Risk Factors for Deep Surgical Site Infection Following Operative Treatment of Ankle Fractures

Mikko T. Ovaska, MD, Tatu J. Mäkinen, MD, PhD, Rami Madanat, MD, PhD, Kaisa Huotari, MD, PhD, Tero Vahlberg, MSc, Eero Hirvensalo, MD, PhD, and Jan Lindahl, MD

Investigation performed at the Department of Orthopaedics and Traumatology, Helsinki University Central Hospital, Helsinki, Finland

Background: Surgical site infection is one of the most common complications following ankle fracture surgery. These infections are associated with substantial morbidity and lead to increased resource utilization. Identification of risk factors is crucial for developing strategies to prevent these complications.

Methods: We performed an age and sex-matched case-control study to identify patient and surgery-related risk factors for deep surgical site infection following operative ankle fracture treatment. We identified 1923 ankle fracture operations performed in 1915 patients from 2006 through 2009. A total of 131 patients with deep infection were identified and compared with an equal number of uninfected control patients. Risk factors for infection were determined with use of conditional logistic regression analysis.

Results: The incidence of deep infection was 6.8%. Univariate analysis showed diabetes (odds ratio [OR] = 2.2, 95% confidence interval [CI] = 1.0, 4.9), alcohol abuse (OR = 3.8, 95% CI = 1.6, 9.4), fracture-dislocation (OR = 2.0, 95% CI = 1.2, 3.5), and soft-tissue injury (a Tscherne grade of ≥1) (OR = 2.6, 95% CI = 1.3, 5.3) to be significant patient-related risk factors for infection. Surgery-related risk factors were suboptimal timing of prophylactic antibiotics (OR = 1.9, 95% CI = 1.0, 3.4), difficulties encountered during surgery, (OR = 2.1, 95% CI = 1.1, 4.0), wound complications (OR = 4.8, 95% CI = 1.6, 14.0), and fracture malreduction (OR = 3.4, 95% CI = 1.3, 9.2). Independent risk factors for infection identified by multivariable analyses were tobacco use (OR = 3.7, 95% CI = 1.6, 8.5) and a duration of surgery of more than ninety minutes (OR = 2.5, 95% CI = 1.1, 5.7). Cast application in the operating room was independently associated with a decreased infection rate (OR = 0.4, 95% CI = 0.2, 0.8).

Conclusions: We identified several modifiable risk factors for deep surgical site infection following operative treatment of ankle fractures.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Surgical site infection is one of the most common complications following ankle fracture surgery. The development of surgical site infection may lead to serious consequences such as permanent disability, amputation, or death[1]. These infections also extend the total hospital stay and may increase health-care costs by >300%[2,3]. Therefore, identification of risk factors for surgical site infection is important.

The reported rate of surgical site infection following operative treatment of ankle fractures varies considerably, ranging from 1.4% to 5.5%[1,4,5]. Infection rates as high as 19% have been reported in diabetic patients[6]. This wide range of reported rates may be partly due to the inconsistent definition of superficial and deep infection. Commonly recognized patient-related risk factors for surgical site infection are diabetes[4,6,7], open fracture[8,9], tobacco use[10], and alcohol abuse[11,12]. Known surgery-related risk factors are improper timing of antibiotic prophylaxis, suboptimal control of perioperative blood glucose levels, and use of a drain or nonocclusive wound dressings[13-16]. However, there are only limited data on surgical risk factors specifically associated with operative treatment of ankle fractures.

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TABLE I Demographic and Preoperative Characteristics of the Age and Sex-Matched Study Groups

Characteristics	No. *(%)* of Patients with Deep Surgical Site Infection (N = 131)	No. *(%)* of Uninfected Controls (N = 131)	P Value
Body mass index >30 kg/m^2	36 (27)	30 (23)	0.405
High-energy injury	17 (13)	13 (10)	0.414
Delay from fracture to admission >2 days	11 (8)	16 (12)	0.297
Fracture type			0.224
Unimalleolar	25 (19)	35 (27)	
Bimalleolar	45 (34)	46 (35)	
Trimalleolar	61 (47)	50 (38)	
Weber classification*			0.873
B	104 (79)	99 (79)	
C	27 (21)	27 (21)	
Time from admission to surgery			0.142
<12 hr	47 (36)	34 (26)	
12-48 hr	52 (40)	53 (40)	
>48 hr	32 (24)	44 (34)	
Use of a temporary external fixator	9 (7)	8 (6)	0.796

*Five isolated medial malleolar fractures in the control group.

