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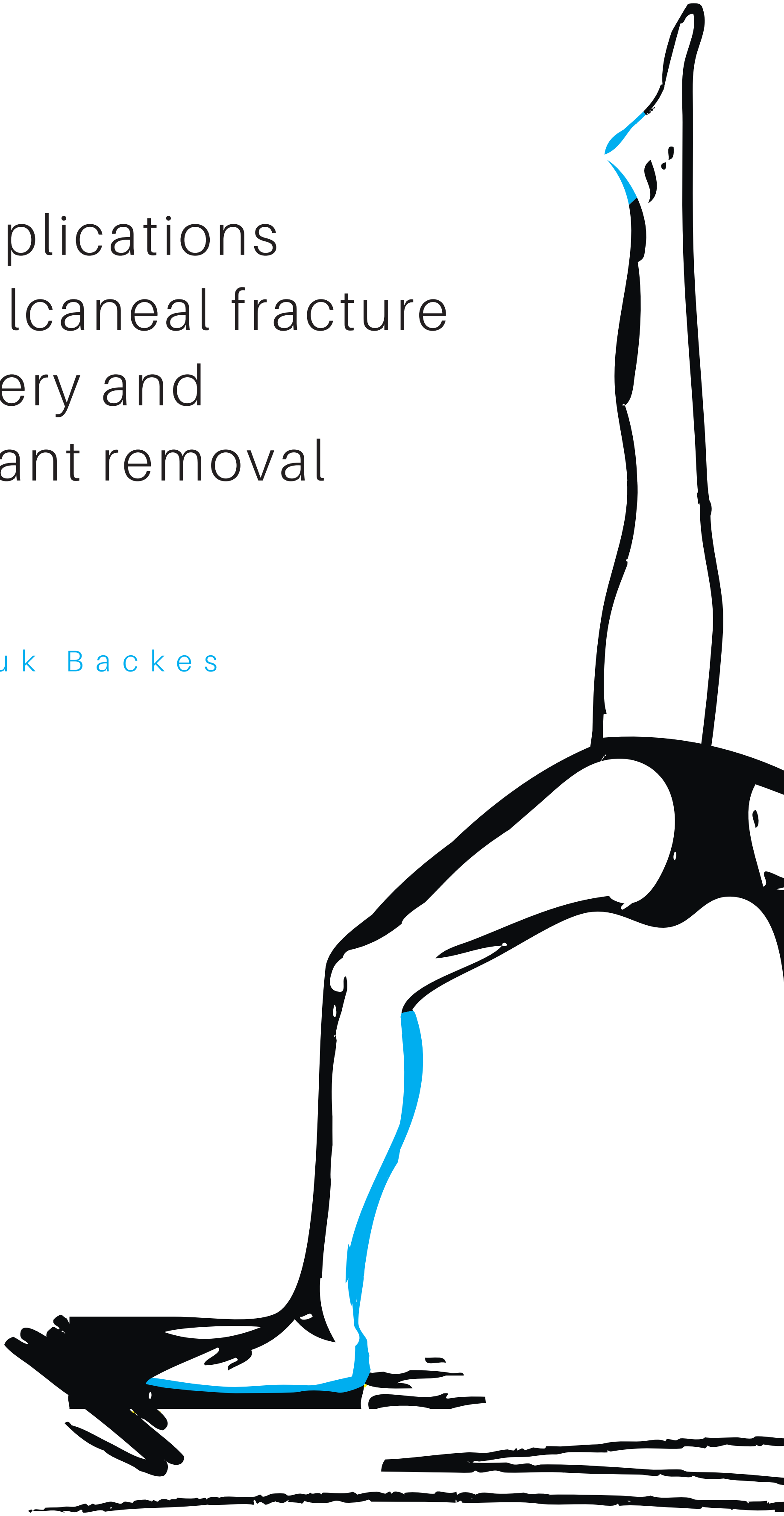

COMPLICATIONS IN CALCANEAL FRACTURE SURGERY AND IMPLANT REMOVAL

Manouk Backes

Complications in calcaneal fracture surgery and implant removal

This thesis was written at the Trauma Unit, Department of Surgery, Academic Medical Center, University of Amsterdam, The Netherlands

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COMPLICATIONS IN CALCANEAL FRACTURE SURGERY AND IMPLANT REMOVAL

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Chapter 1

GENERAL INTRODUCTION, AIM AND OUTLINE OF THIS THESIS

GENERAL INTRODUCTION

Traumatic injuries of the lower extremity have a big impact on physical and psychological function. Six months after a lower extremity fracture patients still experience impairments compared to their pre-injury status.[1] Postoperative wound complications are an integral part of any surgeon's practise and cause a major burden for the patient. Patients suffering from wound infections report substantially bigger physical limitations and a significant reduction in their health related quality of life.[2] Therefore, it is of paramount importance that patients are counselled thoroughly prior to surgical treatment. This thesis focuses on wound complications following two different areas of lower extremity trauma surgery: calcaneal fracture surgery and implant removal below the knee.

PART I CALCANEAL FRACTURE SURGERY

The calcaneus, which means heel in Latin, can be considered a lever that transfers most of the body weight from the lower limb to the ground and from the forefoot to the lower leg. An average person takes 8.000 to 10.000 steps every day, which adds up to about 185.000 kilometres in a lifetime. This is enough to walk around the earth four times, delineating the vast importance of healthy and good functioning lower extremities.

Calcaneal fractures account for less than 2% of all fractures.[3,4] They are typically seen following axial loading of the foot with a fall from a height or high impact trauma. Calcaneal fractures occur mainly in the young, active working population and have a high socioeconomic impact. Dutch trauma surgeons estimate that only 76% of their patients with a calcaneal fracture return to their work.[4] The total annual costs of calcaneal fractures in the Netherlands are estimated around 30 million euro.[4] Calcaneal fractures remain one of the most difficult fractures for trauma and orthopaedic surgeons to manage because of the complexity of the fracture patterns and a limited surrounding soft tissue envelope. Treatment may consist of conservative or operative management. Surgical treatment of displaced intra-articular calcaneal fractures correlates with a better patient-related outcome.[5,6] Patients with surgical treatment are also more likely to resume pre-injury work and report fewer problems when wearing shoes, but this comes at a cost; a higher complication rate is observed following surgical treatment.[7] Randomized studies on surgical or conservative treatment strategies for displaced calcaneal fractures compare the so-called gold standard extended lateral approach (ELA) with a nonoperative regimen.[8] The largest drawback of the ELA is the number of wound complications. In the three largest studies, the percentage of wound complications is 19% to 23%.[9–11] Wound complications following fracture surgery increase health care costs significantly: in the United Kingdom the median total direct costs of hospitalizations per infectious patient were €28.000 compared to €7.600 for patients without infection.[2] In Belgium, treatment costs of patients with a deep infection were approximately 6.5-times higher compared to patients without infection (€44.464 vs. €6.855).[12]

The aim of Part I is

- To determine the incidence, risk factors and effect on functional outcome of wound complications following surgical treatment of displaced intra-articular calcaneal fractures
- To identify the causative organisms of postoperative wound infection in calcaneal fracture surgery
- To compare the incidence of postoperative wound infection and anatomical reduction of the extended lateral approach with the sinus tarsi approach

In **Chapter 2** we determine the incidence of superficial and deep postoperative wound infection (POWI) following calcaneal fracture surgery with the ELA and identify risk factors for POWI. Because high rates of POWI are found following calcaneal fracture surgery with the ELA, a surgical approach that is popular worldwide, our aim is to perform a systematic review on wound complication rates following the ELA and evaluate and quantify geographical differences in **Chapter 3**. Since no literature is available on the causative pathogens of POWI following calcaneal fracture surgery, we determine and compare these in **Chapter 4.** We analyze treatment strategies in patients with POWI and assess the value of wound swabs and deep tissue cultures in the determination of causative pathogens of deep POWI. In **Chapter 5** we investigate the clinical relevance of POWI on functional outcome and assess health-related quality of life and patient satisfaction.

The goal of calcaneal fracture surgery is to restore the anatomy, prevent posttraumatic osteoarthritis and preserve foot and ankle function. Postoperative loss of height of the subtalar joint can occur, which is expressed by a decrease in the Böhler's angle. In **Chapter 6** we try to identify potential risk factors that are associated with a postoperative decrease in this angle.

In recent years, the sinus tarsi approach (STA) has gained interest as an approach for open reduction and internal fixation for calcaneal fractures. This less invasive approach is popular due to a lower rate of postoperative wound complications. In **Chapter 7** we investigate whether the STA allows for a similar anatomical reduction of the posterior talocalcaneal facet as the ELA. In addition, we compare our rate of postoperative wound complications of the ELA and STA.

PART II IMPLANT REMOVAL

The implants used to stabilize calcaneal and lower extremity fractures can be removed at a later stage for various reasons. Indications for implant removal are, for example; pain, functional impairment, prominent material, infection, or patients request.[13] Removal can result in pain relief, improvement in function and a high rate of patient satisfaction.[14,15] Implant removal is a frequently performed procedure and it accounts for up to 29% of all elective surgery and 6.3% of orthopaedic surgical interventions in total.[16] However, high rates of infectious complications following implant removal are reported. Remarkably, in none of these studies a POWI is a primary outcome measurement.[14,15,17–22]

In the Netherlands, a single dose of antibiotic prophylaxis is administered prior to osteosynthesis to lower the risk of development of POWI.[23] It is unclear whether administration of antibiotic prophylaxis prior to implant removal lowers the incidence of postoperative infectious complications as well. National and international guidelines on prevention of postoperative wound complications do not comment on the use of antibiotic prophylaxis prior to implant removal, as there is no evidence on the effectiveness prior to this type of surgery.

The aim of Part II is

- To investigate the incidence of implant removal following (calcaneal) fracture surgery
- To assess the incidence of postoperative wound infection following implant removal in general and in the lower leg
- To evaluate the effect of antibiotic prophylaxis prior to implant removal in the lower leg on the incidence of postoperative wound infection

Because literature on implant removal following operative calcaneal fracture treatment is scarce, the aim of **Chapter 8** is to evaluate the indications and number of wound complications following calcaneal plate removal.

In general, implants placed for fracture stabilization are often removed after fracture healing. Implant removal is considered a 'clean' procedure and low risk surgery. The aim of **Chapter 9** is to assess the incidence and risk factors of wound infection following elective implant removal in an academic and teaching hospital. In the Netherlands about 18.000 procedures with implant removal are performed annually following open or closed reduction and fixation of fractures, of which 28-70% concern the foot, ankle or lower leg region.[15,19] Currently, surgeons individually decide whether administration of antibiotic prophylaxis is indicated, since no evidence-based guideline exists. This leads to undesirable practice variation. Aim of **Chapter 10** is to outline the protocol of **Chapter 11,** in which we evaluate the effect of a single dose of antibiotic prophylaxis on the incidence of wound infection following elective implant removal below the level of the knee.

In **Chapter 12** the main findings of the studies we performed on wound complications in calcaneal fracture surgery and implant removal are summarized and discussed. Also, suggestions for future research are made.

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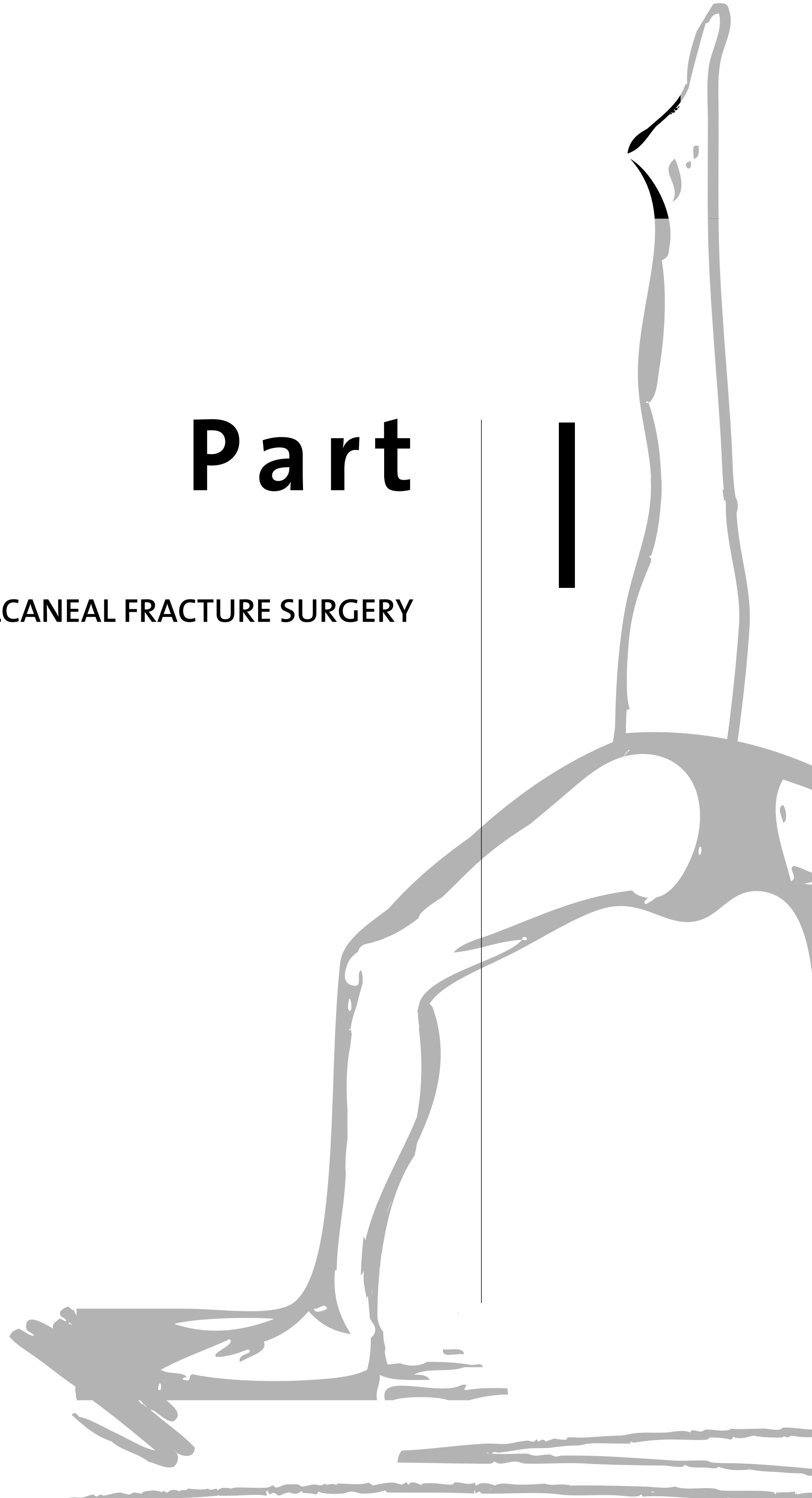
Part I

CALCANEAL FRACTURE SURGERY



Chapter 2

WOUND INFECTIONS FOLLOWING OPEN REDUCTION AND INTERNAL FIXATION OF CALCANEAL FRACTURES WITH AN EXTENDED LATERAL APPROACH

Backes M, Schepers T, Beerekamp MSH, Luitse JSK, Goslings JC, Schep NWL

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ABSTRACT

Purpose

Postoperative wound infections (POWI) following calcaneal fracture surgery can lead to prolonged hospital stay and additional treatment with antibiotics, surgical debridement or implant removal. Our aim was to determine the incidence of superficial and deep POWI and to identify risk factors (RF).

