value 0.01).(24)

Five smaller retrospective case series have reported statistically significant differences in wound complications in smokers versus nonsmokers (P value < 0.05), following open reduction internal fixation via a "conventional" or extensile lateral approach. In total the five studies represent over 840 patients, reporting 182 wound complications (mean 22%) in smoking groups. (25)(26)(27)(28)(29) Although small case numbers, when combined three of the studies demonstrated a total mean infection rate of 16.4% in smokers and 5.0% in non-smokers and odds ratio 3.43 (p value 0.0005). (27)(29)(30) Smoking may also be a dose dependent factor for complications. Folk et al noted significantly increased wound complications (p value 0.04) if a smoker of 10 or more pack years.(25)

With regards to level 1 data, there are several meta-analyses reviewing outcomes following calcaneal fracture treatment. Some have studied sinus tarsi vs. extensile lateral approaches and some have studied non-operative vs. operative treatment. None have looked at studies comparing smokers and non-smokers and outcomes. The meta analyses reviewing surgical approach did not comment on the variable of smoking and outcome. Both meta analyses looked at level 1 data and included similar studies in their analysis,(31)(32) looking at the individual randomised controlled trials (RCT) there was no discussion on smoking and outcome in all but one trial that excluded smokers altogether.(33) The meta-analyses comparing operative and non-operative studies also did not comment on smoking and outcome.(34)(35)(36)(37) The majority of RCTs included in these meta-analyses were the same and once again when RCTs were reviewed individually, smoking was not assessed at all in most.(38)(39)(40)(41)(42)(43)(42)(44)(45) One RCT matched non-operative and

operative groups for smoking prevalence but did not study whether smoking increased complications in either group.(46) One multi centre RCT compared non-operative and operative Calcaneal fracture management. They reported a 16% rate of superficial and deep wound complications and although they hypothesized that smoking contributed to this, the study did not collect sufficient data to confirm this. The study did not comment on the influence of smoking on union rate.(47)

Systematic reviews of studies comparing percutaneous and open calcaneal fracture fixation report a significant reduction in wound complications, however no comments were made as to whether a further risk reduction was noted when comparing non-smokers to smokers.(33)(48)

Fortunately, non-union following calcaneal fracture is rare, none of the studies above reported any non-unions. Case reports have been described in the literature and the commonality in all was active smoking.(49)

In summary there is only level 4 evidence that smoking increases the risk of wound complications when fixing a calcaneus fracture with an extensile lateral approach. There has been no meaningful assessment of smoking in the level 1 literature and a lack of evidence regarding smoking and excess complications in minimally invasive procedures. The influence of smoking on union rates has not been substantially evaluated, however case reports of non-union in smokers have been reported.

**Midfoot and Forefoot Injuries**

Despite numerous studies on the management of midfoot and forefoot injuries, the influence of smoking on outcome was often excluded in their investigation and sometimes only implicated briefly in discussion.(50)(51)(52)(53)(54)(55)(56)(57)(58)(59)(60) Of the few studies to discuss smoking in midfoot injuries, one studied it in sufficient detail. Nolte et al performed a large observational study of 594 consecutive metatarsal fractures and reported that metatarsal fractures are significantly more likely to be associated with a non-union (p value <0.00001) than matched non-smoking counterparts.(61)

One retrospective study reviewed outcomes for 61 patients managed surgically and followed up between 2 and 24 years. Although not statistically significant, there was a positive correlation with smoking history and symptomatic osteoarthritis, with a relative risk 1.35. There was no discussion around wound healing issues and smoking in this study.(62) One further retrospective study of 179 patients also found significantly increased risk of midfoot wound complications following removal of metal in those who smoked when compared to non-smokers (odds ratio 4.93, p value 0.02).(63)

In summary there is level 3 evidence that smoking significantly increases non-union incidence and level 4 evidence for increased risk of symptomatic osteoarthritis and wound complications following hardware removal.

## Foot and Ankle Orthopaedic Surgery

The effects of smoking on complication rates and patient reported outcomes seen in the trauma setting are also reported in elective orthopaedics.