The aim of this case-control study was to identify patient and surgery-related risk factors predisposing patients to deep surgical site infections following operative treatment of ankle fractures. Our hypothesis was that there are previously unidentified risk factors that may affect the incidence of deep surgical site infections. Identifying modifiable risk factors, and implementing appropriate interventions, could provide the means to reduce the incidence of deep surgical site infections.

Materials and Methods

Study Design

We performed an age and sex-matched case-control study at a level-I trauma center. Approval from our institutional review board was obtained prior to the beginning of the study. All patients who had undergone surgery to treat an ankle fracture at our institution from January 2006 through December 2009 were identified by querying the hospital surgical procedure database for diagnoses coded with International Classification of Diseases, Tenth Revision (ICD-10), for fibular fracture (S82.4), medial malleolar fracture (S82.5), lateral malleolar fracture (S82.6), and bimalleolar or trimalleolar fracture (S82.8) and for procedure codes for internal or external fixation of ankle fractures. Eligible surgical procedures were restricted to those performed primarily at our institution in patients eighteen years of age or older. We identified 1923 ankle fracture operations in 1915 patients who were all definitively treated with open reduction and internal fixation (ORIF). The number of treating surgeons was ninety-three. None of the patients had a simultaneous bilateral fracture. In the control group, there were two patients who had sustained a subsequent contralateral ankle fracture during the study period but only the first fracture was studied.

A standardized operative and postoperative protocol was used during the study period. ORIF was performed according to AO principles, and the decision whether to apply a tourniquet depended on the personal preference of the treating surgeon. The wound was closed in three layers (peroneal fascia, subcutaneous layer, and skin). Postoperatively, a cast was applied in all cases either immediately in the operating room or during the following postoperative days. Sutures or staples were removed at two weeks, after which the patients were allowed to begin active ankle motion exercises. Full weight-bearing was allowed at four weeks, and the cast was removed at six weeks.

Identification of Deep Surgical Site Infection

The medical and microbiological records of all 1915 patients with an ankle fracture were reviewed for recorded signs and symptoms of surgical site infection. Two hundred and sixty-seven (13.9%) of the 1915 patients had signs of surgical site infection. We classified infections as deep when all three of the following criteria were met simultaneously: clinical signs of a surgical site infection (redness, swelling, drainage, or dehiscence), positive bacterial cultures of specimens from the wound, and osteosynthesis material visible or palpable in the wound. One hundred and thirty-one (6.8%) of the 1915 patients fulfilled the aforementioned criteria to be classified as having a deep infection. For these 131 patients with a deep infection, an age and sex-matched control group was randomly selected from a cohort of patients who had been treated operatively for an ankle fracture at our institution from January 2006 to December 2009 but did not subsequently develop a surgical site infection. The characteristics of the patients included in the study are shown in Table I.

Data Collection

Potential patient and surgery-related risk factors for deep surgical site infection were identified by a review of medical, operative, microbiological, and radiological records. The charts of each patient and records from other medical specialties (e.g., internal medicine and neurology) were also assessed. We collected the demographic data and possible comorbidities of the patients, injury mechanism (low-energy injury [defined as a same-level fall] or high-energy injury [defined as a motor-vehicle accident or a fall from a height of >1 m), delay from fracture to admission, condition of the soft tissues (Tscherne grade [0 to 4] for closed fractures and Gustilo grade [I, II, or III] for open fractures), presence of a fracture-dislocation, and fracture type (Weber classification [A, B, or C] and whether the fracture was unimalleolar, bimalleolar, or trimalleolar). The delay from admission to surgery (less than twelve hours, twelve to forty-eight hours, or more than forty-eight hours), use of a temporary external fixator, duration of surgery, use of a tourniquet, surgeon experience (specialist, or resident operating without supervision of an attending surgeon), and possible difficulties encountered during the surgery (osteoporotic bone, comminuted fracture, bone loss)