Methods

This study is a retrospective case series. All consecutive patients from 2000 to 2010 with a closed unilateral calcaneal fracture treated with open reduction and internal fixation (ORIF) via an extended lateral approach (ELA) were included. Patient, fracture, trauma and peri-operative characteristics were collected, including RF such as smoking, diabetes mellitus, time to operation, pre-operative in- or outpatient management and wound closure technique. The primary end point was a POWI as defined by the US Centers for Disease Control and Prevention.

Results

A total of 191 patients were included of which 47 patients (24.6%) had a POWI; 21 (11.0%) and 26 (13.6%) patients had a superficial and deep wound infection, respectively. American Society of Anaesthesiologists (ASA) classification higher than ASA 1 was associated with an increased risk. Placement of a closed suction drain at the end of surgery was associated with less POWI (35% vs. 15%, $p=0.002$). In this study, none of the previously reported RF were associated with an increased risk for POWI.

Conclusions

Open reduction and internal fixation of displaced calcaneal fractures is associated with a high rate of POWI of 25%. Factors that were associated with an increased risk were ASA classification other than 1 and absence of closed suction drain placement. A closed suction drain may be a protective measure to avoid wound complications.

INTRODUCTION

Calcaneal fractures account for less than 2% of all fractures.[1,2] Treatment may consist of operative or conservative management. Patients treated with open reduction and internal fixation (ORIF) are more likely to develop wound complications. However, surgery correlates with better patient-related outcome.[3,4]

Calcaneal fracture surgery is infamous for its postoperative wound infection (POWI) rate leading to prolonged hospital stay and secondary operations. The incidence of a wound infection following operative treatment of closed calcaneal fractures varies between 2% and 25% and rates of complications requiring surgery are up to 21% (Table 1).[5-19]

Some studies identified covariates associated with an increased risk of wound complications such as a higher body mass index (BMI), smoking and drug abuse.[12,15,20] In addition, the incidence of wound infections increased in patients who were managed as outpatients pre-operatively or underwent surgery more than five or 14 days following trauma.[5,20,21] However, another recent retrospective study showed no correlation with surgical timing.[22] Intra-operative risk factors were surgical experience and a single layered closure technique.[12,20,23]

In the decision to treat patients operatively or conservatively it is important to consider risk factors for wound complications. The main drawback of previous research is that many risk factors were identified in small case series. The aim of this study was to assess the incidence of POWI and associated risk factors in a large series of patients with unilateral closed displaced calcaneal fractures treated with ORIF through an extended lateral approach (ELA) in an academic Level 1 Trauma Center.

PATIENTS AND METHODS

All consecutive patients over a 12-year period (January 2000 until December 2011) with a unilateral calcaneal fracture treated with ORIF through an ELA were included in this retrospective study. Patients with open fractures and/or treatment with an external fixator prior to ORIF were excluded because of the increased risk of postoperative wound complications.[9,11,12] Patients with bilateral calcaneal fractures were excluded because of the unfeasibility of performing an independent analysis of two fractures in the same patient. Other exclusion criteria were patients who were operated with a different approach than the ELA (including patients with a primary arthrodesis through an ELA), referred patients with a pre-existing wound infection, reconstructive surgery following conservative treatment for calcaneal fracture and patients with incomplete follow-up. Polytrauma patients who underwent surgery on other extremities or body parts in the same operative session as calcaneal fracture surgery were excluded from analysis considering operation time. Minimal follow-up was one year. To prevent observer bias, the treating surgeons were not part of the review team. The Institutional Review Board approved the study.

Table 1. Rates of postoperative wound complications, wound infections and complications requiring surgery in studies including more than 100 calcaneal fractures treated with open reduction and internal fixation.

Investigator	N of Fractures (N of patients)	Postoperative wound complication in % (N)	Postoperative wound infection in % (N)	Superficial infection in % (N)	Deep infection in % (N)	Complication requiring surgery in % (N)
Folk et al 1999[5]	190 (179)[a]	25.3 (48)	NA	NA	NA	20.9 (40)
Harvey et al 2001[6]	218 (181)[a]	10.8 (23)	3.3 (7)	1.4 (3)	1.9 (4)	0.47 (1)
Naovaratanophas and Thepcharti, 2001[7]	114 (98)	NA	2.6 (3)	NA	NA	NA
Buckley et al 2002[8]	249 (206)	NA	18.9 (47)	17 (36)	5 (11)	NA
Benirschke et al 2004[9b]	341 (322)	NA	1.8 (6)	NA	NA	1.2 (4)
Zwipp et al 2004[10]	553 (496)[a]	17.9 (99)	6.5 (36)	4.3 (24)	2.2 (12)	NA
Koski et al 2005[11]	148 (126)	24 (35)	16 (23)	NA	NA	14 (20)
Court-Brown et al 2009[12]	178 (NA)	NA	25.3 (45)	19.7 (35)	5.6 (10)	NA
Demcoe et al 2009[13]	278 (246)	24.3 (67)	17.7 (49)	14.4 (40)	3.3 (9)	3.3 (9)
Kienast et al 2009[14]	136 (NA)	5.9 (8)	5.1 (7)	4.4 (6)	0.7 (1)	1.5 (2)
Gaskill et al 2010[15]	158 (146)	36.1 (57)	8.2 (13)	2.5 (4)	5.7 (9)	10.8 (16)[c]
Bergin et al 2012[16]	102 (97)	31.4 (32)	15.7 (16)	8.8 (9)	6.9 (7)	3.9 (4)
Wu et al 2012[17]	170 (148)	11.8 (20)	8.2 (14)	7.1 (12)	1.2 (2)	2.4 (4)
Ding et al 2013[18]	490 (479)	17.8 (87)	7.3 (36)	5.1 (25)	2.2 (11)	12.0 (59)
Rammelt et al 2013[19]	149 (127)[a]	22.8 (34)	NA	NA	5.4 (8)	5.4 (8)

[a] includes open fractures, [b] 106 patients (31.8%) of patients received oral antibiotics at discharge, [c] removal of implants,
N; Number, NA; not available

Clinical data

Data were obtained from the hospital's electronic and paper medical records: patient characteristics were gender, age at the time of trauma, insurance status, BMI, past medical history (psychiatric/cardiac/pulmonary/peripheral vascular disease/diabetes mellitus), known substance abuse and American Society of Anaesthesiologists (ASA) classification. Duration of postoperative hospital stay and type of management were also recorded. Following trauma, patients were either hospitalised (inpatient management) or admitted to the hospital a day prior to surgery (outpatient management).

The following trauma characteristics were documented: polytrauma patient (defined as Injury Severity Score ≥16) and trauma mechanism, classified as low- and high-energy trauma (LET and HET) and subdivided in fall from height, fall from stairs, motor vehicle accident (MVA), direct trauma or other mechanism. Fracture characteristics were: side of injury, presence of ipsilateral foot or lower extremity fractures and fracture type. All fractures were classified according to the Sanders and the Essex-Lopresti classifications by a specialised trauma surgeon and a radiologist, and radiographic analysis for Böhler's angle was performed on pre- and direct postoperative lateral images.[24,25] The increase in Böhler's angle was measured to analyse a possible association with POWI due to increased tension on the wound edges in intra-operative adjustment to a normal angle. Finally, pre-operative and intra-operative characteristics were collected such as time to surgery, the surgeon's experience, duration of surgery, tourniquet use and duration, closed suction drain placement and wound closure technique.

The primary outcome, postoperative wound infection, was classified as superficial or deep infection by applying the criteria of the US Centers for Disease Control and Prevention for defining a surgical site infection.[26] A superficial wound infection was defined as a wound with dehiscence or signs of infection (confirmed with a positive culture) amenable to conservative treatment with antibiotics. Deep wound infections were confirmed with a positive culture and defined as osteomyelitis, infected implants or a plate fistula needing implants removal, (readmission with) intravenous antibiotics or wound debridement with or without local antibiotic treatment with gentamicin beads or vacuum-assisted closure.

Surgical procedure

All patients were advised to strictly elevate the foot and ankle in between trauma (no cast) and surgery and intravenous antibiotics were administered to all patients 30 minutes prior to surgery (1500 mg cefuroxime). The patient was placed in the contralateral decubitus position of the injured leg on a radiolucent operating table. The ELA (Seattle/modified Kocher) was used in which the full-thickness flap was retracted according to the no-touch technique, with temporary K-wires in the talus to facilitate operative exposure (Figure 1).[10,24] A non-locking stainless steel AO/Synthes calcaneal plate with stainless steel 3.5-mm screws (Synthes, West Chester, PA, USA) was used. A tourniquet was not used routinely.

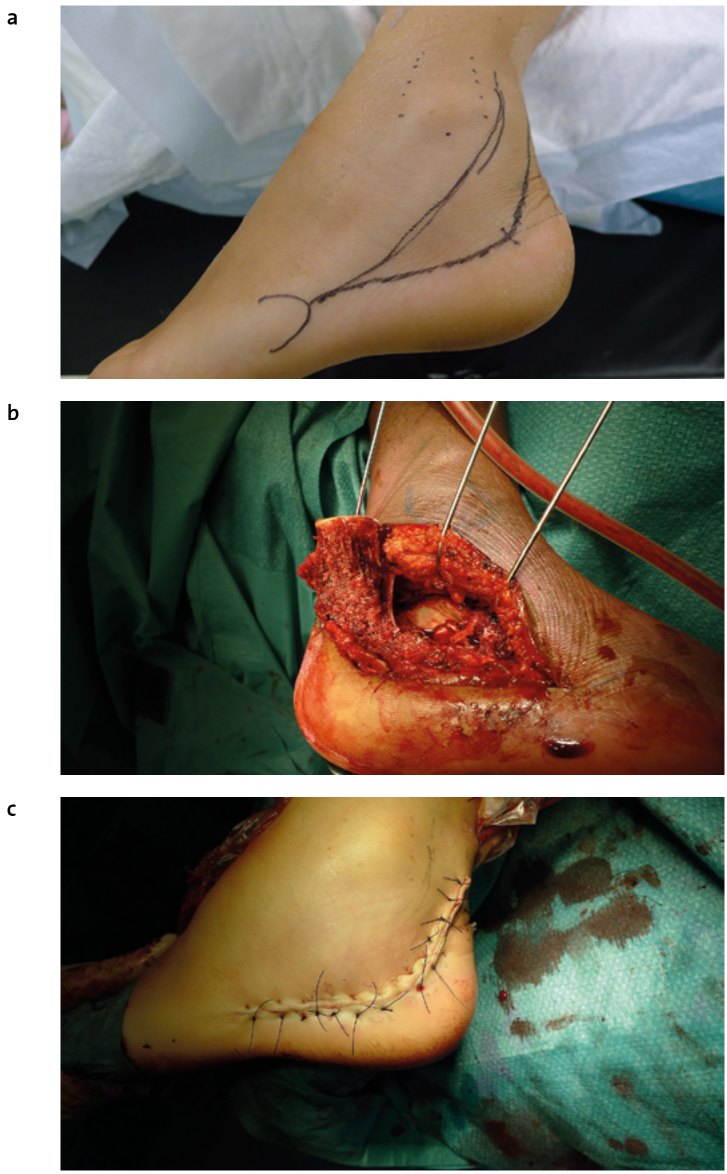

Figure 1. **a** Pre-surgical demarcation: the *inverted C line* is the base of the fifth metatarsal, the *dotted line* is the head of the fibula, the *upper line* is the wrong approach and the *lower line* is the ELA. **b** Surgical view in which the full-thickness flap is retracted according to the no-touch technique, with temporary K-wires in the talus to facilitate operative exposure. **c** Postoperative view with Donati Ethilon® sutures and a closed suction drain.

The goal of surgery was restoration of articular surfaces, calcaneal height, width and length, and correction of varus. Intra-operatively the positions of the fragments, plate and screws were evaluated by the surgeon with fluoroscopy. Wound closure was either performed with subcuticular inverted Vicryl sutures combined with Steri-Strips

(3M, St. Paul, MN, USA) and/or (Allgöwer-)Donati Ethilon sutures (Ethicon, Division of Johnson & Johnson, Somerville, NJ, USA) depending on the preference of the surgeon as well as placement of a closed suction drain (8 Fr). Postoperatively the drain was removed when production was less than 30 cc in the last 24 hours or after 48 hours. All patients were hospitalised following surgery and none were treated in day care. Postoperative antibiotics were not prescribed routinely. Patients were kept non-weight bearing for a period of 12 weeks and were instructed to perform flexion and extension exercises of the ankle.

Statistical analyses

Data were analysed using the Statistical Package for the Social Sciences (SPSS) version 19.0 (SPSS Inc., Chicago, IL, USA). Normality of continuous data was tested with the Kolmogorov-Smirnov test and by inspecting the frequency distributions (histograms). Descriptive analysis was performed to compare baseline characteristics between patients with and without an infection. For continuous data, mean SD (parametric data) or medians and interquartile ranges (non-parametric data) were calculated. Differences were assessed using Student's t test (parametric data) or the Mann-Whitney U test (non-parametric data). Categorical data were compared using the $\chi 2$ test. A p-value <0.05 was taken as the threshold of statistical significance. Firstly, a univariate analysis was performed followed by a multivariate logistic regression analysis to model the relationship between different covariates and wound infection. Covariates with a p value <0.2 and expected associated risk factors were selected for the multivariate regression analysis. This was done for the total population of patients with a wound infection and for a subgroup of patients with a deep wound infection.