### *Total Ankle Replacement*

With regards to smoking and total ankle replacement (TAR), there is a relative paucity in reported literature discussing its influence on outcome. One prospective review of 668 patients reported that ccurrent smoking was shown to reduce mean Short Musculoskeletal Function Assessment (SMFA) scores even up to 5 years. In this study there were only 6 current smokers recorded and although proven to be statistically significant, some caution should be taken as other patient reported outcomes used in the study did not show any difference. No comment on wound complications related to tobacco use was made.(64)

These findings were further corroborated by Lampley et al's retrospective review of 646 primary TARs. They reported a significantly decreased SMFA at both 1 and 2 years follow up. Additionally, they also reported no difference in SMFA between non-smokers and ex-smokers, suggesting an element of reversibility regarding the ill effects of smoking on patient reported outcomes. Lampley et al also reported a significantly increased rate of wound breakdown in active smokers (11.8% vs 3.9% p value 0.047). Unfortunately the variation in time free from smoking and numbers

involved preclude an analysis of minimum time required to be free from smoking and have a non-smoking level of functional outcomes and complications.(65)

Whalen et al was able to quantify the amount of smoking in pack years that significantly increased risk of wound complications. They performed a retrospective review of 57 patients and identified 12 pack years as a threshold for significantly increased risk of wound complications.(66) Other retrospective studies could not demonstrate a correlation between smoking and adverse outcome following TAR. These studies were smaller and despite appropriate statistical analysis are open to type 2 error.(67)(68)(69)(70)

In summary there is level 3 evidence that smoking increases risk of wound complications and decreased patient reported outcomes. This may be dose dependent.

***Ankle and Hindfoot Arthrodesis***

Delayed union and non-union in smokers following osteotomies and arthodeses have also been well recognized. Cobb et al performed a retrospective review of 44 patients and found that the risk for ankle arthrodesis non-union in smokers was 3.75 times that of non–smokers (p value 0.0275). All patient had open joint preparation and screw fixation. This was after adjustments for co-morbidities such as diabetes, cardiovascular disease and steroid use. (71) Studies utilising alternative fixation techniques such as ilizarov method also report similarly high non-union rates. Fragomen et al performed a retrospective review of 101 patients underwent complex ankle arthrodesis using Ilizarov method. They reported union rates of 93% in non-

smokers and 46% in smokers (p value 0.0008). (72)

Post traumatic arthritis following calcaneal fracture leads to a considerable proportion of subtalar arthrodeses. One recent retrospective study from Van der Vliet et al reported the functional outcomes of such a group. The median interval between arthrodesis and outcomes survey was 8.8 years. FAAM, MFS, PROMIS PF, EQ-5D and EQ-VAS scores were used. Most were fused with 2 screws and around half received autograft. Of the 159 eligible patients, only 84 responded and 21 of those were smokers. Using multivariable regression analysis smokers scored significantly less in all functional scores tested (p value < 0.05). This study was limited in that smoking status was only checked at time of subtalar joint arthrodesis and not after.

Chahal et al reported multi-centre results following a retrospective review of 88 patients, that underwent subtalar arthrodesis. The cases were age matched, smokers had a significantly lower union rate of 68.4% when compared to 89.8% in non-smokers (p value < 0.05). This equated to an odds ratio of 3.87.(73) Furthermore, a large retrospective review of 184 subtalar arthrodeses by Myerson and co-authors reported a union rate in non-smokers of 92% and a union rate in smokers of 73% (p value <0.05). (74)

Ishikawa et al' s retrospective review looked at a mix of 160 hind foot arthrodeses (any combination of subtalar, talonavicular and calcaneocuboid arthrodeses) and identified a significant increase of non-unions in smokers compared to nonsmokers (18.6% vs. 7.1% respectively, p value 0.04).(75) Mulligan et al performed a retrospective comparative study of both ankle and hindfoot arthrodeses in 139 cases.

They reported in smokers an overall complication rate of 43% (odds ratio 2.2, p value 0.11), major complication rate of 19% (odds ratio 5.32, p value 0.02) and a re-operation rate of 29% (odds ratio 2.22, p value 0.14). Deep infections were significantly more frequent in smokers (p value < .01), wound complications and non-unions were also more common in smokers, however statistical significance was not reached (p value > 0.05).(76) This may have been due to under powering of study.