TABLE II Univariate Conditional Logistic Regression Analyses for Individual Risk Factors in Age and Sex-Matched Patients with and without Deep Surgical Site Infection Following Ankle Fracture Operations

Patient-Related Characteristics	No. (%) of Patients with Deep Surgical Site Infection (N = 131)	No. (%) of Uninfected Controls (N = 131)	Odds Ratio (95% Confidence Interval)	P Value
Tobacco use	47 (36)	17 (13)	4.8 (2.2, 10.2)	<0.001
Alcohol abuse	29 (22)	12 (9)	3.8 (1.6, 9.4)	0.003
Diabetes	20 (15)	9 (7)	2.2 (1.0, 4.9)	0.047
Fracture-dislocation	71 (54)	49 (37)	2.0 (1.2, 3.5)	0.007
Tscherne grade ≥1	38 (29)	19 (15)	2.6 (1.3, 5.3)	0.006

were recorded. Additionally, suboptimal timing of antibiotic prophylaxis (administered more than sixty minutes before the incision or administered after the incision, or administered less than five minutes before inflation or administered after inflation of the tourniquet), wound closure method (staples or interrupted monofilament sutures), and application of a cast in the operating room were assessed. Postoperative noncompliance (defined as not adhering to the postoperative weight-bearing regimen) and wound complications (skin necrosis or blistering) were recorded, as were fracture malreduction (>2 mm in any projection) on postoperative radiographs. C-reactive protein values, blood leukocyte counts, and the causative pathogens were recorded at infection onset.

Data Analysis

An independent biostatistician performed the statistical analysis of the data. The differences in demographic and preoperative characteristics between the case and control groups were tested with use of the McNemar test (dichotomous variables) and the test of marginal homogeneity (polytomous variables). The McNemar test was also used to analyze differences between the groups with regard to postoperative noncompliance. The Mann-Whitney U test was used to compare the duration of surgery between residents and specialists, and the Kruskal-Wallis one-way analysis of variance on ranks was used to compare the operative time among unimalleolar, bimalleolar, and trimalleolar fractures. Conditional logistic regression analysis was used to determine significant risk factors for deep surgical site infection. Multivariable conditional logistic regression analysis with use of a forward stepwise procedure was applied to identify independent risk factors for deep surgical site infection. Sixteen risk factors (with p values of <0.20 in the univariate analysis) were selected at step zero, and three risk factors were included into the final multivariable model. In the final model, multicollinearity between the risk factors was not detected (tolerance of >0.97 for all three variables). Results of logistic regression analyses are expressed with use of odds ratios (OR) with their 95% confidence interval (CI). P values of <0.05 were considered significant.

Sources of Funding

There were no external funding sources for this study.

Results

The incidence of deep surgical site infection following ankle fracture surgery was 6.8% (131 of 1923). The mean age of the patients was fifty-six years (range, twenty to ninety years), and 56% were women. The mean time from the injury to the operative fracture reduction (ORIF or temporary external fixation) was two days in both groups. The mean operative time was eighty-eight minutes (range, seventeen to 382 minutes) for the patients with deep infection and sixty-nine minutes (range, fourteen to 240 minutes) for the controls ($p < 0.001$). A tourniquet was not used for eighteen patients (14%) with a deep infection and for twenty-two control patients (17%). Five patients (4%) with postoperative infection had multiple concomitant risk factors (diabetic smoker with compromised soft tissue), whereas none of the controls had this risk factor combination.