RESULTS

There were 260 patients with 279 calcaneal fractures treated operatively during the 12-year study period. A total of 191 patients were included (Figure 2).

Patient characteristics are found in Table 2. Forty-seven patients (24.6%) had a POWI confirmed with a positive culture. Of these patients, 21 (11.0%) had a superficial and 26 (13.6%) had a deep wound infection. In 20 (42.6%) of the 47 patients with a POWI, the infection was treated with oral antibiotics. In one patient (2.1%) the infection resolved spontaneously with local wound care without the use of antibiotics. In 18 patients (38.3%) with a deep POWI intravenous antibiotics were administered. In general, the indication for operative debridement was a POWI without clinical improvement with intravenous antibiotics (on-going drainage, septic signs). This decision was left to the discretion of the attending surgeon. In eight patients (20%) intravenous antibiotic treatment and surgical debridement were not successful and the implant had to be removed because of an on-going infection. No amputations were performed.

In the univariate analysis, ASA classification other than 1 (p=0.001) showed an development of a POWI. Patients with a POWI were hospitalised two days longer on

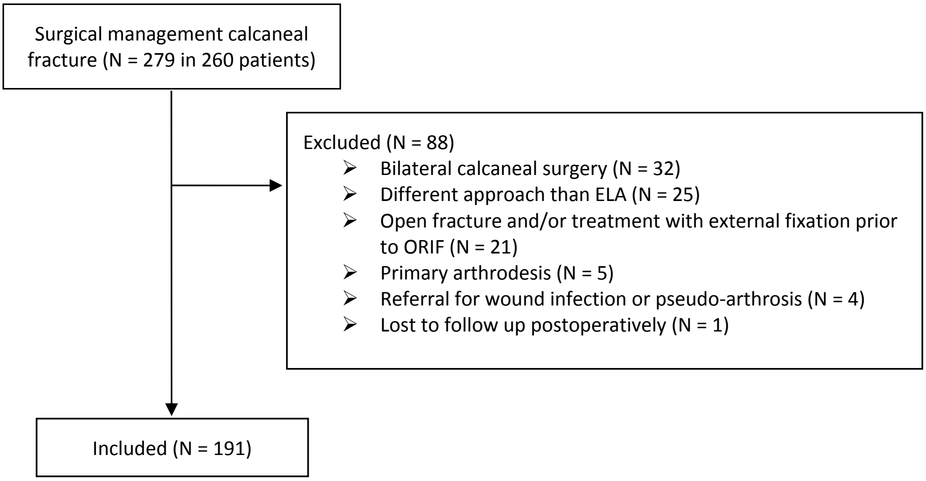

Figure 2. Flow diagram of all patients with a calcaneal fracture treated operatively and included patients between 2000 and 2010. N; Number

average compared to the group without a POWI (seven vs. five days, p<0.001). Patients with a deep POWI were hospitalised for an average of an extra four days compared to patients without a deep POWI (nine vs. five days, p<0.001). In 83.2% the operation was performed by a single senior surgeon. In 99 patients (53.6%) a closed suction drain was placed and this was associated with less POWI (35 vs. 15%, p=0.002). This association was not seen when looking at deep POWI only. In the 86 patients without drain placement there were 34.9% POWI of which 16.3% were deep infections. Finally, multivariate analysis of six possible risk factors was performed based on results in the univariate analysis of this study and previously reported risk factors from the literature. This also showed a decreased risk of POWI after placement of a closed suction drain at the end of surgery (p=0.003) (Table 3).

DISCUSSION

In this case series of 191 unilateral calcaneal fractures the postoperative wound infection rate was 25%, of which 13.6% were deep infections. Factors that were associated with an increased risk for wound infections were ASA classification other than 1 and absence of a closed suction drain placement at the end of surgery. None of the previously reported risk factors (higher BMI, drug abuse, smoking, outpatient management and surgery after more than five or 14 days) showed a relation with a POWI in our study (Table 3).[5,12,20,21] As there was no difference in POWI between pre-operative in- or outpatients we find that pre-operative outpatient management is acceptable. As could be expected, hospital stay for the index fracture was longer in patients with a POWI.

In the literature on drain placement in surgery of the musculoskeletal system no significant differences were found in incidence of POWI, dehiscence or re-operation.[27]

Table 2. Patient-, trauma-, fracture-, perioperative characteristics and incidence of deep and superficial wound infections in 191 patients with unilateral calcaneal fractures treated with open reduction and internal fixation via an extended lateral approach.

	Number of patients (%)	Deep wound infection	p-value (two-sided)	Superficial + deep wound infection	p-value (two-sided)
Patient characteristics					
Male	131/191 (68.6)	19	NS	32	NS
Age (median in years)	45 (12 - 75)	45.1	NS	46.7	NS
BMI (range)	24.0 (16.6 - 38.3)	24.4	NS	24.6	NS
No Insurance	13/191 (6.8)	1	NS	3	NS
Past Medical History					
Psychiatric	24/191 (12.6)	3	NS	6	NS
Cardiac	18/191 (9.4)	1	NS	4	NS
Pulmonary	13/191 (6.8)	3	NS	5	NS
Peripheral vascular disease	1/191 (0.5)	0	NS	0	NS
Diabetes Mellitus	12/191 (6.3)	3	NS	4	NS
ASA-classification[a]					**0.001**
I	131 (68.6)	14		24	
II	55 (28.8)	12		23	
III	5 (2.6)	0		1	
Substance Abuse					
Nicotine	85/182 (46.7)	11	NS	22	NS
Drugs	34/182 (19.8)	3	NS	10	NS
Alcohol	103/174 (59.2)	10	NS	24	NS
Hospital stay					
Pre-operative inpatient management	49/191 (25.7)	8	NS	15	NS
Postoperative time to discharge (mean in days)	4 (1-60)	8.9	**0.005**	7.1	**<0.001**
Trauma characteristics					
LET	91/173 (52.6)	11	NS	25	NS
Trauma mechanism			NS		NS
Fall from height	124/191 (65.3)				
Fall from stairs	40/191 (20.9)				
MVA	8/191 (4.2)				
Direct trauma	5/191 (2.6)				
Unknown/other	14/191 (7.3)				
Polytrauma, ISS ≥ 16	13/191 (6.8)	1	NS	2	NS

Table 2. (continued)

	Number of patients (%)	Deep wound infection	p-value (two-sided)	Superficial + deep wound infection	p-value (two-sided)
Fracture characteristics					
Right	101/191 (52.9)	14	NS	29	NS
Concomitant foot or cruris fracture	21/191 (11.0)	5	NS	8	NS
Essex-Lopresti classification	181		NS		NS
Joint depression type	99/181 (54.7)	13		28	
Tongue type	76/181 (42.0)	13		19	
Combined type	3/181 (1.7)	0		0	
Sanders classification	183		NS		NS
I	17/183 (9.3)	0		4	
II	121/183 (66.1)	19		30	
III	39/183 (21.3)	11		11	
IV	2/183 (1.1)	2		2	
Peri-operative characteristics					
Time to surgery (days)	14 (1-37)	14.5	NS	14.5	NS
Surgery within 1 week	20/191 (10.5)	5	NS	5	NS
Surgery within 2 weeks	98/191 (51.3)	13	NS	24	NS
Surgery within 3 weeks	170/191 (89.0)	22	NS	41	NS
Surgery time (minutes)	115 (68-231)	123	NS	115	NS
Single senior surgeon	159/191 (83.2)	19	NS	38	NS
Use of tourniquet during surgery	10/186 (5.4)	2	NS	4	NS
Duration of use (minutes)	123 (90-180)	NA	NA	180	NS
Use of closed suction drain	99/185 (53.6)	10	NS	15	**0.002**
Incision closure technique	182		NS		NS
Single layered	130/182 (71.4)	16		32	
Double layered	52/182 (28.6)	8		13	
Böhler's angle					
Mean pre-operative angle in degree (range)	7.4 (-43.0–39.4)	NS	NS	NS	NS
Mean increase in angle in degree (range)	23.5 (-9.3-75.6)	NS	NS	NS	NS

[a] $\chi 2$ difference between ASA I and II+III
N; number, NS; not significant, NA; not available, ORIF; open reduction and internal fixation, ELA; extended lateral approach, BMI; body mass index, PVD; peripheral vascular disease, DM; Diabetes Mellitus, ASA; American Society of Anesthesiologists, LET; low energy trauma, MVA; motor vehicle accident, ISS; Injury Severity Score

Table 3. Multivariate regression analysis of possible risk factors for postoperative wound infections in patients with a unilateral calcaneal fracture surgery with open reduction and internal fixation via an extended lateral approach.

Risk factor	p-value	Odds ratio	Confidence Interval
ASA classification	0.015	0.377	(0.172-0.828)
BMI[a]	0.138	1.070	(0.978-1.171)
Concomitant foot or cruris fracture	0.650	0.756	(0.225-2.534)
In-or outpatient management[a]	0.630	0.801	(0.325-1.974)
Closed suction drain placement	0.003	0.294	(0.133-0.651)

[a] previously appointed risk factor in literature
BMI; body mass index, ASA; American Society of Anesthesiologists

Unfortunately no specific data on calcaneal fracture surgery were available in this study. Closed suction drain placement has previously not been shown to reduce wound healing complications.[20] However, in our study placement of a closed suction drain during surgery resulted in a significant decrease of POWI. As 83% of surgeries were performed by a single senior surgeon who decided on drain placement in 85 patients (54%) vs. no drain placement in 69 (43%) with missing data in five patients we cannot exclude selection bias. Because of the retrospective character of the study we do not have information about haemostasis before wound closure. Surprisingly, the effect of a closed suction drain on POWI was only found for the total population of patients with wound infections. In the subgroup of patients with deep infections this effect could not be detected. We suspect this is due to the small number of patients in this group (N=26).

Our study shows a considerable percentage of POWI. As previously noted, infection rates in the literature vary between 2% and 25% (Table 1).[5-19] The policy at our facility is to treat the vast majority of patients with dislocated intra-articular calcaneus fracture operatively, irrespective of any unfavourable factors for wound healing, which could contribute to the high rate of infections. This considerable rate of POWI is more likely the result of our type of surgical approach. As we recently started performing calcaneal surgery more often via an even more extended lateral approach according to Freeman et al. and (in less complex fractures) via the sinus tarsi approach, the severe wound complication rates appear to have decreased.[28-30] In the latter type of approach a wound complication rate of 29% in the ELA versus 6% in the less invasive sinus tarsi approach was described.[31]

In summary, we present a large series of consecutive patients with a closed displaced calcaneal fracture treated with ORIF. A postoperative wound complication rate of 25% was detected and ASA classification other than 1 and no closed suction drain placement at the end of surgery were identified as risk factors for POWI. We therefore conclude that a closed suction drain may be a protective measure to avoid wound complications.

Future studies are required to further investigate the long-term clinical outcome in patients with a postoperative wound infection.

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Chapter 3

EVALUATION AND QUANTIFICATION OF GEOGRAPHICAL DIFFERENCES IN WOUND COMPLICATION RATES FOLLOWING THE EXTENDED LATERAL APPROACH IN DISPLACED INTRA-ARTICULAR CALCANEAL FRACTURES – A SYSTEMATIC REVIEW OF THE LITERATURE

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ABSTRACT

Aims

Calcaneal fracture surgery is often performed via the extended lateral approach (ELA). Large differences are reported in literature on wound complication rates. As the ELA is an approach that is used frequently worldwide our aim was to perform a systematic review on reported wound complication and infection rates following the ELA and evaluate and quantify geographical differences.

Methods

A literature search was conducted in the MEDLINE and EMBASE databases and Cochrane Library for articles in which calcaneal fracture surgery was performed with the ELA. Studies in which both the ELA and wound complication rates were described were included. Studies before Jan 2000, studies with <10 patients, biomechanical studies and reviews were excluded. No restrictions regarding language were applied.

Results

A total of 3068 articles were identified, of which 1867 remained to be reviewed for title and abstract, resulting in 217 articles. After reading the full text, 123 articles were included. In these studies 10942 calcaneal fractures were described, of which 8584 were treated with the ELA in 28 different countries spread over 5 continents. Most studies came from China (N=42). The average total number of postoperative wound complications and infections was respectively 14,3% and 6,3%, with an average of 3,8% of superficial and 2.2% of deep infections. The highest rate of postoperative wound infection (POWI) was found in Europe (12,1%) and the lowest in North America (2,8%). A significant difference in the incidence of POWI between continents was detected, varying between a median of 0% versus 3.8% of deep POWI. A total of 29 studies were prospective studies and 88 retrospective, but no differences were found in incidence of postoperative wound complications and infections (respectively $p=0.970$ and $p=0.748$). Also, no statistically significant difference was found in postoperative wound complications and infections between studies with <10 or ≥10 calcaneal fracture surgeries via the ELA per year (respectively $p=0.326$ and $p=0.378$). However, lower rates of POWI were found in studies with a follow up of >3 months ($p=0.01$).

Conclusions

We found large differences in incidence of postoperative wound complications and infections following calcaneal fracture surgery with the extended lateral approach between countries and continents. We did not find a lower wound complication or infection rate in retrospective studies compared to prospective studies, larger studies or in studies in which more patients were treated annually. However, the rate of POWI was significantly lower in studies with a follow up of >3 months. We advise the use of a reliable postoperative complication registration system and uniformity in the use of standardized definitions of wound complications for calcaneal fracture surgery.

INTRODUCTION

Patients with a displaced intra-articular calcaneal fracture (DIACF) are often treated surgically.[1–5] Goals of surgery are restoration of articular surfaces, calcaneal height, width and length and correction of axis. Since the 1990s, the extended lateral approach (ELA) has been considered the standard approach for performing open reduction and internal fixation (ORIF) of DIACF's.[6] In the ELA, a full-thickness sub-periostial flap is retracted, with the use of no touch technique, to facilitate operative exposure.[6–9]

The ELA is associated with high postoperative wound complication rates and several reasons have been identified as a cause. The vascular distribution of the lateral foot is known to be dependent upon the lateral calcaneal branch of the peroneal artery, which can be compromised by the ELA. Lower wound complication rates are found when the lateral calcaneal branch of the peroneal artery is patent.[10] Patient characteristics that are associated with the occurrence of a postoperative wound infection (POWI) are a higher body mass index (BMI), smoking, diabetes and drug abuse.[11–13] Surgical characteristics associated with POWI are outpatient management, surgery after more than five days or two weeks following trauma, surgical experience, a single layer closure technique and no placement of a closed suction drain.[11,13–18]

We noticed large differences in the literature of the incidence of postoperative wound complications operative treatment with the ELA in patients with a calcaneal fracture. As the ELA is an approach that is still used frequently worldwide, our aim in this study was to perform a systematic review of the literature on wound complication rates following the ELA for DIACF's and evaluate and quantify geographical differences.