Thevendran et al. completed a current concepts review on the risks of non-union in foot and ankle arthrodeses. The papers they included were discussed above.(74)(71)(73) (75) (77) All papers were level 4 except for Ishikawa et al's level 3 paper They concluded that there was enough evidence to support a grade B recommendation on smoking as a risk factor for non-union.(77)

Results of more complex procedures, namely tibiotalarcalcaneal arthrodeses have also been reported to be influenced by smoking. Steele et al performed a retrospective comparative cohort study of 86 patients whom underwent tibiotalarcalcaneal arthrodesis. In this study surgical approach or postoperative rehabilitation was not described and the comparison was made between dynamic compression and static locking intramedullary nailing methods. There was no difference in union between fixation groups although union time was quicker with dynamic compression groups. This was despite all 7 current smokers being in the dynamic compression group. When variables were analysed for non-union, smoking was found to have an odds

ratio of 2.63, however this was not statistically significant. This study had lower numbers particularly with smokers and their results are therefore open to type 2 error.(78)

More recently Pitts et al, reported results of a retrospective single centre study of 101 patients. arthrodeses were performed using an intramedullary nail. Their indications for use was varied and includes in the treatment of osteoarthritis, avascular necrosis, Charcot arthropathy, failed total ankle arthroplasty and severe deformity. There was a median follow-up of 13 months. This was a heterogeneous group of patients and numbers were insufficient to study smoking within the subgroups of indications for surgery. Overall, smoking increased risk of non-union with relative risk of 1.372, this was not statistically significant (p value 0.324). Smoking did not influence below knee amputation rate, return to theatre or post-operative infection.

To summarise, there is level 3 evidence that smoking significantly increases the risk of non-union and major complications such as deep infection in ankle and hindfoot arthrodesis.

***Midfoot Arthrodesis***

There was relatively little in the literature with regards to detailed evaluation of complications in midfoot arthrodesis related specifically to smoking.(79)(80) One retrospective single surgeon series comparing union rates of both hindfoot and midfoot arthrodeses in smokers and non-smokers reviewed 381 consecutive arthrodeses. Revisions and Charcot cases were excluded. Patients were matched for

age, diabetes status and BMI. The relative risk for non-unions in smokers was 5.81 (p value < 0.001).(81) This finding may also be dose dependent, with increasing non-unions noted with heavier smokers. However this did not quite reach statistical significance (p value 0.054).(81)

One retrospective review from Buda et al studied results from two centres and 9 surgeons performing single or multiple tarsometatarsal joint arthrodesis. 88 patients were included and they were fused with a combination of screws alone, screw and plates and plates alone. Perioperative smoking was found to increase the risk of non-union with an odds ratio 7.9, p value 0.002), There was no significant difference between smoking prevalence in the three different fixation groups. There was one confounder in particular that may have influenced results, 70 patients received autograft bone and of those 33 also had demineralised bone matrix. It is not clear whether smoking groups were matched for use of bone graft and therefore non-union rates quoted for smoking may in part be influenced by bone graft adjuncts. This study unfortunately did not comment on wound complications in smokers.(82)

One prospective study from Coetzee et al reported outcomes for Lapidus procedure for failed treatment of hallux valgus in 26 cases. Smoking was associated with significantly poorer AOFAS hallux metatarsophalangeal-interphalangeal scale and visual analogue score at six and twelve months (p value < 0.05). The three non-unions in this study all occurred in smokers.(83)

To summarise, there is level 4 evidence that non-union risk is significantly increased in smokers. There is level 2 evidence that significantly poorer functional outcomes

can also be expected in smokers (p value <0.05).

***Forefoot Surgery***

Bettin et al. performed a retrospective comparative study of 602 patients who underwent forefoot surgery. This included fracture fixation, elective surgery, soft tissue and bony procedures. Patients were grouped into active smoking, ex-smoker and non-smoker groups. They found active cigarette smokers were 4.3 times more likely to have a complication than nonsmokers and ex-smokers were 1.9 times more likely to have a complication when compared to non-smokers.(65) The increased complications in active smokers includes; delayed union (relative risk 6.9, p value 0.0323), non-union (relative risk 6.9, p value 0.0452), infection (relative risk 4.6, p value 0.0101), delayed wound healing (relative risk 9.7, p value 0.00025), and persistent pain (relative risk 3.8, p value 0.0025). Complication rates were a dose dependent phenomenon, with those smoking less than 14 cigarettes a day not suffering a complication and those who smoke 18 cigarettes or more all suffered a complication. (84)

