■ FOOT AND ANKLE

The impact of lifestyle risk factors on the rate of infection after surgery for a fracture of the ankle

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Aims

Lifestyle risk factors are thought to increase the risk of infection after acute orthopaedic surgery but the evidence is scarce. We aimed to investigate whether smoking, obesity and alcohol overuse are risk factors for the development of infections after surgery for a fracture of the ankle.

Patients and Methods

We retrospectively reviewed all patients who underwent internal fixation of a fracture of the ankle between 2008 and 2013. The primary outcome was the rate of deep infection and the secondary outcome was any surgical site infection (SSI). Associations with the risk factors and possible confounding variables were analysed univariably and multivariably with backwards elimination.

Results

A total of 1043 patients were included; 64 (6.1%) had a deep infection and 146 (14.0%) had SSI. Obesity was strongly associated with both outcomes (odds ratio (OR) 2.21, p = 0.017 and OR 1.68, p = 0.032) in all analyses. Alcohol overuse was similarly associated, though significant only in unadjusted analyses. Surprisingly, smoking did not yield statistically significant associations with infections.

Conclusion

These findings suggest that obesity and possibly alcohol overuse are independent risk factors for the development of infection following surgery for a fracture of the ankle. This large study brings new evidence concerning these common risk factors; although prospective studies are needed to confirm causality.

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Post-operative infection is a feared complication in surgery. Smoking, obesity and alcohol overuse are risk factors, but their role in acute fracture surgery remains unclear. These factors have been theoretically linked to impaired wound healing and an increased risk of infection through several mechanisms.[1] Studies in elective orthopaedic and general surgery confirm smoking, alcohol overuse and possibly obesity as risk factors for wound complications and infection.[2-4] However, the evidence in acute orthopaedics and thus following surgery for fractures of the ankle remains scarce.

The incidence of these fractures has been reported to be 107 in 100 000 population per year and open reduction and internal fixation (ORIF) is often required, and is considered to be a low-risk procedure.[5,6] However, infection is a relatively frequent complication. Deep infection is reported in between 1.1% and 6.8% of cases, and superficial infections are reported in between 2.9% and 10.8%.[6-12] Infection is associated with an increased risk of a poor outcome, an economic burden for the healthcare system, and can, in severe cases, lead to amputation or death.[6,11,13,14]

Smoking, obesity and alcohol overuse have been suggested to be some of many factors which might increase the risk of complications after surgery for a fracture of the ankle.[15] However, their specific role, particularly related to infection, remains sparsely studied. Smoking and the increased risk of both deep infection and surgical site infection (SSI) as a broader definition seem to be associated in some studies.[9,11,12,16-18] Alcohol overuse also appears to be a risk factor.[8,9,11,19] Few studies have assessed the role of obesity and the evidence there is conflicting and sparse.[8,10,12,18]

The aim of this retrospective cohort study was to investigate whether smoking, obesity

Table I. Demographics of the patients

Variable	n (%)*
n	1043 (*100.0*)
Age (range) (yrs)	54.8 (9 to 95)†
Gender	
Male	431 (*41.3*)
Female	612 (*58.7*)
Diabetes	51 (*4.9*)
BMI ≥ 30 kg/m^2	164 (*17.3*)
Alcohol overuse	243 (*23.6*)
Smoking	283 (*27.3*)
ASA score	
I	445 (*47.9*)
II	397 (*42.7*)
III	87 (*9.4*)
IV	1 (*0.1*)
Fracture type	
Lateral	398 (*38.2*)
Medial	61 (*5.9*)
Bimalleolar	374 (*35.9*)
Trimalleolar	210 (*20.1*)

* percentage of available data. Number of patients with missing data regarding; BMI (96), alcohol (15), smoking (7), ASA (113)
† age is displayed as mean (range)
BMI, body mass index; ASA, American Society of Anesthesiologists

and alcohol overuse are risk factors for developing infection after surgery for a fracture of the ankle.

Patients and Methods

Through retrospective screening, we included consecutive patients who underwent surgery for a fracture of the ankle between 2008 and 2013. They were identified from the operation notes or post-operative registration. Exclusion criteria were fractures not involving the ankle and pilon-type fractures, those treated by external fixation or arthrodesis, patients with other fractures in the same limb and those who underwent surgical treatment elsewhere, those who failed to attend for follow-up and those whose fracture was wrongly coded.

We identified 1197 eligible patients; 154 were excluded leaving 1043, who were included. Five were registered twice as they had sustained two fractures of the ankle which were treated surgically on separate occasions during the period of the study. The demographics of the patients are shown in Table I.