METHODS

This systematic review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A computerized literature search was conducted on the 17th of April 2017 in the databases of MEDLINE (Pubmed), EMBASE (Ovid) and the Cochrane Library (Figure 1).[19] Search terms were: Calcaneus, Calcaneal, Fractures, Bone, Fracture*, Surgical Procedures, Operative, Surgical, Operat*. There was no language restriction and only papers after Jan 1st 2000 were included. An article in a foreign language in which none of the authors was proficient was translated. All titles and abstracts were reviewed by three independent readers (MB, TS, KS) using Covidence.[20] Based on the title and abstract, a list of full text articles was created. Full texts were assessed using the following inclusion criteria: (I) publication after Jan 1st 2000 (II) inclusion of adults (III) inclusion of >10 patients with ELA and (IV) data available on wound complications following the ELA. Publications that were excluded were (V) biomechanical studies (VI) reviews and (VII) studies with the same patient cohort as an already included full text (VIII) and no availability of full text (IX). In case of a disagreement, the full text was discussed and consensus was reached after discussion.

The number of calcaneal fractures surgically approached with the ELA and number of wound complications following the ELA were extracted from each study that was included for the quantitative synthesis. In studies in which wound complications were subdivided in minor and major, these numbers were used for analysis. In studies in which postoperative wound infection (POWI) (deep and superficial), wound dehiscence and wound necrosis were described, these numbers were used. In studies in which both were mentioned, both were used for analysis. Superficial POWI, wound dehiscence and wound edge necrosis without the need for surgical intervention were considered minor wound complications. Wound edge necrosis or dehiscence requiring surgical intervention or intravenous antibiotics, osteomyelitis and a deep POWI were considered a major wound complication. Conflicts were discussed until an agreement was reached. Additional data that were collected were the duration of the inclusion period and the minimal follow up in months.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 24.0 (SPSS, Chicago, Illinois, USA). Data are shown as percentages with the median and interquartile ranges or means and standard deviations as appropriate. The Kruskal-Wallis test was used to test for differences in reported complication rates between continents and countries and a Mann-Whitney U-test for differences between retrospective and prospective studies. A p-value <0.05 was taken as the threshold of statistical significance.

RESULTS

The search produced a total of 3068 articles, of which 1201 were duplicates and were removed (Figure 1). A total of 1867 articles remained to be reviewed for title and abstract, after which 1650 articles were eliminated. Of the remaining 217 articles, another 92 were excluded after reading the full text. Twenty-one articles were excluded because the surgical approach was not described or another approach than the ELA was used (4 papers had included <10 patients, in 23 articles on calcaneal fracture surgery with the ELA postoperative wound complications were not described, 4 articles had a difficult to understand study design, 3 articles had an incorrect patient population, 7 articles had the patient cohort already included in another article that was included, 8 articles did not have the full text available, 12 articles were not original research (e.g. congress abstract, review) and 12 articles turned out to be double papers (e.g. English and Chinese version of same paper). A total of 123 articles were included in this systematic review (Figure 1). In these papers, 10942 calcaneal fractures were included of which 8584 were treated with the ELA in 28 different countries spread over 5 continents (Table 1). Most studies came from China (N=42) and from only one study was found in 13 countries (Table 2). A total of 29 studies were prospective studies, 88 were retrospective and in 6 studies, the type of study was not described.

We found 66 publications from Asia, 44 from Europe, 10 from North America, 2 from Africa, 1 from South America and none from Oceania (Table 1). The average number of postoperative wound complications and wound infections was respectively 14,3% and 6,3%. Rates of superficial and deep POWI were respectively 3,8% and 2,2%. The highest

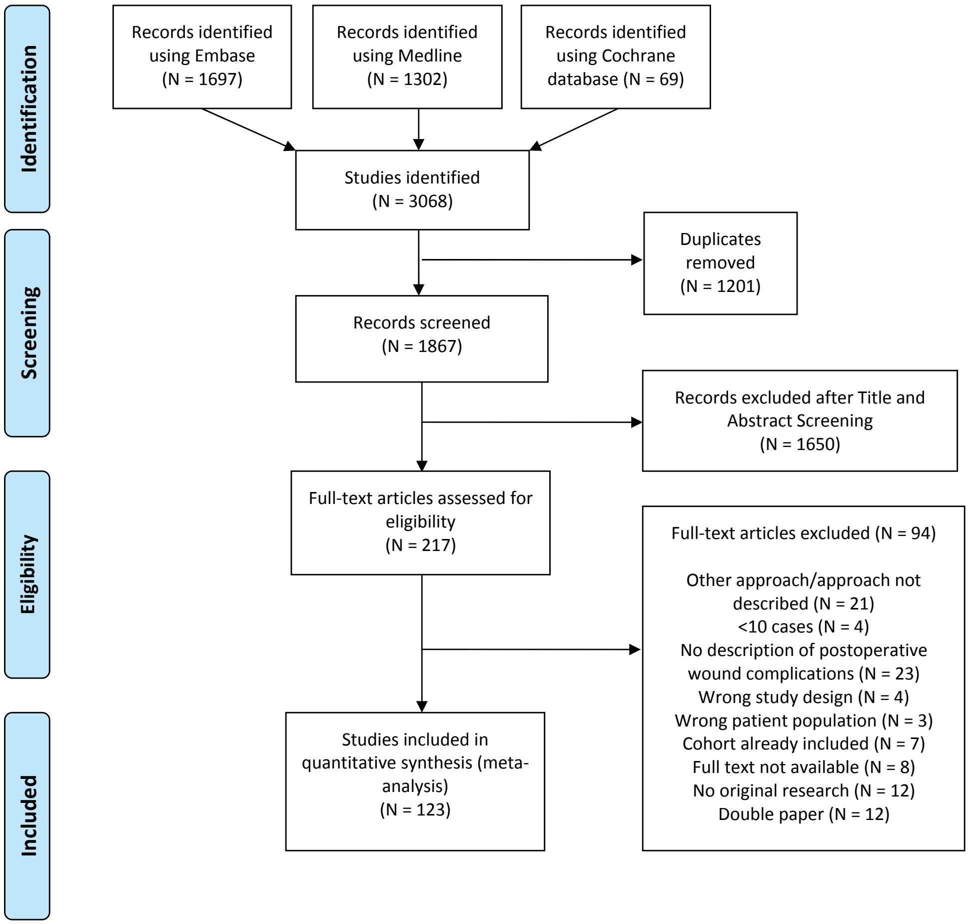

Figure 1. Flowchart of the literature search according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 guidelines.

rate of POWI was found in Europe (12,1%), followed by Africa (11,1%), Asia (4,5%), South America (4,4%), and North-America (2,8%) (Table 1). The lowest reports on POWI are from Iran, Italy and Malaysia (0%) and Croatia and USA (1,9%) (Table 2). The highest rates are reported in Morocco (33%) and Nepal (21,4%) (Table 2). A significant difference in the incidence of POWI between continents was found, varying between a median of 0% versus 3.8% of deep POWI (Table 1).

The incidence of postoperative wound complications per continent and country are presented in Figure 2 and 3. Most studies report on <100 cases and a wide variety in incidence of postoperative wound complications and infections is presented (Figure 4 and 5).

Table 1. Postoperative wound complication and infection rates per continent.

Continent	Asia	Europe	North America	South America	Africa	p-value
Studies (N)	66	44	10	1	2	
Calcaneal fractures (N)	5353	4254	1228	60	47	
Surgery with ELA (N)	4300	3201	1013	23	47	
Patients (ELA) per study (N)^	65	73	101	23	24	
Total wound complications (%)±	13,5 (5,4-20,2)	16,7 (10,6-21,0)	9,6 (6,8-31,9)	8,7	19,5	0,452*
Total POWI (%)±	4,5 (0-8,4)	12,1 (3,8-16,3)	2,8 (2,1-11,6)	4,4	11,1	0,019*
Total superficial POWI (%)±	0,0 (0-7,1)	7,9 (2,6-13,7)	1,2 (0,0-5,7)	NR	2,9	0,007*
Total deep POWI (%)±	0,0 (0-5,1)	3,8 (0-6,1)	2,4 (1,4-7,0)	NR	9,8	0,034*

*Kruskal-Wallis test
± Data are in median and IQR
^ Data are in mean
N; number, ELA; extended lateral approach, NR; not reported, POWI; postoperative wound infection

The median follow up of patients was 12 months (IQR 6-18). The rate of POWI was significantly lower in studies with a follow up of more than three months (p=0.01). A median of 1,1 patient was treated per month (IQR 0,68-1,82) per study. No statistically significant differences were found in postoperative wound complications and infections between studies with <10 or ≥10 calcaneal fracture surgeries with the ELA per year (respectively p=0.326 and p=0.378). Also, no difference was found between prospective and retrospective studies in incidence of postoperative wound complications and infections (respectively p=0.970 and p=0.748).

DISCUSSION

This is the largest review of the literature on calcaneal fracture surgery with the ELA. We have found a significant difference in reports on wound complication and wound infection rates between countries and continents (Figure 2 and 3).

There could be several explanations for geographical differences in the incidence of postoperative wound complications. Large differences are found in POWI rates between continents; 4,5% in Asia and 12,1% in Europe (Figure 2). Possibly orthopaedic and trauma surgeons really have less postoperative wound complications in Asia. This could be a result of their expertise or timing in this type of surgery, as incorrect timing can result in wound necrosis and POWI.[13,21–23] In China, for example, a very low percentage of wound complications is reported, while the amount of publications coming from China is the highest (N=42). The number of patients in published articles from China is substantially higher than numbers from other countries. However, we did not find a lower wound complication or infection rate in larger studies (Figure 4 and 5) or in

Table 2. Postoperative wound complication and infection rates per country.

Country	Studies (N)	Surgery with ELA (N)	Calcaneal fractures (N)	Total wound complications (%) ±	Total POWI (%) ±	Total superficial POWI (%) ±	Total deep POWI (%) ±
Brasil	1	23	60	8,7 (NA)	4,4 (NA)	NR	NR
Canada	3	341	563	18,9 (NA)	18,9 (NA)	14,5 (NA)	4,1 (NA)
China	42	3103	3952	11,3 (4,9-15,8)	3,6 (0-6,9)	0,0 (0,0-5,6)	0,0 (0-3,8)
Croatia	1	103	103	5,8 (NA)	1,9 (NA)	1,9 (NA)	0 (NA)
Czech Republic	4	301	494	20,8 (18,9-21,0)	7,9 (4,5-10,1)	7,4 (NA)	2,3 (0,2-10,1)
Finland	1	148	148	23,7 (NA)	15,5 (NA)	10,1 (NA)	5,4 (NA)
France	3	327	346	24,1 (NA)	3,2 (NA)	3,2 (NA)	0 (NA)
Germany	8	690	795	11,4 (7,6-18,2)	10,0 (1,7-12,1)	3,0 (0,2-6,4)	4,9 (1,7-12,1)
India	7	562	599	13,1 (3,3-30,4)	3,0 (0,0-9,2)	0,0 (0,0-2,2)	2,1 (0,0-8,4)
Iran	1	14	61	0 (NA)	0 (NA)	0 (NA)	0 (NA)
Ireland	4	133	210	20,2 (15,9-29,4)	20,2 (15,9-29,4)	14,4 (12,5-17,1)	5,3 (1,1-15,1)
Israel	1	24	24	20,8 (NA)	8,3 (NA)	8,3 (NA)	0 (NA)
Italy	4	82	183	13,1 (8,8-39,3)	0,0 (0,0-11,8)	0 (NA)	0,0 (0,0-11,8)
Kuwait	1	55	94	16,4 (NA)	5,5 (NA)	0 (NA)	5,5 (NA)
Malaysia	1	12	27	0 (NA)	0 (NA)	0 (NA)	0 (NA)
Morocco	1	12	12	33,3	16,7	NR	16,7
Nepal	1	14	14	21,4 (NA)	21,4 (NA)	14,3 (NA)	7,1 (NA)
Netherlands	4	352	472	20,5 (13,6-36,4)	14,3 (11,3-22,5)	7,8 (5,3-10,8)	6,6 (5,6-12,0)
Poland	2	58	158	15,1 (NA)	13,7 (NA)	11,5 (NA)	2,1 (NA)
Romania	1	29	66	20,7 (NA)	13,8 (NA)	13,8 (NA)	0 (NA)
South Korea	1	60	100	13,3 (NA)	NR	NR	NR
Switzerland	3	148	149	14,5 (NA)	14,5 (NA)	13,7 (NA)	4 (NA)
Taiwan	3	124	133	9,4 (NA)	5,1 (NA)	0 (NA)	1,9 (NA)
Thailand	1	114	114	14 (NA)	14 (NA)	11,4 (NA)	2,6 (NA)

Table 2. (continued)

Country	Studies (N)	Surgery with ELA (N)	Calcaneal fractures (N)	Total wound complications (%) ±	Total POWI (%) ±	Total superficial POWI (%) ±	Total deep POWI (%) ±
Tunisia	1	35	35	5,7 (NA)	5,7 (NA)	2,9 (NA)	2,9 (NA)
Turkey	7	218	235	22,2 (16,3-27,8)	16,3 (14,8-21,1)	14,0 (7,7-14,8)	6,6 (0,0-7,7)
United Kingdom	6	489	567	12,6 (3,9-20,7)	12,6 (3,6-20,7)	4,8 (2,1-15,6)	4,3 (0,0-9,6)
United States of America	10	1013	1228	9,6 (6,8-31,9)	2,8 (2,1-11,6)	1,2 (0,0-5,7)	2,4 (1,4-7,0)
p-value				0,218*	0,004*	<0.001*	0,138*

*Kruskal-Wallis test

± Data are in median and IQR

N; number, ELA; extended lateral approach, NR; not reported, NA; not applicable, POWI; postoperative wound infection