Krannitz et al performed a prospective study comparing outcomes in smokers, second-hand smokers and non-smokers after undergoing an Austin bunionectomy.(85) 46 patients were recruited and split into three smoking status groups. They found that the osteotomy of a smoker took 1.73 times longer to reach

radiographic bone consolidation than that of a nonsmoker, equating to an increase in time to bone healing of 42% (p value 0.01). Krannitz also found an increase in healing time was dose dependent in relation to smoking activity.(85)

To summarise, there is level 2 to 3 evidence of increased complications in smokers undergoing forefoot surgery. With union rate taking 1.73 and complications occurring up to 4 times more frequently.

***Smoking in Diabetics***

Diabetes is a significant risk factor to bone healing and wound complications in foot and ankle surgery.(77) However, in diabetics the evidence for a relationship between tobacco and ulcers or amputation is variable. Some studies have implicated smoking as a causal link in diabetic foot complications. A cross-sectional study of 1142 patients with type 2 diabetes in Jordan found smoking to be a strong predictor of amputation.(86) A population-based cohort study in Wisconsin of people with type 1 diabetes age greater than 18 years found an association between ulcers and 10+ pack year history of smoking (odds ratio 1.3) and current smokers (odds ratio 2.3), however they found no link in type 2 diabetics.(87) In contrast, Adler et al, reported smoking to not increase the rate of amputation in a prospective study of 776 patients (rate of smoking in amputees of 87% and in non-amputees of 84%, p value 0.61). (88)

**Smoking cessation, testing and electronic cigarettes**

Animal studies have demonstrated reversible effects of nicotine, suggesting a role for smoking cessation therapy in the perioperative period. Animal studies into the effects of nicotine have demonstrated decreased capillary blood flow, distal perfusion and compromised skin viability. Reversibility was noted if Nicotine was withheld for two weeks.(54) In a level 1 comparative study, cessation of smoking for 4 weeks preoperatively, reduced the risk of wound infection to equal to that of non-smoking patients.(89) Immune function appears to recover after 2-6 weeks of abstinence; wound-healing after 3-4 weeks; and pulmonary function after 6-8 weeks.(90) A meta-analysis of randomized trials evaluating the effects of smoking cessation on postoperative complications in all operatively treated patients, demonstrated an overall relative risk reduction of 41% across many different surgical subspecialties.(91)

There may also be some reversibility of the effects of smoking on bone may at least be partially reversible. Former smokers have been found to have lower fracture risk than current smokers and had consistently improved outcomes in systemic post-operative complications, infections, outcome scores, return to work and recovery rates.(90) Cessation programs have had some success, with Moller and colleagues noting a postoperative complication rate of 18% in a preoperative intervention group (4 weeks of counseling and nicotine replacement therapy) compared with 52% in the

smoking group.(92) Similar findings were also noted by Lindstorm's group.(93) Despite these findings, there are no definitive guidelines on peri-operative smoking cessation and future work is needed to evaluate the various strategies for smoking cessation and the implementation of these strategies. Cook et al. showed in a randomized control trial that the negative effects of smoking in fracture healing could be mitigated using an active ultrasound device. (94)

On occasion, it may be important to determine whether a patient has ceased smoking. Although no studies have been performed in the reliability of patient reporting of smoking status in foot and ankle surgery, it has been stated that self-reporting likely leads to an underestimation of up to 25% of true smoking status.(95) The two most common methods of smoking assessment currently in use are exhaled carbon monoxide or cotinine measurement. Deveci et al reported that an exhaled carbon monoxide measurement of 6.5 parts per million had a sensitivity of 90% and specificity of 83%.(96) Etzel et al performed a review of the use of saliva cotinine as a marker of tobacco smoke exposure.(97) They found that passive smokers usually have cotinine concentrations in saliva below 5 ng/ml. Levels between 10 and 100 ng/ml may result from infrequent active smoking and levels >100 ng/ml from regular active smoking.