All fractures were classified as lateral unimalleolar, medial unimalleolar, bimalleolar or trimalleolar. Surgically treated isolated rupture of the syndesmosis without bone fracture was classified as a lateral unimalleolar fracture.

The standard surgical procedure involved ORIF with screws and plates. Occasionally, wires or staples were used. Standard prophylactic antibiotics involved 2 g of dicloxacillin given intravenously during surgery. Post-operative treatment involved a plaster cast or a walker cast with no weight-bearing for the first three weeks and partial weight-bearing for the following three weeks. The patients were reviewed as outpatients two to three weeks post-operatively with standard radiographs, and at six weeks after the operation.

Data were collected from the hospital records. We reviewed the progress of each patient in detail from presentation to a minimum of 30 days post-operatively. Those treated between 2008 and 2011 were identified from a database created for other studies about pain management.[20,21] We included patients treated in 2012 and 2013, added data on alcohol intake and re-operations, and further reviewed all those who developed an infection.

The type of fracture was recorded from the operation notes, and the American Society of Anaesthesiologists (ASA) score[22] and body mass index (BMI) from the anaesthetic records. Obesity was defined as BMI ≥ 30 kg/m^2. Smoking status and alcohol overuse were recorded from the anaesthetic or admission records. Alcohol overuse was defined as a weekly intake of > 7 units for women or > 14 units for men. One unit equals 12 g of alcohol.

We identified re-operations through cross-matching patients included in the study with all patients registered as having had two or more operations on the ankle between 2008 and 2014.

We chose deep infection as the primary outcome and SSI as secondary outcome. We defined deep infection as being present if a re-operation was performed for this indication as recorded by the surgeon. According to established guidelines,[23] we considered SSI to be present if antibiotic treatment was initiated and clinical signs of infection were documented within 30 days of the initial operation or if the indication for the first re-operation was infection. Thus, patients with deep infection acquired within the first 30 days were also recorded in the SSI group. SSIs occurring after re-operations for other indications were not included.

The study was approved by the Danish Data Protection Agency (J.nr.750.16-32). In accordance with Danish legislation, the study required neither individual consent nor approval by an ethics committee.

Statistical analysis. The three hypothesised risk factors were analysed for association with the primary and secondary outcomes. We adjusted for possible confounding factors by further including gender, age, diabetes, ASA score type of fracture. ASA scores III and IV were pooled due to low volumes. The analysis was conducted in two steps.

Firstly, all factors were analysed in a univariable model. We used the chi-squared or Fisher's exact test for nominal variables and simple logistic models for numerical values, where the p-value was calculated with the Wald test. Secondly, all significantly associated factors in the initial analysis (i.e. $p < 0.05$) were included in a multivariable logistic regression model. We calculated the p-values using a likelihood ratio test. For factors with more than two sub-levels (e.g. ASA score) the p-values for the individual sub-levels were found using the Wald test. The multivariable regression was repeated using backwards elimination, thus excluding the element with the highest p-value and re-running the model until only elements returning a p-value

Table II. Deep infections after surgery for a fracture of the ankle

	Crude measures	**Univariable**		**Initial multivariable model***		**Final multivariable model†**	
	Deep infections, n (%)	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Obesity							
BMI < 30	39 (*5.0*)	ref.					
BMI ≥ 30	17 (*10.4*)	**2.21 (1.19 to 3.97)**	**0.008‡**	**2.09 (1.10 to 4.00)**	**0.031¶**	**2.21 (1.19 to 4.11)**	**0.017¶**
Alcohol overuse							
No	42 (*5.4*)	ref.					
Yes	22 (*9.1*)	**1.77 (1.01 to 3.00)**	**0.037‡**	1.75 (0.96 to 3.20)	0.080¶		
Smoking							
No	43 (*5.7*)	ref.					
Yes	21 (*7.4*)	1.33 (0.76 to 2.26)	0.310‡				
Gender							
Female	34 (*5.6*)	ref.					
Male	30 (*7.0*)	1.27 (0.76 to 2.12)	0.350‡				
Diabetes							
No	56 (*5.7*)	ref.					
Yes	8 (*15.7*)	**3.10 (1.20 to 7.11)**	**0.010§**	2.18 (0.88 to 5.40)	0.110¶	**2.72 (1.16 to 6.36)**	**0.032¶**
ASA score							
I	13 (*2.9*)	ref.	**< 0.001‡**		0.120¶		
II	26 (*6.6*)	**2.31 (1.19 to 4.73)**	**0.001‡**	1.41 (0.65 to 3.08)	0.390**		
III+IV	15 (*17.1*)	**6.78 (3.07 to 15.15)**	**< 0.001‡**	2.74 (1.01 to 7.46)	**0.049****		
Fracture type							
Lateral	25 (*6.3*)	ref.	0.530§				
Medial	1 (*1.6*)	0.25 (0.01 to 1.58)	0.230§				
Bimalleolar	25 (*6.7*)	1.07 (0.58 to 1.98)	0.880§				
Trimalleolar	13 (*6.2*)	0.98 (0.45 to 2.05)	1.000§				
Age††	-	**1.03 (1.01 to 1.04)**	**< 0.001****	1.02 (1.00 to 1.04)	0.050¶	**1.03 (1.01 to 1.05)**	**< 0.001¶**
Total	64 (*6.1*)						