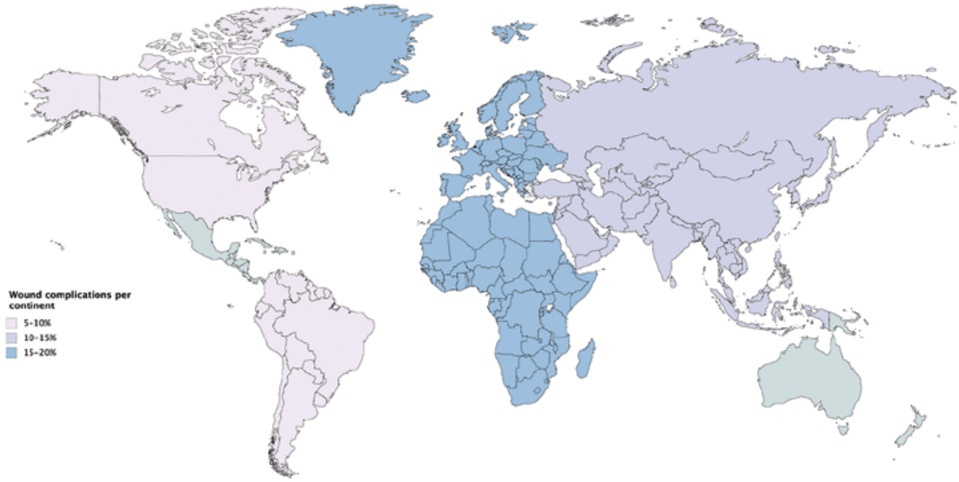

Figure 2. Incidence of postoperative wound complications per continent. NA; not available

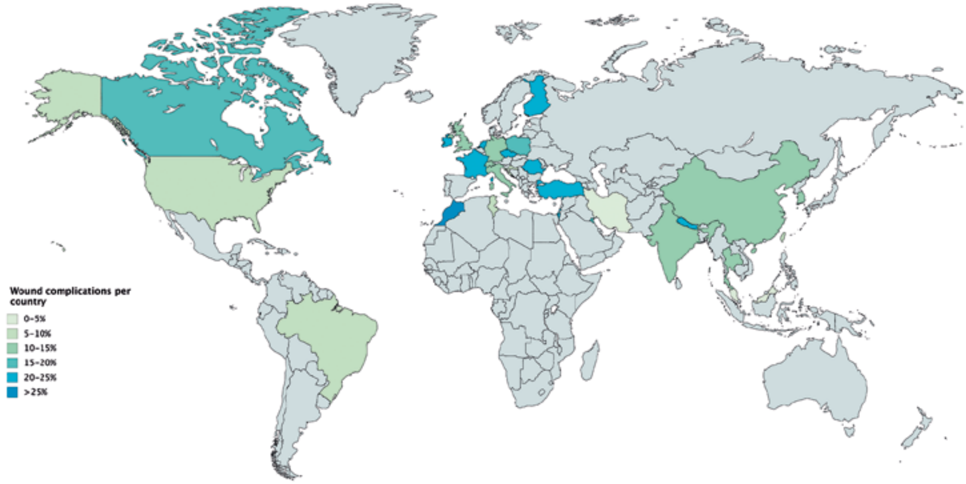

Figure 3. Incidence of postoperative wound complications per country. NA; not available

studies in which more patients were treated per year. This is in contrast with a review of the literature by Poeze et al., in which 21 studies were included with 1656 patients and a significant relationship between the deep infection rate and the fracture load was found.[24]

The variation in incidence of postoperative wound complications could be the result of differences in the definition of a postoperative wound complication and a POWI between surgeons and countries, which results in a reporting bias.[25,26] For example, one surgeon might classify a complication as a wound dehiscence while another might

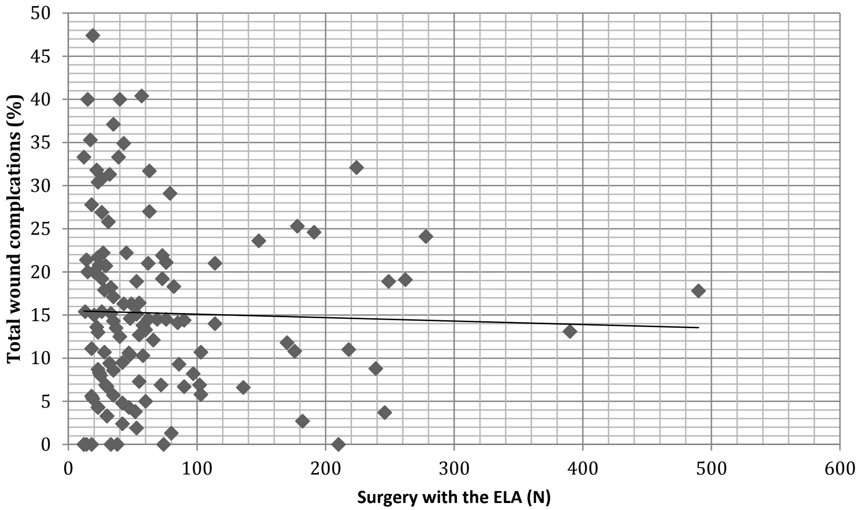

Figure 4. Number of calcaneal fractures treated with the ELA per study versus the incidence of postoperative wound complications.

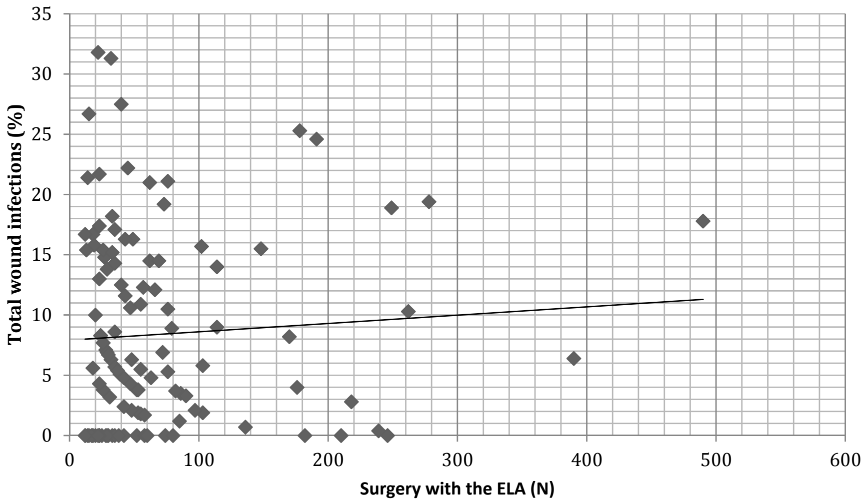

Figure 5. Number of calcaneal fractures treated with the ELA per study versus the incidence of postoperative wound infections.

classify the same wound as a superficial POWI. We advise the use of criteria of the Centers for Disease Control and Prevention for reports on POWI to prevent reporting bias.[27–29]

Another explanation for the observed geographical differences could be caused by a selection bias: e.g. variance in in- and exclusion criteria. For example, publications with exclusion of high-risk patients (e.g. drug abusers or heavy smokers) are more likely to report lower complication rates. Also, the difference could be result of difficulties in detection of a POWI in studies (retrospective) with a longer follow up. This is reflected by a significant difference in POWI rates between studies with a follow up of <3 or ≥3 months.

Finally, the variability in incidence of postoperative wound complication rates could be a result of underreporting. This may be because surgeons are unaware of an occurrence, choose to underreport a POWI or it could be result of an inadequate complication registration system.[30,31] There is a growing focus on quality and safety in healthcare. Complication outcomes are increasingly used as an indicator to compare hospital performance and to rank hospitals.[32] In addition, as there is a general trend towards reducing hospital stay, adequately detecting a POWI post-discharge is a major challenge.[33] This might especially be the case in specialized centers in which high numbers of referred patients are treated and where the follow-up is performed at a local hospital. Unfortunately, we don’t have data to support this hypothesis. However, a POWI rate of 0% in studies with a large cohort of patients remains highly unlikely. The above highlights the need for an adequate surgical complication registration system with an adequate follow up after patient discharge.

We performed the largest systematic review on calcaneal fracture surgery with the ELA with a thorough literature search. A limitation of this study is that the number of patients that were lost to follow up was not reported in most studies. Also, we were unable to correct for selection bias, so studies with inclusion of less severe injuries or exclusion of less fit patients might be included.

In conclusion, we found large differences in incidence of postoperative wound complications and infections following calcaneal fracture surgery with the extended lateral approach between countries and continents. We did not find a lower wound complication or infection rate in retrospective studies compared to prospective studies, larger studies or in studies in which more patients were treated annually. However, the rate of POWI was significantly lower in studies with a follow up of >3 months. We advise to use of a reliable postoperative complication registration system and use of a standardized definition of wound complications for calcaneal fracture surgery. We suggest the criteria set by the Centers for Disease Control and Prevention.[27,28]

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Chapter 4

DETERMINATION OF PATHOGENS IN POSTOPERATIVE WOUND INFECTIONS IN SURGICALLY REDUCED CALCANEAL FRACTURES AND IMPLICATIONS FOR PROPHYLAXIS AND TREATMENT

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ABSTRACT

High rates of postoperative wound infection have been reported following operative treatment of calcaneal fractures. Aim of this retrospective cohort study was to determine the causative pathogens of these infections and subsequent treatment strategies. In addition, microbacterial growth from superficial wound swabs and deep fluid or tissue cultures were compared.

Patients with a unilateral surgically treated calcaneal fracture in a 15-year period were included. Patient-, fracture- and surgical characteristics were collected from the electronic medical charts. An infection was categorized into deep or superficial according to the CDC criteria. Secondary outcomes were wound edge necrosis and wound dehiscence. Type of collection of culture swabs, their results and treatment strategies were documented.

Ninety-two of 357 (26%) patients developed a postoperative infection; 55 (60%) deep and 37 (40%) superficial. Most frequent causative pathogens were Enterobacteriaceae and *Staphylococcus aureus*. Thirty-three of 55 (60%) patients with deep infection were treated with intravenous antibiotics (IV) and surgical debridement, 2 (4%) with IV antibiotics only and 22 (40%) with implant removal. In 33 of 92 (36%) patients with a POWI both superficial and deep cultures were obtained, in which a microorganism was not cultured from the superficial swab 13 (39%) times.

In conclusion, we found that a quarter of patients with operative calcaneal fracture treatment are diagnosed with a postoperative wound infection, which are mainly caused by Enterobacteriaceae or *Staphylococcus aureus*. Physicians cannot rely on results of superficially obtained cultures for adequate treatment of deep infection. As the spectrum of sensitivity profiles varies greatly between hospitals and countries, we recommend to aim empiric antibiotic treatment to both gram-positive and gram-negative microorganisms upon suspicion of deep infection.

INTRODUCTION

Patients with a displaced intra-articular calcaneal fracture are often treated surgically to restore anatomy and preserve foot function.[1–3] High rates of postoperative wound infection (POWI) from 7 to 25% have been reported following calcaneal fracture surgery.[4–11] However, to our knowledge, only limited data is available on the causative pathogens of wound infection following calcaneal fracture surgery.[6,12] In these studies *Staphylococcus aureus* was the microorganism isolated most often.[12]

Upon suspicion of POWI the attending physician can decide to start empirical antibiotic treatment in anticipation of results of bacterial specification from a (tissue) culture. The antibiotic regimen can be changed after bacterial specification, which sometimes takes several days to a week. As a result, patients are not always treated adequately initially. Remarkably, we only found one study on determination of pathogens and antibiotic resistance in deep infections after operative fixation of fractures.[13]

Our aim was to determine the type of causative pathogens of POWI following calcaneal fracture surgery and subsequent treatment strategies. We hypothesize most infections are caused by a *Staphylococcus aureus*. In addition, microbacterial growth from superficial wound swabs and deep fluid or tissue cultures are compared.

PATIENTS AND METHODS

This is a case series of consecutive patients in a Level-1 Trauma Center between January 2000 and June 2014 (N=357). Inclusion criteria were adult patients with surgical treatment of a displaced intra-articular calcaneal fracture with open reduction internal fixation (ORIF) by the extended lateral approach (ELA) or the sinus tarsi approach (STA), percutaneous fixation or external fixation. Exclusion criteria were bilateral calcaneal fracture surgery, patients referred with a wound infection and patients with reconstructive surgery following initial non-operative treatment for a calcaneal fracture. Minimal follow up was six months.

The Institutional Reviewing Board approved the study and waived the need for informed consent.

Clinical Data

Data were obtained from the hospital's electronic medical records. A search was performed from Jan 2000 until June 2014 using surgical code 338732 (Current Procedural Terminology, American Medical Association, Chicago, IL). In addition, a hand search was performed with the key word calcaneus. Collected were; patient characteristics (i.e. gender, age at the time of surgery and type of fracture (open or closed), surgical characteristics (i.e. type of approach in the primary procedure subdivided in extended lateral approach, sinus tarsi approach, minimally invasive or percutaneous approach and external fixation prior to ORIF.

Outcome

The occurrence of POWI, their causative pathogen(s) and subsequent treatment strategies were distinguished. Data on wound edge necrosis and wound dehiscence were also collected.

Postoperative wound infection was classified according to the criteria of the US Centers for Disease Control and Prevention and further subdivided into deep and superficial.[14,15] Superficial wound infections were wounds with signs of infection amendable for conservative treatment with antibiotics. Deep wound infections were confirmed with a positive culture and defined as osteomyelitis, infected hardware or a plate-fistula in need for implant removal, (readmission with) intravenous antibiotics or wound debridement with or without local antibiotic treatment with gentamicin beads or vacuum assisted closure. The medical files and database of the Department of Microbiology was available for data collection of cultures.

Different treatment strategies were distinguished from the medical charts: for superficial POWI; oral antibiotics or local non-antibiotic wound care and for deep POWI; intravenous (IV) antibiotics, surgical debridement with IV antibiotics or implant removal with debridement and IV antibiotics.

Culture swabs

In case of suspicion of superficial POWI bacterial specimens were obtained by wound swabs (by cotton tipped swabs in Amies transport medium (Medical Wire & Equipment, Corsham, England)) and in case of suspicion of deep POWI tissue or (purulent) fluid samples were collected during surgical debridement or implant removal because of ongoing infection (in sterile containers). Specimens were sent to the laboratory for aerobic and anaerobic culture. The wound swabs were cultured on several agar plates (Biomerieux, Marcy l'Etoile, France), incubated during four days and pathogens (such as *Staphylococcus Aureus*, Streptococci, Pseudomonas, yeasts) were identified by mass spectrometry (Malditof; Bruker, Karlsruhe, Germany). Flora considered as commensals were also described (for example skin flora or coliform rods). Tissue and fluid samples were cultured on several agar plates and in a thioglycolate broth, incubated during seven days and all bacterial growth was identified and reported. Gram stain was carried out for all tissue and fluid cultures, and for wound swabs only when a slide was sampled.