Grana and coauthors completed an in depth review of the current evidence of the health impact on the introduction of e-cigarettes. (98) They found that e-cigarettes

deliver lower levels of some of the toxins found in cigarette smoke. However, their health benefits are negated by its common dual use with cigarettes in the majority of the studies.(98) Similarly, Farsalinos and Polosa performed a systematic review of clinical studies on e-cigarette use and also concluded that e-cigarettes were far less harmful than tobacco.(99) There are currently no clinical studies on the effect of e-cigarettes in surgical outcomes available in the literature. At a cellular level, Romagna et al. found a significant reduction in cytotoxicity, when studying the effect of electronic cigarette vapor extract on cultured mammalian fibroblasts as compared to tobacco smoke.(100)

To summarize, it appears that there is a theoretical reduced risk profile of e-cigarettes in comparison to tobacco use in the perioperative period, however caution must be taken with this assumption without firm evidence.

Table 1. Summary of levels of evidence and available statistical analysis. Table 1 was created by selected data from studies with the highest level of construction within each category. If more than one studies were wound in each level, then the largest study with adequate data was used. Some studies reported relative risk (RR), some odds ratio (OR) and some neither. Where available data from each study was collected to calculate post hoc RR and OR for the table.

| Table 1 | **Summary of Best Available Evidence** | | | |
|---|---|---|---|---|
| **Foot & Ankle subgroup** | **Level of Evidence** | **Complications in smokers vs. non-smokers** | **P value** | **Association and probability** |
| **Trauma** | | | | |
| **Ankle** | 2 | General complications | 0.0045 | RR 1.5<br>OR 1.7 |
| | 2 | Superficial infection | <0.032 | RR 1.5<br>OR 1.7 |
| | 2 | Deep Infection | <0.001 | RR 5.8<br>OR 6 |
| | 2 | Decreased physical function | 0.009 | Not applicable |
| | 4 | Wound complications in the elderly | <0.05 | RR 3.3<br>OR 4.6 |

| | | | | |
|---|---|---|---|---|
| | 4 | Delayed union | 0.0034 | OR 4.6<br>RR 1.5 |
| **Calcaneus** | 4 | Increased wound complications | 0.028 | OR 1.9 |
| | 4 | Infection | 0.00005 | RR2.9<br>OR 3.3 |
| **Midfoot** | 4 | Wound Complication After Metal Removal | 0.02 | RR 2.9<br>OR 4.9 |
| **Forefoot** | 3 | Non-union | <0.0000 1 | Insufficient data |
| **Orthopaedics** | | | | |
| **TAR** | 3 | Wound breakdown | 0.047 | RR 3<br>OR 3.3 |
| **Ankle arthrodesis** | 3 | Non-union | 0.0275 | RR 3.8<br>OR 4.6 |
| **Hindfoot arthrodesis** | 3 | Non-union | <0.05 | RR 3.1<br>OR 3.9 |
| **Midfoot arthrodesis** | 2 | Functional Outcome | <0.05 | Not applicable |
| | 4 | Non-union | <0.001 | RR 5<br>OR 8.5 |
| **Forefoot surgery** | 3 | Delayed Union | 0.0323 | RR 6.9<br>OR 7.1 |
| | 3 | Non-union | 0.0452 | RR 6.9<br>OR 7.0 |
| | 3 | Infection | 0.0101 | RR 4.6<br>OR 5.0 |
| | 3 | Persistent Pain | 0.0025 | RR 3.8<br>OR 4.4 |

## Conclusion

The majority of evidence for smoking in foot and ankle surgery is level 3-4 data, with most being retrospective with little quantification of level of tobacco use. In the trauma setting evidence does indicate that wound complications and non-unions are significantly higher in the smoking population. There is also suggestion that smoking may significantly reduce functional outcome, at least in ankle fractures.

In the elective orthopaedic setting similar levels of evidence are noted. There appears

to be a significantly increased risk of non-union in ankle and hindfoot arthrodeses in smokers. Forefoot arthrodeses have also been shown to take significantly longer to unite. Again, there is a suggestion of poorer functional outcome in midfoot arthrodeses in smokers. There may also be a dose related effect regarding the amount of smoking and complication rate.

In the setting of diabetes, ulceration rate in smokers is higher and there may be a higher risk of amputation. Use of e cigarettes requires further study but likely reduces complication rates.

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Figure 1