Results in bold are statistically significant (p < 0.05)
* significant elements from univariable analysis included
† non-significant elements excluded with backwards elimination
‡ chi squared test
§ Fisher's exact test
¶ likelihood ratio test
** Wald test
†† increased risk per year of age
OR, odds ratio; CI, confidence interval; ref., reference value; BMI, body mass index; ASA, American Society of Anesthesiologists.

< 0.05 were left. Missing data only led to exclusion from the models in which these data were needed.

The results of the univariable and the multivariable analyses were recorded as odds ratios (OR) with 95% confidence intervals (CIs). In a separate analysis all factors in the initial multivariable model were tested for interactions amongst each other.

We used the statistical software "R" version 3.1.2 (The R Foundation for Statistical Computing, Vienna, Austria), with the statistical package "EpiTools" version 0.5.7, for the statistical analyses.

Results

Of the 1043 patients included, 164 (17.3%) were obese, 283 (27.3%) were smokers and 243 (23.6%) overused alcohol. There were few missing data (Table I). Re-operation was recorded for 416 patients (39.9%), including the planned removal of a syndesmosis screw. Deep infection was recorded in 64 patients (6.1%). Of these, 51 had positive microbiological cultures and the results were negative, missing or flawed in 13. SSI was found in 146 patients (14.0%).

Table II shows an overview of the primary outcome including correction for the confounding factors. A total of 17 obese patients (10.4%) had deep infection resulting in an OR of 2.21 for sustaining a deep infection when obese, in both the univariable analysis (p = 0.008) and the final multivariable model (p = 0.017). A total of 22 patients (9.1%) who overused alcohol had a deep infection with an OR of 1.77 (p = 0.037). However, this became non-significant in the multivariable model (OR 1.75, p = 0.080) and was thus excluded through the backwards elimination process. Smoking yielded an OR for a deep infection of 1.33 (p = 0.310) and was not included in the multivariable model. ASA score, age and diabetes were univariably associated with an increased risk and included in the multivariable model where only age and diabetes had statistical significance (Table II). No significant interactions were found between the elements of the multivariable model.

Table III shows the secondary outcome. Of the 146 patients with SSI, 97 (66.4%) were managed with antibiotics as outpatients, 17 (11.6%) required admission and intravenous antibiotics and 32 (21.9%) underwent a re-operation, thus also fulfilling the criteria for deep infection.

Table III. Surgical site infections after surgery for a fracture of the ankle

	Crude measures	**Univariable analysis**		**Initial multivariable model***		**Final multivariable model†**	
	Infections, n (%)	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Obesity							
BMI < 30	100 (*12.8*)	ref.					
BMI ≥ 30	33 (*20.1*)	**1.72 (1.10 to 2.64)**	**0.014‡**	**1.79 (1.12 to 2.86)**	**0.019¶**	**1.68 (1.06 to 2.67)**	**0.032¶**
Alcohol overuse							
No	97 (*12.3*)	ref.					
Yes	47(*19.3*)	**1.70 (1.15 to 2.49)**	**0.006‡**	1.43 (0.93 to 2.19)	0.110¶		
Smoking							
No	106 (*14.1*)	ref.					
Yes	39 (*13.8*)	0.98 (0.65 to 1.44)	0.900‡				
Gender							
Female	86 (*14.1*)	ref.					
Male	60 (*13.9*)	0.99 (0.69 to 1.41)	0.950‡				
Diabetes							
No	134 (*13.5*)	ref.					
Yes	12 (*23.5*)	**1.99 (0.97 to 3.79)**	**0.044‡**	0.99 (0.45 to 2.18)	0.970[f]		
ASA score							
I	31 (*7.0*)	ref.	**< 0.001‡**		**0.005¶**		**0.002¶**
II	69 (*17.4*)	**2.80 (1.80 to 4.44)**	**< 0.001‡**	**1.76 (1.05 to 2.94)**	**0.031****	**1.89 (1.14 to 3.13)**	**0.014****
III+IV	29 (*33.0*)	**6.53 (3.66 to 11.66)**	**< 0.001‡**	**3.21 (1.58 to 6.51)**	**0.001****	**3.40 (1.71 to 6.74)**	**< 0.001****
Fracture type							
Lateral	50 (*12.6*)	ref.	0.060§				
Medial	3 (*4.9*)	0.36 (0.07 to 1.18)	0.088§				
Bimalleolar	62 (*16.6*)	1.38 (0.91 to 2.12)	0.130§				
Trimalleolar	31 (*14.8*)	1.20 (0.72 to 2.00)	0.450§				
Age††	-	**1.03 (1.02 to 1.04)**	**< 0.001****	**1.02 (1.01 to 1.03)**	**0.002¶**	**1.02 (1.01 to 1.03)**	**0.002¶**
Total	146 (*14.0*)						