If bacterial growth was observed in wound and intraoperative collected samples, only the result of the intraoperative tissue culture was used for determination of the causative organism.

Surgical procedure

Single dose IV antibiotic prophylaxis was administered to all patients preoperatively (1500 mg cefuroxime or 1000mg cefazolin). Patients with an open fracture received (extended) IV antibiotic prophylaxis for a maximum of three days (cefazolin for Gustillo grade 1 and 2 and cefazolin and gentamicin for grade 3) upon hospital admission. Wound closure was either performed with subcuticular vicryl sutures combined with Steri-Strips (3M, St. Paul, MN) and/or Allgöwer-Donati ethilon sutures (Ethicon, Division of Johnson & Johnson, Somerville, NJ) with placement of a closed suction drain (8Fr) depending on the preference of the surgeon. This drain was removed postoperatively when production was less than 30cc in the last 24 hours, or after a maximum of 48 hours. All patients were hospitalized following primary surgery. Patients were discharged when pain was under control and remained non-weight bearing for a period of 8-12 weeks postoperatively.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 22.0 (SPSS, Chicago, Illinois, USA). Normality of continuous data was tested with the Kolmogorov-Smirnov test and by inspecting the frequency distributions (histograms). Descriptive analysis was performed to compare baseline characteristics between patients with and without POWI. Categorical variables are presented as counts and proportions, continuous variables as means and standard deviations or medians and interquartile ranges as appropriate. A $\chi 2$-test was used to test for differences in categorical variables and an independent t-test or Mann-Whitney-U test for differences in continuous variables where appropriate. Univariate analysis was performed to compare gender, age, fracture type and type of approach for patients with and without POWI and patients with and without deep POWI. Statistical significance was defined at the 5% ($p \leq 0.05$) level.

RESULTS

A total of 357 patients were included. Baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics of patients with surgical calcaneal fracture treatment

Baseline characteristics	N (%)	N (%) of POWI	p-value (2 sided)	N (%) of deep POWI	p-value (2 sided)
Patient					
Male gender	245/357 (68.6)	60/245 (24.5)	NS	40/55 (16.3)	NS
Age (median)	12-77 (44)	14-75 (46)	NS	14-69 (44)	NS
Fracture*			< 0.001		< 0.001
Open	21/357 (5.9)	14/21 (66.7)		10/21 (47.6)	
Closed	335/357 (93.8)	78/335 (23.3)		45/335 (13.4)	
Treatment**			0.006		NS
ELA/STA/percutaneous	343/357 (96.1)	84/343 (24.5)		46/343 (13.4)	
External fixation	12/357 (3.4)	8/12 (66.7)		7/12 (58.3)	

*1 missing data **2 missing data
NA: not applicable, NS: not significant, ELA: extended lateral approach, STA: sinus tarsi approach

Of these 357 patients, 92 (25.8%) patients had a POWI of which 55 (60%) were deep and 37 (40%) were superficial infections (Figure 1). Fourteen of 21 (67%) patients with an open calcaneal fracture had a POWI, of which 71% were deep and 29% superficial, compared to 78 of 336 (23%) patients with a closed fracture, of which 58% were deep and 42% superficial ($p \leq 0.05$) (Table 1). A total of 21 (6%) patients had wound edge necrosis or wound dehiscence without signs of infection.

The top 3 most frequently cultured microorganisms in patients with a POWI were Enterobacteriaceae, *Staphylococcus aureus* and Streptococci. In patients with a deep POWI this was respectively 56%, 33% and 7% and in patients with a superficial POWI respectively 38%, 51% and 3% (Figure 2). In 36 (41%) cultures growth of >1 microorganism was found. The same types of pathogens were found in deep POWI following surgery of open and closed calcaneal fractures.

Treatment strategies in patients diagnosed with POWI are presented in Figure 1. In 31 (56%) patients with a deep POWI surgical debridement was performed (mean 4 times, range 1-11) in combination with IV antibiotics and in 22 (40%) patients implant removal with debridement and IV antibiotics was deemed necessary following failed prior treatment. Two (4%) patients with deep infection, both with an open calcaneal fracture, were successfully treated with antibiotics without surgery (Figure 1). Seventeen (31%) patients with a deep POWI were initially unsuccessfully treated as a superficial POWI with oral antibiotics. Five of 55 (9%) patients with a deep POWI no growth was observed after obtaining a culture swab. All these five patients had received IV antibiotics at the time of tissue sample collection. The median duration between start of infection and a disease free status was 90 days (IQR 50 - 314). No partial or total calcanectomies or below the knee amputations were necessary. Debridement with collection of deep

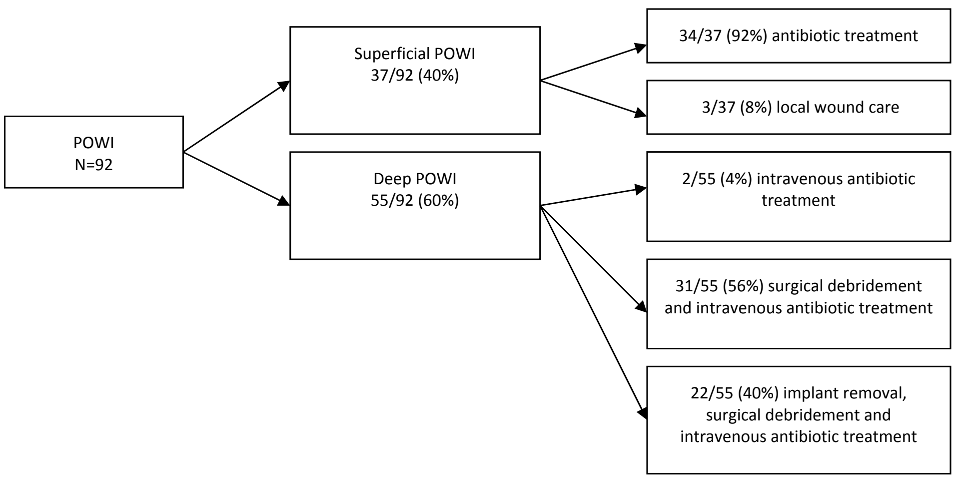

Figure 1. Flow chart of patients with a postoperative wound infection and subsequent treatment. POWI; postoperative wound infection, N; number

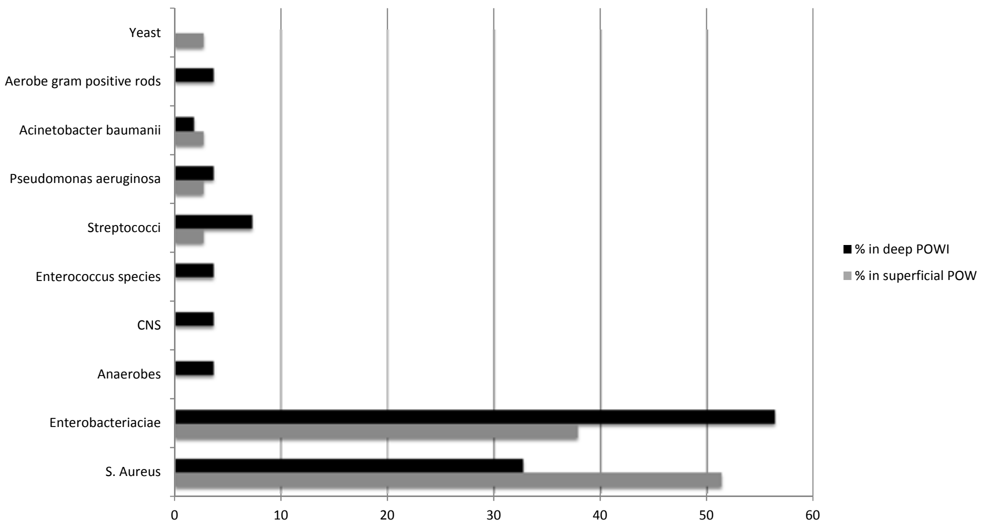

Figure 2. Type of microorganisms (Y-axis) in percentages (X-axis) in patients with deep and superficial postoperative wound infection. CNS; coagulase negative staphylococci, S. Aureus; *Staphyloccus aureus*

tissue samples because of a clinical suspicion upon a deep POWI was performed mainly in the early postoperative period, within 30 days (median 28 days, IQR 13 - 123).

In 87 of 92 (95%) patients with a POWI cultures were collected (Table 2). A deep tissue culture during debridement or implant removal was collected in 52 of 92 (57%) patients with POWI. Sixty-two percent of cultured microorganisms in deep POWI were aerobic gram-negative rods and 47% of the cultured microorganisms in deep POWI were not sensitive to cefazolin (antibiotic prophylaxis). In 33 of 92 (36%) patients both a deep and a superficial culture swab was obtained. In these 33 patients a microorganism grew from a deep culture that did not grow in the superficial culture 13 (39%) times (*Staphylococcus aureus* (N=6), Enterobacteriaceae (N=2), Streptococci (N=2), nonfermenting gram-negative rods (N=2) and multiple anaerobic microorganisms (N=1), skin flora was not included). Another different microorganism was cultured in the superficial swab 16 (48%) times compared to the deep swab obtained preoperatively.

DISCUSSION

We found a wound infection rate of 25.8% following operative treatment of calcaneal fractures, which are most commonly caused by Enterobacteriaceae, *Staphylococcus aureus* and Streptococci (Figure 2). *Staphylococcus aureus* commonly colonize the skin of feet[16] and the skin in about one third of patients and is a well-known causative pathogen in POWI.[17,18] To our knowledge there are no studies available on determination on causative pathogens of POWI following operative treatment of calcaneal fractures,

Table 2. Superficial and deep cultures in patients with superficial and deep POWI.

	N (%) of patients without POWI	N (%) of patients with superficial POWI	N (%) of patients with deep POWI
No culture collected	254/265 (96)	4/37 (10.8)	1/55 (1.8)
Superficial culture	11/254 (4.3)	30/37 (81)	38/55 (69.1)
Deep culture	0 (0)	4/37 (10.8)	48/55 (87.3)
Both	0 (0)	1/37 (2.7)	32/55 (58.2)

POWI; postoperative wound infection, N; number

but some studies specify pathogens of calcaneal osteomyelitis. Overall, these studies reported *Staphylococcus aureus* as a main culprit.[19-21] In a study on infection following all types of orthopaedic open fractures the most frequently identified microorganisms were Enterobacter species and Pseudomonas (31%) followed by Enterococcus species in 27% of cases.[22] We also found a high rate of POWI caused by Enterobacter species or other Enterobacteriaceae in open fractures (54%).

The antibiotic prophylaxis and empirical treatment upon suspicion of postoperative wound infection in calcaneal fracture surgery should cover for the most common pathogens of POWI. In our center the standard antibiotic prophylaxis is cefazolin and empirical treatment for a POWI is amoxicillin and clavulanate potassium or flucloxacillin, which is not adequate for the treatment of Enterobacteriaceae. The current study resulted in a change of empiric treatment regimen in our hospital for POWI following calcaneal fracture surgery to IV flucloxacillin in combination with gentamicin. Also, the antibiotics given as extended prophylaxis in open fractures was changed to cover for Enterobacter species and Pseudomonas species as potential pathogens in grade 3 open fractures. Follow-up of the incidence of infection in open calcaneal fractures will reveal whether this is related to the specific antibiotics that were given in the past. As almost half of the cultured microorganisms in deep POWI were not sensitive to cefazolin the question remains whether the preoperative prophylaxis for operative treatment of closed calcaneal fractures should be extended in the gram-negative spectrum as well. Further research needs to be performed to investigate this.

In nearly all patients with a deep POWI surgical debridement was performed (96%), partly in combination with implant removal (40%) (Figure 1). Thirty one percent of patients with a deep POWI were diagnosed and treated as a superficial POWI prior to adequate treatment for a deep infection. Apparently, it is a challenge to differentiate between superficial and deep infection and better diagnostic tools should be developed. We recommend surgeons to intervene (more) aggressively upon the slightest suspicion on a deep POWI and obtain tissue cultures during surgical debridement.

Finally, we tried to value superficial wound swabs for bacterial cultures in comparison to cultures of intraoperative tissue samples in the determination of causative pathogens of deep POWI. In the 33 patients in whom both superficial and deep cultures were collected a microorganism was not cultured in the superficial wound swab 13 times (39%). Therefore, physicians cannot rely on results of a superficially obtained culture for treatment of deep POWI.

A limitation of the current study is that we found incomplete registration or lack of differentiation between purulent fluid or regular wound swab collection. This missing information is a drawback inherent to the retrospective character of the study. We realize that our use of a CPT code to identify potential eligible patients may have been subject to coding biases. However, the risk is small, as we performed a manual search for calcaneal fracture surgery as well.

In conclusion, a quarter of the surgically treated calcaneal fractures was complicated by POWI that was mainly caused by Enterobacteriaceae and/or *Staphylococcus aureus*. The spectrum of sensitivity profile for pathogenic organisms varies greatly between hospitals and countries, but we recommend aiming empiric antibiotic treatment to both gram-positive and gram-negative microorganisms upon suspicion of deep POWI. In addition we recommend collection of deep tissue samples and analysis of your local sensitivity profile for pathogenic organisms, as we show that you cannot rely on the results of a superficially obtained culture for adequate antibiotic treatment of deep POWI.

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Chapter 5

THE EFFECT OF POSTOPERATIVE WOUND INFECTIONS ON FUNCTIONAL OUTCOME FOLLOWING INTRA-ARTICULAR CALCANEAL FRACTURES

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ABSTRACT

Introduction

High rates of postoperative wound infection (POWI) are reported following operative treatment of calcaneal fractures. This leads to additional therapy, prolonged hospital stay, burden for patients and increased costs. The primary aim of this study is to evaluate the effect of POWI following surgery via the extended lateral approach of displaced intra-articular calcaneal fractures on functional outcome. Secondary aims are assessment of health-related quality of life and patient satisfaction.

Patients and methods

All consecutive adult patients with a calcaneal fracture treated between 2000 and 2011 with open reduction and internal fixation through an extended lateral approach were retrospectively included and sent a questionnaire. Functional outcome was measured using the Foot Function Index (FFI, best score 0 points) and the American Orthopaedic Foot and Ankle Society (AOFAS, best score 100 points) hindfoot score. The EuroQOL-5D was used for quality of life (QOL) and a Visual Analogue Scale (VAS, best score 10 points) for overall patient satisfaction.