In the group with deep infection, the mean duration of surgery was sixty-three minutes (range, nineteen to 149 minutes) for the patients with a unimalleolar fracture and 102 minutes (range, thirty-two to 260 minutes) for those with a trimalleolar fracture ($p < 0.001$). The mean duration of surgery was eighty minutes (range, seventeen to 204 minutes) for the residents and 103 minutes (range, twenty-four to 382 minutes) for the specialists ($p = 0.139$).

The deep infection was diagnosed at an average of 127 days after the internal fixation of the fracture. At the time of infection onset, 60% of the patients presented with an elevated C-reactive protein value (>10 mg/L). Similarly, 52% of the patients had an elevated blood leukocyte count (>8.2 E^9/L). Eighty-eight (67%) of the 131 infections were monobacterial, and the three most prevalent causative pathogens in these eighty-eight infections were *Staphylococcus aureus* (n = 43), *Staphylococcus epidermidis* (n = 34) and *Pseudomonas aeruginosa* (n = 3). The remaining forty-three infections (33%) were multibacterial, and the most frequent pathogens were *Staphylococcus epidermidis* (n = 23), *Staphylococcus aureus* (n = 16), and *Enterococcus faecalis* (n = 8).

Local wound irrigation and debridement was performed, and empiric antibiotic treatment was initiated in all patients. If necessary, the antibiotic treatment was later modified according to the results of the antimicrobial sensitivity tests. Patients with a deep infection underwent an average of two additional surgical procedures (range, zero to ten). Thirty-seven patients (28%) required flap coverage, and hardware removal was performed in seventy-one patients (54%). Altogether, 103 (79%) of the 131 patients had at least one subsequent operation due to the infection. Only twenty-five patients responded to a prolonged course of antibiotic therapy and local wound care without a need for additional surgery.

Patient-related factors that were associated with a significantly increased risk of deep surgical site infection in the univariate analysis are shown in Table II. In addition to these factors, postoperative noncompliance significantly increased the risk of deep surgical site infection (thirteen patients with deep infection and no patients in the control group were noncompliant, $p < 0.001$). However, obesity (body mass index of >30 kg/m^2) ($p = 0.406$), an American Society of Anesthesiologists score of 3 or 4 ($p = 0.051$), neuropathy ($p = 0.080$), schizophrenia ($p = 0.054$), a delay from

TABLE III Univariate Conditional Logistic Regression Analyses for Surgical Risk Factors in Age and Sex-Matched Patients with and without Deep Surgical Site Infection Following Ankle Fracture Operations

Operative Characteristics	No. *(%)* of Patients with Deep Surgical Site Infection (N = 131)	No. *(%)* of Uninfected Controls (N = 131)	Odds Ratio (95% Confidence Interval)	P Value
Suboptimal timing of prophylactic antibiotic therapy*	42 (32)	27 (21)	1.9 (1.0, 3.4)	0.035
Duration of surgery >90 min	46 (35)	22 (17)	2.7 (1.5, 5.0)	0.001
Difficulties encountered during surgery†	39 (30)	23 (18)	2.1 (1.1, 4.0)	0.019
Postoperative skin necrosis or blistering	19 (15)	4 (3)	4.8 (1.6, 14.0)	0.005
Fracture malreduction on postoperative radiographs‡	19 (15)	6 (5)	3.4 (1.3, 9.2)	0.016
Application of a cast in the operating room	31 (24)	59 (45)	0.4 (0.2, 0.7)	<0.001

*Administered more than sixty minutes before the incision or administered after the incision, or administered less than five minutes before inflation or administered after inflation of the tourniquet. †Osteoporotic bone, comminuted fracture, bone loss. ‡Dislocation of >2 mm in any projection.

fracture to admission of more than two days (p = 0.301), the injury mechanism (p = 0.416), the fracture type (p = 0.631), the presence of an open fracture (p = 0.280), and a delay from admission to surgery (p = 0.157) did not increase the risk of deep surgical site infection. The univariate associations of surgery-related factors and deep surgical site infection are shown in Table III. No significant associations were found with regard to tourniquet use (p = 0.494), wound closure method (p = 0.564), surgeon experience (p = 0.273), or use of a syndesmotic screw (p = 0.436).