Results in bold are statistically significant (p < 0.05)
* significant elements from univariable analysis included
† non-significant elements excluded with backwards elimination ‡chi squared test §Fisher's exact test
¶ likelihood ratio test
** Wald test
†† increased risk per year of age
OR, odds ratio; CI, confidence interval; ref, reference value; BMI, body mass index; ASA, American Society of Anesthesiologists.

A total of 33 obese patients (20.1%) had a SSI with an OR of 1.72 in the univariable analysis (p = 0.014) and an OR of 1.68 in the final multivariable analysis (p = 0.032). A total of 47 patients who overused alcohol (19.3%) had a SSI with an OR in the univariable analysis of 1.70 (p = 0.006). The multivariable OR was not significant and alcohol was eliminated. A total of 39 smokers (13.8%) had a SSI which was similar to non-smokers and the difference was not significant with an OR of 0.98 (p = 0.900). In the univariable analyses ASA score, diabetes and age were significantly associated with an increased risk but ultimately only age and ASA score had significance (Table III). Again, no significant interactions were found among the elements included in the multivariable model.

Discussion

We conducted this large retrospective analysis of associations between lifestyle risk factors and post-operative infections in 1043 patients who had undergone surgery for a fracture of the ankle to provide further information about the complications following this treatment. Our primary finding was that obesity is associated with a markedly increased risk of both deep infection and SSI in these patients, even when adjusting for confounding factors. Alcohol overuse yielded a similar risk, although statistical significance was not upheld after adjustments. Surprisingly, we did not find a statistically significant association between smoking and infection.

Besides obesity and alcohol overuse, age and diabetes were also associated with an increased risk of infection. This has been previously described.[6,8,9,12] We also found ASA score to be of significance, which seems plausible as comorbidity has been reported to be a risk factor.[24]

A few authors have studied associations between obesity and the risk of infection in patients with a fracture of the ankle who undergo surgery,[8,10,12,18] and in contrast to our results, none reported an increased risk of deep infection or SSI. However, none had obesity as the primary focus. One retrospective study comparing obese with non-obese patients found no difference in unspecified complications, but did not report the rates of infection.[25] Most authors considered it in relation to diabetes, which is a known risk factor for infection.[26] Even when adjusting for diabetes, our findings suggest an increased risk of deep infection and SSI in obese patients. Obesity should therefore be borne in mind when choosing treatment.

The large sample size in our study might explain why we were able to identify obesity as a risk factor. A limitation, however, is the method of defining obesity by BMI from the patient-reported height and weight as recorded in the notes. BMI derived in this way has been shown to be 0.8 kg/m^2 less than if measured directly.[27] In order to accommodate for this we re-ran the analyses with obesity defined as BMI ≥ 29.2 and this only lowered the ORs slightly and did not change the overall conclusion.