Results

Of 135 eligible patients, 94 returned the questionnaire (response rate 70 %). The median FFI was 12 points (IQR 3–33) and AOFAS 79 points (IQR 61–90). The FFI and AOFAS were, respectively, 17 and 9 points higher in favour of patients without POWI (N = 69) compared to patients with POWI (N = 25). Albeit large differences, they were not statistically significant given the current number of patients. Patients without POWI scored better on all health-related aspects of QOL in the EQ-5D, but this did not reach statistical significance. However, the VAS on overall patient satisfaction did show a statistically significant difference of 1.3 points (9.0 vs. 7.7; $p = 0.01$) in favour of patients without POWI. Importantly, a clinically relevant difference was found with the FFI, as the estimated minimal clinical important difference of the FFI is 10 points.

Conclusion

Our results implicate that postoperative wound infection leads to lower functional outcome scores following calcaneal fracture surgery, but no statistical significance was reached. In addition, patients do not report significant worse QOL or physical impairment. Overall patient satisfaction measured by a VAS was significantly lower in case of a POWI, reflecting the burden caused by a wound complication.

INTRODUCTION

In the last two decades, several studies showed improved outcome following operative treatment in patients with displaced intra-articular calcaneal fractures compared with non-operative treatment.[1-5] Moreover, initial operative management has proven better long-term functional results in case a secondary arthrodesis is required.[6]

However, open reduction and internal fixation (ORIF) of the calcaneus through an extended lateral approach (ELA) is infamous for its high rate of postoperative wound infection (POWI) and various risk factors have been identified.[7-11] Wound complications can be divided into minor complications (superficial infection, dehiscence, wound edge necrosis) and major complications (deep infection, osteomyelitis, plate fistula).[12] Rates of minor and major complications reported in literature are, respectively, 0–21.4% and 0–14.3%.[7,9]

Costs in patients with a displaced intra-articular calcaneal fracture and a postoperative complication (including wound, implant and neurologic complications, thromboembolism and compartment syndrome) are approximately $2000 higher compared to patients without a complication. In addition, costs in patients requiring a secondary fusion can be up to $74.000 higher.[13]

Besides additional medical costs and lengthened hospital stay, a postoperative wound complication leads to an increased burden for the patient.[14] One previous study on wound complications specifically did not find a negative relation between wound complications and outcome; however, this study was hampered by a relatively small number of patients and mainly superficial wound complications.[14] Therefore, little information is available on the effect of POWI on long-term functional outcome.

The primary aim of the current study was to evaluate the effect of POWI following calcaneal fracture surgery on functional outcome. The secondary aims were measuring the effect of POWI on health-related quality of life and overall patient satisfaction.

PATIENTS AND METHODS

We conducted a retrospective cohort study. All consecutive adult patients over an eleven-year period (January 1st, 2000 to December 31st, 2010) with ORIF of a closed displaced intra-articular calcaneal fracture through an ELA were assessed for eligibility. Exclusion criteria were patients with a primary arthrodesis, a different surgical approach and inability to fill in a questionnaire (unknown address, not attending outpatient department visits, death or imprisonment).

Clinical data

Patient characteristics obtained from the electronic hospital's medical charts were gender, age at trauma and past medical history such as diabetes and nicotine abuse. Trauma characteristics included injured side and trauma mechanism, further subdivided into fall from height or stairs, motor vehicle accident or other. All fractures were classified according to the Essex-Lopresti and Sanders classifications. Initial Böhler's angle was measured by a trauma surgeon specialized in foot and ankle trauma.[15,16]

All patients were seen within 30 days postoperatively by an attending physician. Postoperative wound infections were subdivided in superficial or deep infections by applying the criteria of the US Center for Disease Control and Prevention.[12] A superficial POWI was defined as a wound with signs of infection (confirmed by a positive culture) amendable for conservative treatment with antibiotics. A deep wound infection was confirmed with a positive culture, osteomyelitis, infected hardware or a plate fistula in need for implant removal, (readmission with) intravenous antibiotics or wound debridement with or without local antibiotic treatment with gentamicin beads or vacuum assisted closure. Finally, secondary intervention such as implant removal, secondary arthrodesis and number of additional surgical procedures following the initial procedure were registered.

Primary outcome was functional outcome as measured by two area specific outcome scores. Functional outcome was measured using the Foot Function Index (FFI, best score 0 points)[18], and the American Orthopaedic Foot and Ankle Society hindfoot score (AOFAS, best score 100 points).[19] The AOFAS score was divided into groups according to the literature: a score of 90–100 was graded as an excellent result; 75–89 as good; 50–74 as fair, and less than 49 points was graded as a failure or poor outcome. Both outcome measurements are frequently used in foot and ankle research.[17] Range of motion and alignment was documented for all patients at their final visit to the outpatient clinic in follow-up and these data were obtained from the outpatient medical charts. From the literature, it is known that little additional improvement in the AOFAS score can be expected after 1.5 years of follow-up.[18]

Secondary outcome was quality of life (QOL), which was measured by the EuroQol-5D (EQ-5D).[23] This included assessment of perceived general health on a Visual Analogue Scale (VAS) of zero to 100, in which 100 represented excellent general health (EQ-VAS). In addition, a ten-point VAS, with zero implying maximum dissatisfaction and ten full satisfaction, was used to measure patient satisfaction with overall outcome.[21]

In addition, questions were asked on ability to work and type of employment; classified as either heavy physical labour or light physical labour. Finally, patients were asked to report on time to return to work and occupational adjustments as a result of their calcaneal fracture.

Surgical procedure

Open reduction and internal fixation was achieved via an extended lateral approach[9,15,24] with a stainless steel 3.5-mm non-locking AO calcaneal plate and screws. A 'no touch' technique was applied with K-wires in the talus and cuboid and a tourniquet was rarely used. The goal of surgery was restoration of articular surfaces, calcaneal height, width, length, and correction of varus. Postoperatively a standard pressure bandage was applied. Patients were kept non-weight bearing for a period of 12 weeks and instructed for active range of motion exercises.

Statistical analyses

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS, Chicago, Illinois, USA). Normality of continuous data was tested with the Kolmogorov–Smirnov test and by inspecting the frequency distributions. Descriptive analysis was performed to compare baseline characteristics between patients with and without POWI. For continuous data, the mean and standard deviation (SD) (parametric data) or medians and interquartile ranges (non-parametric) data were calculated. Differences were assessed using the Student's T test (parametric data) or the Mann–Whitney U-test (non-parametric data). Categorical data were compared using the $\chi 2$ test. Finally, the relation between functional outcome and type of fracture, timing of intervention and age was assessed. Also, the relation between POWI and functional outcome/QOL was assessed and corrected for the confounders fracture type and secondary interventions by means of multivariate logistic regression. A p value of <0.05 was taken as the threshold of statistical significance. All p values are two tailed.

RESULTS

Demographics

During the 11-year study period, a total of 182 patients with 195 fractures were treated surgically with ORIF through an ELA. A total of 135 of these patients were included in the study and sent a questionnaire. Patients were excluded because of an unknown address (N = 19), not attending the outpatient department (N=17), primary arthrodesis (N=5), death (N=4) or imprisonment (N=2). A total of 94 patients returned the questionnaire, resulting in a 70% response rate with a median follow-up of almost 6 years (71 months). Of these, 25 patients suffered from a POWI, of which 12 patients had a deep POWI.

Patient characteristics and secondary interventions of both the responding patients and non-responding patients are displayed in Table 1. Patients not responding were more frequently male, smokers and younger of age ($p<0.05$). In univariate analysis, no association was found between the occurrence of POWI and male gender (p=0.344), younger age (p=0.854) or nicotine abuse (p=0.826). The median follow-up was 33 months following ORIF.

Functional outcome and quality of life

Primary and secondary outcomes are presented in the first row of Table 2. Patients with superficial or deep POWI showed a difference in FFI (26-9=17 points) and AOFAS (81-72=9 points) compared to patients without POWI. However, these differences were not statistically significant given the current number of patients. According to

Table 1. Patient, trauma, fracture, surgical characteristics and secondary intervention of respondents and non-respondents following intra-articular calcaneal fracture surgery

	Patients with response (N=94)	Patients without response (N=41)	p-value
Patient characteristics			
Male (%)	57 (61)	32 (78)	<0.05
Median age in years at time of trauma (range)	48 (14-75)	44 (12-68)	<0.05
Diabetes mellitus (%)	8 (8)	3 (7)	NS
Nicotine abuse (%)	33 (35)	24 (59)	<0.05
Median follow up in months (range)	71 (26-157)	NA	NA
Trauma characteristics			
Unilateral (%)	81 (86)	41 (100)	<0.05
Trauma mechanism (%)			NS
Fall from height or stairs	81 (86)	38 (93)	
MVA	6 (6)	1 (2)	
Other	7 (7)	2 5)	
Fracture characteristics			
Concomitant foot/ankle injury (%)	15 (16)	2 (5)	NS
Essex-Lopresti classification (%)			<0.05
Joint depression type	37 (39)	27 (66)	
Tongue type	49 (52)	9 (22)	
Combined type	1 (1)	1 (2)	
Unknown	6 (6)	4 (10)	
Sanders classification (%)			NS
I + II	64 (68)	30 (73)	
III + IV	23 (24)	8 (20)	
Unknown	7 (7)	3 (7)	
Median pre-operative Böhler's angle in degree (range)	6.8 (-7.5-15.2)	8.2 (-.2-8.2)	NS
Surgical characteristics			
Wound complications (%)	29	9	NS
Minor			NS
Wound dehiscence	4 (4)	2 (5)	
Superficial POWI with oral antibiotics	13 (16)	2 (5)	
Major			NS
Deep POWI with iv antibiotics/surgical debridement	5 (5)	5 (12)	
Deep POWI with implant removal	7 (7)	-	
Secondary intervention			
Implant removal (%)	50 (53)	15 (37)	NS
Secondary arthrodesis (%)	9 (10)	2 (5)	NS
Median number of surgeries including implant removal (range)	2 (1-9)	1 (1-5)	NS

POWI; postoperative wound infection, NA; not available, NS; not significant MVA; motor vehicle accident the AOFAS score, a good to excellent result was reached in 54% of patients (62% in group without POWI and 32% in group with POWI). A POWI occurred significantly less often in the group with good or excellent outcome and more often in the group with poor or fair outcome (p=0.017).

On the other hand, the VAS on overall patient satisfaction did show a significant difference of 1.3 points (9.0 vs. 7.7; p=0.01) in favour of patients without POWI (Table 2). When looking at the QOL measurements and the percentage of patients reporting a problem, patients without (deep) POWI scored better on all health-related aspects of QOL in the EQ-5D (Figure 1). However, this did not reach statistical significance.

Median time to return to work following calcaneal fracture treatment was 4 months (IQR 2–9). Return to work was 6.5 months (IQR 3.5–9.5) in patients with heavy

Table 2. Functional outcome and quality of life measurements in patients with or without a postoperative wound infection following intra-articular calcaneal fracture surgery.

Patients (N)	FFI (SD)	AOFAS (SD)	EQ-5D index (SD)	EQ-VAS (SD)	VAS (SD)
All (94)	12 (20)	79 (21)	0.83 (0.11)	80 (15)	8.7 (2.1)
No POWI (69)	9 (20)	81 (22)	0.86 (0.11)	78 (13)	9.0 (1.6)
POWI (25)	26 (19)	72 (17)	0.81 (0.12)	80 (19)	7.7 (2.9)*
Deep POWI (12)	23 (21)	72 (17)	0.82 (0.13)	78 (25)	7.6 (3.5)**

*p=0.01 comparing patients with a POWI to patients without a POWI
**p=0.03 comparing patients with a deep POWI to patients without a POWI
SD; Standard Deviation, N; Number, POWI; postoperative wound infection, FFI Foot Function Index, AOFAS; American Orthopaedic Foot and Ankle Society, EQ-5D; EuroQol-5D, VAS; Visual Analog Scale on patient satisfaction

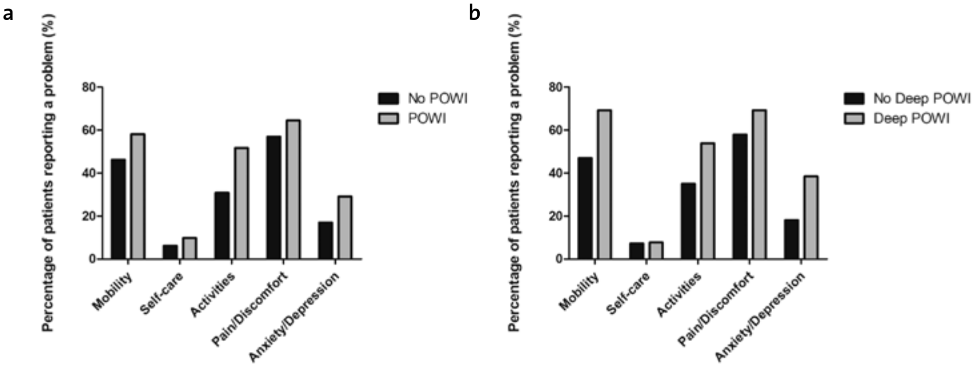

Figure 1. a Percentage of patients with a postoperative wound infection versus patients without a postoperative wound infection reporting a problem in the EQ-5D (not significant). **b** Percentage of patients with a deep postoperative wound infection versus patients without a postoperative wound infection reporting a problem in the EQ-5D (not significant). POWI postoperative wound infection, EQ-5D EuroQol-5D

physical labour and 3.5 months (IQR 2–9) in patients without heavy physical labour. In patients performing heavy or light physical labour, the occurrence of POWI, return to work following trauma, adjustment of work environment and inability to work following fracture treatment were not statistically different (p>0.05). Seventeen percent of patients (N=16) were not able to return to their previous work and another 31% (N=33) required adaptations regarding work environment. In addition, no significant association was found in physical impairment between patients with and without POWI (p>0.05) (Table 3).

Secondary interventions

In 50 patients (52.1%) implants were removed (vs. 37% in non-responding patients). In seven patients, this was the result of on-going infection following initial fracture surgery and in four patients because of a fistula or infection after more than 30 days. In nine patients (9.6%), a secondary arthrodesis of the posterior talocalcaneal (PTC) joint was deemed necessary, of which three patients suffered from a deep and one from a superficial POWI following the initial procedure. Need for implant removal and secondary arthrodesis was both associated with the occurrence of POWI (p<0.05).