In the multivariable analysis, the variables that remained independently associated with an increased risk of deep surgical site infection included tobacco use (OR = 3.7; 95% CI = 1.6, 8.5) and a duration of surgery of more than ninety minutes (OR = 2.5; 95% CI = 1.1, 5.7). Application of a plaster cast in the operating room (OR = 0.4; 95% CI = 0.2, 0.8) was independently associated with a decreased risk of infection.

Discussion

The focus of the present study was to identify significant patient and surgery-related risk factors for deep infection following operative treatment of ankle fractures. The study identified several modifiable risk factors, including prolonged operative time, nonanatomic fracture reduction, and delayed cast application. To our knowledge, these factors have not previously been shown to increase the rate of deep infections in this setting. The results of the current study also suggest that special attention should be paid to certain patient groups, since smokers, alcohol abusers, and patients with diabetes are clearly at high risk for deep infection. Although the detrimental effects of chronic diseases cannot be resolved in the acute setting, several risk factors are modifiable and should be addressed in the operative treatment of ankle fractures. Our findings could serve as a basis for optimizing treatment algorithms for patients undergoing ankle fracture surgery, thereby reducing morbidity and associated health-care costs.

In our study, the rate of deep surgical site infection was 6.8%, which is slightly higher than the rates in previous reports[1,4,5]. The reported incidence of surgical site infection following ankle fracture surgery varies considerably, partially because the depth of the infection has not been clearly defined. The relatively high infection rate reported in our study may be due in part to overrepresentation of complex fractures and patients with multiple comorbidities referred from other community or smaller tertiary-care hospitals.

Although patient-related risk factors can rarely be eliminated, their effect should be minimized. In this study, diabetes was associated with an increased risk of deep surgical site infection. Uncontrolled diabetes is one of the most commonly recognized harbingers of postoperative infection[4]. As the incidence of diabetes increases[17], so does the role of perioperative blood glucose level optimization to reduce the rate of postoperative infections[18]. Smoking is another modifiable risk factor; it has been found to increase the risk of surgical site infection up to fivefold following ankle fracture surgery[10]. Our results support this finding, as tobacco use was the strongest predictor of deep infection even after adjustment for all other variables. Therefore, every smoker undergoing ankle fracture surgery should be encouraged to quit. Even a reduction in smoking should be encouraged, since this may have beneficial effects, especially in cases with compromised soft tissue[19].

A delay from admission to surgery did not increase the risk of deep infection in this current study. Previous studies have shown that, in the subgroup of patients with ankle fracture-dislocation, a delay in surgery increases the risk of postoperative infection[20,21]. Similarly, we noted that a fracture-dislocation or even a superficial skin abrasion increases infection risk. On the basis of these findings, judicious timing of surgery allowing for soft-tissue recovery may be warranted in cases without an associated ankle fracture-dislocation.

The goal of fracture surgery should be achieving and maintaining an anatomic reduction while minimizing the duration of surgical wound exposure to surrounding pathogens. In this study, we chose ninety minutes to be the threshold for prolonged surgery since this was reasonably close to the mean operative time in our cohort. On the basis of the multivariable analysis, prolonged operative time was an independent risk factor for deep infection. This was further corroborated by the finding that encountering intraoperative problems also significantly increased infection risk in the univariate model. Tourniquet use has been linked to postoperative pain[22], but it provides a bloodless operative field, facilitating reduction and helping to shorten operative time. Although tourniquet use does not increase the infection rate following plating of tibial fractures[23], it has been related to a higher incidence of postoperative wound complications after foot and ankle surgery[22]. In the present study, tourniquet use was not associated with an increased risk of infection. The optimal wound closure method is not known, but there is some evidence to indicate that subcutaneous wound closure with monofilament sutures minimizes tissue ischemia and is associated with decreased bacterial contamination[15]. We found that the use of staples did not increase the risk of infection when compared with interrupted monofilament sutures. The above findings together support the use of a tourniquet and staples as measures to reduce operative time.