Alcohol overuse has been reported to be related to various post-operative complications including delayed wound healing and infection.[3] A Cochrane review[28] concluded that stopping the consumption of alcohol one month pre-operatively reduces the complications after elective surgery. In surgery for a fracture of the ankle, some authors have reported results similar to ours.[19,29] Ovaska et al[8] retrospectively investigated deep infection following ORIF of a fracture of the ankle and reported increased risk with alcohol abuse (OR 3.8; 1.60 to 9.40), although this was not significant in multivariable analysis. In contrast, other retrospective studies did not find the same association.[9,11] This incongruity stems partly from different definitions of alcohol overuse. The definition we used is based on the Danish National Board of Health's low-risk recommendations,[30] and is more restrictive than most,[3,11,19,28,29] while the term is poorly defined in some studies.[7-9] Even with the restrictive definition we found a univariably significant association between alcohol overuse and an increased risk of infection. Choosing a higher alcohol limit could yield an increased rate of infection in the exposed group, assuming a dose-response relationship between alcohol and infection. Some alcohol data were not reported quantitatively but as "no abuse" or "only on social occasions". These were interpreted as non-overuse, which might not be consistently true, especially for young people who are more prone to binge-drinking.[31] Moreover, alcohol data were based on patient-reporting, which may underestimate consumption and thereby weaken the results.[32]

Smoking has been identified as a risk factor for wound complications including infection following orthopaedic procedures.[33,34] A number of authors have reported similar results after surgery for a fracture of the ankle. Ovaska et al[8] reported an increased risk of deep infection (OR 4.8; 2.2 to 10.2). Nåsell et al[9] reported an increased risk of both superficial (OR 1.7; 1.0 to 2.9) and deep infection (OR 6.0; 2.0 to 18.7) in smokers in a retrospective study similar to ours. Hence, we expected also to identify smoking as a risk factor, but we found no such significant association. Although this was surprising, a few authors have reported similar findings.[11,12,18]

The negative results might be biased by surgeons generally accepting smoking as a risk factor and adjusting the peri-operative regime, surgical procedure or prophylactic antibiotics accordingly. We did not have the data necessary to adjust for this. Moreover, some patients reduce or stop smoking following hospitalisation, which could reduce the risk of infection. Smoking might also be under reported in patients' records resulting in an under estimation of the potential risk; although smoking status in hospital records is reported to have a high validity.[35] Our study is large but may still be under powered to detect an increased risk.

The definition of deep infection varies among studies.[7,9-12,16] The definition we chose is a pragmatic approach to identifying deep infections in a retrospective study and is similar to that used by Nåsell et al.[9] Our rate of deep infection is high compared with theirs and that of Miller et al,[12] who reported rates of < 2%, and is much more similar to that of Ovaska et al,[8] who reported 6.8%. In our study, one in five deep infections either had negative or missing microbiological cultures. Although infection was not verified with certainty in these patients, the clinical suspicion was the indication for further surgery with resulting risks, inconveniences and costs, thus making the definition of the outcome clinically meaningful. Pre-operative treatment with antibiotics was not recorded and may have resulted in false negative bacterial cultures.[36] A limitation of this study is a lack of data on the use of antibiotics pre- and post-operatively.

Rates of SSI of between 2.9% and 10.8% have been reported in these patients.[9-12,18,24] We found a rate of 14%. This could even be an under estimation if antibiotic treatment initiated by general practitioners was not consistently recorded at follow-up. An over estimation may be more likely due to possible over treatment. Access to general practitioners is free and widely available in Denmark and frequent visits to physicians without an orthopaedic background presumably gives lower thresholds for prescribing antibiotics. Furthermore, the diagnosis of SSI after discharge from hospital has been reported to have a low sensitivity.[23] Despite these issues, we consider our definition of the outcome to be clinically relevant. Whenever treatment is initiated it carries the cost of antibiotics, further outpatient visits and the potential spread of antibiotic resistance, regardless of whether the diagnosis of SSI was correct.

Our study is also limited by its retrospective design, which risks the effects of residual confounding variables, which cannot be adjusted for. Nonetheless, it has strengths. The infection outcomes are clinically meaningful and the study is based on a large consecutive cohort compared with most studies in this area. This enabled us to show an association between alcohol overuse and infection even with a restrictive definition of 'overuse'. Importantly, to our knowledge, no previous studies have had a primary focus on obesity and post-operative infections in patients with a fracture of the ankle who undergo surgery, which adds strength to our findings. Large, prospective studies are needed to substantiate the relationship between obesity and infection in these patients as well as for both moderate and severe alcohol overuse.

In conclusion, these findings suggest that obesity and possibly alcohol overuse are independent risk factors for infection following surgery for a fracture of the ankle. We

were not able to show any significant correlation between smoking and post-operative infection.

Take home message:

- Our study indicates that obese patients and possibly patients who overuse alcohol are at an increased risk of infection following ankle fracture surgery.

- This should be taken into consideration by the clinician when choosing treatment strategy.

Author contributions:
L. L. Olsen: Study planning, Data collection, Data analysis and interpretation, Writing first draft, Approving final manuscript.
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