A noteworthy finding of our study was the significantly lower number of infections when a cast was applied in the operating room. This is not surprising because immobilization may have a beneficial effect on soft-tissue recovery. Furthermore, cast application in the operating room may protect the surgical wound from bacterial contamination. It has been recommended that dressings remain unopened for twenty-four to forty-eight hours postoperatively to reduce the infection rate[14]. The above conclusion seems rational, but the soft-tissue condition may be a confounding factor, since patients with more severe swelling are more likely to have delayed cast application. Although we do not believe that immediate cast application itself prevents deep infection, our findings suggest that a cast should be applied in the operating room provided that soft-tissue injury is minimal.

Properly administered antibiotic prophylaxis significantly reduces the incidence of surgical site infections, and the efficacy of single-dose prophylactic antibiotic therapy has been described[15,24-26]. To have the desired effect, antibiotic prophylaxis has to be administered within sixty minutes before the incision[15]. In addition, it has to be fully administered before the tourniquet is inflated[14]. Olsen et al. demonstrated that suboptimal timing of antibiotic prophylaxis significantly increased the number of postoperative infections following spinal operations[16]. In the present study, we also noted that suboptimal timing of antibiotic prophylaxis increased the risk of deep surgical site infection following ankle fracture surgery. We observed that, even in our group without infection, antibiotic prophylaxis had been administered suboptimally in 21% of the patients. This is a cause for concern because similar results have recently been reported in another study, reflecting the possible magnitude of this problem[16]. Suboptimal timing of antibiotic prophylaxis is an important risk factor for infection, and is easily modifiable.

The retrospective study design has inherent limitations. Since deep surgical site infections are relatively uncommon, conducting a prospective study is not feasible. A retrospective age and sex-matched case-control study is an accepted design for an investigation of risk factors for postoperative infection[27]. However, an important limitation of this study design is the reliance on data provided by the medical and surgical charts. Since patient data are not always properly documented, complications may be underreported. To control for these unavoidable reporting deficiencies, the charts of each patient were scrutinized, and records from all other medical specialties were assessed as well. Another limitation is that some occult infections may not have been identified, and the proportion of deep infections preceded by a superficial infection was not recorded. However, had occult or superficial infections progressed to a deep infection, they would probably have been included in the study population. The strengths of this study include the large number of deep infections identified and treated at a single institution, and an extensive array of evaluated potential risk factors. Furthermore, we believe that the large number of treating surgeons increases the generalizability of the results. Another strength was the inclusion of only deep infections because they can be diagnosed with high specificity and have the greatest impact on clinical outcome. To our knowledge, this is the most comprehensive analysis of risk factors for deep surgical site infection specifically targeting ankle fracture surgery.

Our study revealed several modifiable risk factors predisposing patients to the development of deep surgical site infection following operative treatment of ankle fractures. In the absence of a panacea for postoperative infections, we rely primarily on preventive measures, and therefore recognition of risk factors such as diabetes, smoking, alcohol abuse, and compromised soft tissues is important. Meticulous preoperative planning and implementation of a checklist may be valuable adjuncts in reducing operative time as well as human error. Taken together, the expected impact of these measures on both patient morbidity and health-care costs could be substantial. ■

Mikko T. Ovaska, MD
Tatu J. Mäkinen, MD, PhD
Rami Madanat, MD, PhD
Eero Hirvensalo, MD, PhD
Jan Lindahl, MD
Department of Orthopaedics and Traumatology,
Helsinki University Central Hospital,
Topeliuksenkatu 5,
00260 Helsinki, Finland.
E-mail address for M.T. Ovaska: mikko.ovaska@hus.fi

Kaisa Huotari, MD, PhD
Division of Infectious Diseases,
Department of Medicine,
Helsinki University Central Hospital,
Peijas Hospital, Sairaalakatu 1,
01400 Vantaa, Finland

Tero Vahlberg, MSc
Department of Biostatistics,
University of Turku,
Lemminkäisenkatu 1,
20014 Turku, Finland

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