Patients in which implants were removed scored significantly better on the FFI (p=0.023) compared to patients without implant removal with a median of 17 vs. 8.

Table 3. Patient reports on physical impairment prior to and following closed calcaneal fracture surgery.

Parameter (N of responders)	Pre-trauma (%)	Post-trauma (%)	No POWI, N = 69 (%)	POWI, N = 25 (%)	p-value
Practicing sports (91)	49 (52)	37 (40)	27 (39)	10 (40)	0.81
Running (89)	89 (95)	44 (47)	37 (54)	7 (28)	0.09
Ankle stiffness (90)					0.17#
Never		23 (24)	20 (29)	3 (12)	
In morning		42 (45)	33 (48)	9 (36)	
Always		25 (27)	14 (20)	11 (44)	
Walk on bare foot (91)					0.32##
Easily		**57 (61)**	45 (65)	12 (48)	
Experience difficulties		**28 (30)**	19 (28)	9 (36)	
Not possible		**6 (6)**	4 (6)	2 (8)	
Shoe wear (94)					0.45###
Normal footwear		64 (68)	45 (65)	19 (76)	
Orthopaedic adjustments		18 (19)	13 (19)	5 (20)	
Orthopaedic shoes		12 (13)	11 (16)	1 (4)	

no ankle stiffness compared to stiffness and morning stiffness ($\chi 2$)
easily compared to experiencing difficulties and not possible ($\chi 2$)
normal footwear compared to orthopaedic footwear ($\chi 2$)
N; Number, POWI; Postoperative wound infection

The AOFAS (73 vs. 79), QOL measurements EQ-5D (0.83 vs. 0.87), EQ-VAS (75 vs. 80) and VAS of overall treatment (8.0 vs. 9.0) showed no significant difference.

Patients with secondary PTC arthrodesis did score significantly worse than patients without secondary arthrodesis on FFI (44 vs. 9, $p<0.001$), AOFAS (57 vs. 81, $p=0.001$), QOL EQ-5D Index (0.71 vs. 0.86, $p<0.001$) and VAS for satisfaction (6.5 vs. 9.0, $p=0.001$).

Multivariate regression analysis

No statistical significance was found between the AOFAS score and surgery within 1 or 2 weeks following trauma (respectively, 0.517 and 0.186) and neither for the FFI (respectively $p=0.586$ and $p=0.146$). Therefore, no association was found between timing of intervention and functional outcome. The median age of the responding patients was 48 years and no differences were found in functional outcome between patients older or younger than 48 years and their AOFAS or FFI. Also, no association was found between the type of fracture using the Sanders classification and functional outcome/QOL (Table 4).

Multivariate analysis was performed to assess the relation between POWI and functional outcome/QOL corrected for the confounders fracture type and secondary interventions. No association was found for functional outcome. However, patient satisfaction on overall treatment remained significantly higher in patients without POWI ($p=0.008$).

Table 4. Functional outcome and quality of life measurements in patients with or without a postoperative wound infection per Sanders classification.

Patients (N)	FFI (p-value)	AOFAS (p-value)	EQ-5D index (p-value)	EQ-VAS (p-value)	VAS (p-value)
Sanders 1 (8)	0.456	0.763	0.169	0.099	0.153
POWI (3)					
No POWI (5)					
Sanders 2 (55)	0.263	0.553	0.743	0.467	0.144
POWI (15)					
No POWI (40)					
Sanders 3 (21)	0.238	0.133	0.296	0.587	0.088
POWI (5)					
No POWI (15)					
Sanders 4 (2)	NA	NA	NA	NA	NA
POWI (2)					
No POWI (0)					

N; Number, POWI; postoperative wound infection, FFI Foot Function Index, AOFAS; American Orthopaedic Foot and Ankle Society, EQ-5D; EuroQol-5D, VAS; Visual Analog Scale on patient satisfaction

DISCUSSION

No statistically significant association was found with postoperative wound infection on functional outcome following calcaneal fracture surgery. However, patients with a POWI reported a poor and fair outcome significantly more often compared to patients without a POWI. Unfortunately, the minimal clinically important difference (MCID) is unknown for both the AOFAS and the FFI.[25] However, the estimated MCID can be calculated as one half of the standard deviation (0.5 SD).[26] The 0.5 SD of the FFI and AOFAS were 10 and 10.5, respectively. Patients with POWI score a 17 points difference compared to patients without POWI, resulting in a worse FFI. This implicates that a clinically relevant difference exists between the two groups. The estimated MCID was not reached in the AOFAS hindfoot score. Even though patients scored higher on all items of the EQ-5D, the occurrence of POWI was not statistically associated with worse health-related QOL.

The VAS on overall patient satisfaction was significantly higher in patients without POWI ($p=0.01$). Additional admissions, a prolonged hospital stay, additional surgical procedures and costs of wound dressings could all contribute to this inconvenience.

Importantly, almost one-third of patients required adjustment of work environment following calcaneal fracture surgery. This emphasizes the impact a calcaneal fracture has on day-to-day life and supports the statement that a calcaneal fracture is a life-changing event.[27]

We found a high rate of implant removal of 52.1%. This is in concordance with the literature.[28] Patients without implant removal scored higher in the FFI and therefore show worse functional outcome as opposed to a previous study.[14] Patients with implant removal scored better with a median score of 17 versus 8. This might be a result of implant removal because of symptoms (e.g. pain, palpable screws, stiffness), which are reported in about three quarters of patients.[29] This is in line with previous literature with 79% of patients reporting less complaints as a result of implant removal following calcaneal fracture surgery.[29]

Of interest, we showed that a secondary fusion is indicated more frequently following POWI. This might be explained by additional joint damage caused by infection.[30] In addition, patients reported on ankle stiffness more frequently following POWI, which further contributes to this hypothesis. Patients with secondary arthrodesis scored worse on all outcome scores.

To the best of our knowledge, only three studies have been performed on foot and ankle surgery, with a main focus on postoperative wound complications and outcome effects.[14,31,32] In the study by de Groot et al., a retrospective analysis was performed on outcome in 39 patients with an intra-articular calcaneal fracture. They revealed no significant difference between patients with and without a wound complication.[14] However, two-thirds of the reported complications were wound dehiscences, which were not included in the current study. Korim et al. found that both deep and superficial infections result in lower functional outcome scores in a case–control study following operative fixation of fractures of the ankle.[31] Schepers et al. investigated the effect of delay in surgery in closed ankle fractures on occurrence of POWI.[32] Delay in surgery was associated with a significant increase in wound complications, resulting in a lower functional outcome at follow-up of almost 4 years. Delay of definite fixation of closed, intra-articular calcaneal fractures did not decrease wound complication rates when using the ELA and an increased wound complication rate when using less invasive approaches was found.[10]

The current study is mainly limited by its retrospective character. Even though we received an above average response rate of 70%, we were unable to locate a considerable percentage of patients. Our non-attenders showed no differences in incidence of POWI, but were more often male and younger, which is similar to a study of Murnaghan and Buckley.[33]. This most likely did not affect our results, because no association was found between these characteristics and outcome in the univariate analysis.

In conclusion, our results implicate that postoperative wound infection leads to lower functional outcome scores following calcaneal fracture surgery, but no statistical significance was reached. In addition, patients do not report significant worse QOL or physical impairment. Overall patient satisfaction was significantly lower in case of a postoperative wound infection.

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Chapter 6

PREDICTING LOSS OF HEIGHT IN SURGICALLY TREATED DISPLACED INTRA-ARTICULAR FRACTURES OF THE CALCANEUS

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ABSTRACT

Purpose

The goal of calcaneal fracture surgery is to restore its anatomy and good foot function. However, loss of height of the subtalar joint can occur postoperatively, as expressed by a decrease in Böhler's angle (BA). The aim of this study was to identify potential factors associated with a postoperative decrease in BA.

Methods

All consecutive adult patients treated with open reduction and internal fixation (ORIF) via an extended lateral approach (ELA) between 2000 and 2013 were retrospectively included. Primary outcome was the occurrence of a calcaneal collapse, defined as a postoperative decrease of ≥10° in BA. The BA was measured pre-operatively, directly following surgery and at one-year follow-up. Patient characteristics (body mass index, diabetes mellitus, smoking/alcohol/substance abuse, American Society of Anaesthesiologist classification), fracture classification and treatment characteristics: peroperative increase in BA and occurrence of postoperative wound infection (POWI) were collected.

Results

A total of 262 patients with 276 calcaneal fractures were included. A calcaneal collapse occurred in 46 cases (17%). The median preoperative BA, peroperative increase in BA and postoperative decrease in BA were, respectively, 2°, 27° and 4°. A calcaneal collapse was seen more often following a peroperative increase of >25° in BA, but no significant association was found ($p=0.056$). Uni- and multivariate analysis showed that patients with substance abuse and those with POWI had significantly more calcaneal collapse ($p<0.05$). No association was found between substance abuse and the occurrence of POWI ($p=0.293$).

Conclusions

In nearly one in six patients with an intra-articular calcaneal fracture treated with ORIF via an ELA, a postoperative collapse of ≥10° was found during follow-up. Calcaneal collapse was correlated with the occurrence of a POWI and substance abuse.

INTRODUCTION

In 1931, Böhler proposed that radiological measurements of the calcaneus could be useful to evaluate initial damage as well as reduction quality in posterior-facet fractures of the calcaneus.[1] The Böhler's angle (BA) is the angle formed by the intersection of an imaginary line joining the highest point of the anterior calcaneal process and the highest point of the posterior talocalcaneal joint with a line drawn from the most superior point of the posterior talocalcaneal joint to the highest point of the calcaneal tuberosity measured on a lateral foot radiograph (Figure 1). A normal BA ranges between 25° and 40° [1,2,3] and a BA of ≤20° following trauma is highly accurate for determining the presence of a calcaneal fracture.[4]

The goal of calcaneal fracture surgery is to restore the anatomy of the calcaneus with its articular surfaces and thereby maintain foot function. However, the subtalar joint frequently collapses (calcaneal collapse) postoperatively to some extent, which can be seen at radiological follow-up.[5-7] Several authors noted a correlation between initial BA and outcome.[7-12] The BA at time of admission appears to be a valuable prognosticator for functional long-term results.[11]. A poor clinical outcome is more common when the BA is decreased.[9] Surgical restoration of the BA leads to a better outcome compared with nonoperative treatment;[10,13] however, operative overcorrection of a reduced BA should be avoided.[11] Patients treated conservatively have a larger definitive reduction in BA than patients treated operatively.[8]

The aim of this study was to investigate the trend in Böhler's angle in patients with a displaced intra-articular calcaneal fracture treated surgically with an extended lateral approach (ELA) and to identify factors associated with a postoperative calcaneal collapse.

MATERIALS AND METHODS

The hospital database of a Level 1 trauma center was used to identify patients with calcaneal fracture surgery using the appropriate procedure code. All consecutive adult patients treated with open reduction and internal fixation (ORIF) via an ELA between 2000 and 2013 were retrospectively included. Exclusion criteria were patients with an open fracture who were initially treated with external fixation prior to ORIF, surgery via a different approach than an ELA, patients with a primary subtalar arthrodesis, referred patients with a pre-existing wound infection and patients with reconstructive surgery following conservative treatment of a calcaneal fracture. Patients in whom a secondary arthrodesis was performed during follow-up were not excluded.

Primary outcome was calcaneal collapse, which was defined as a post-operative decrease of ≥10° in BA. This cutoff value was chosen following an extensive literature search: in patients treated with ORIF, the highest reported decrease in BA ranged from 6° to 10.4° at 1-year follow-up[5,6,14] and in patients treated conservatively an 11° collapse was detected.[8]

a

b

c

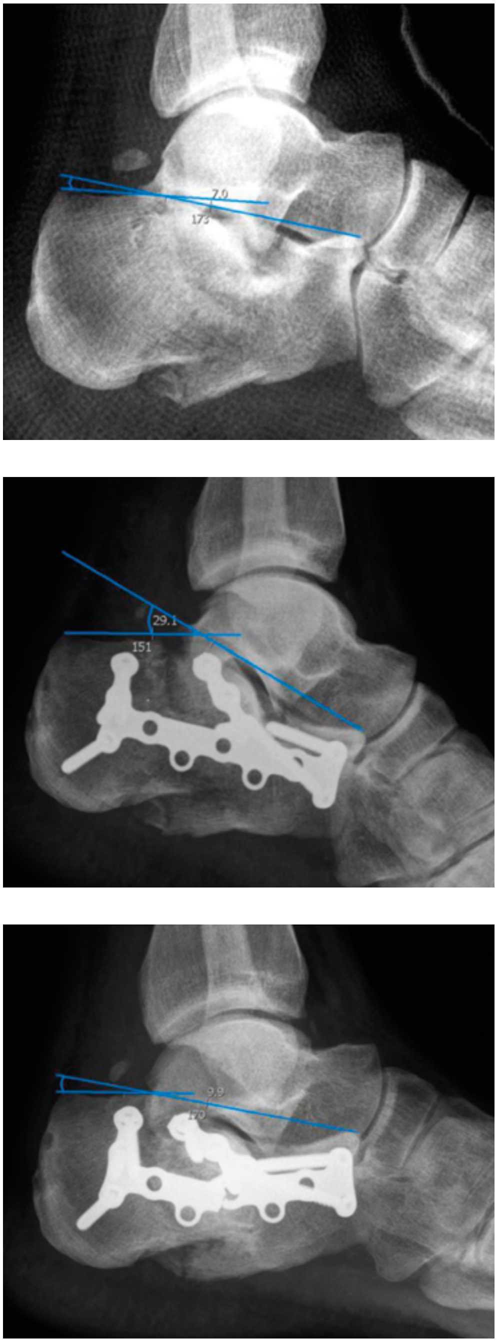

Figure 1. Böhler's angle (BA) is the angle from the intersection of an imaginary line joining the highest point of the anterior calcaneal process and the highest point of the posterior talocalcaneal joint, with a line drawn from the most superior point of the posterior talocalcaneal joint to the highest point of the calcaneal tuberosity, as measured on lateral foot radiograph. **a** Preoperative BA of 7°. **b** Postoperative BA of 29°. **c** Calcaneal collapse of 10° at one year follow-up.

Radiographic evaluation

The BA was measured on a lateral radiograph, as described previously, at three different time points: pre-operatively, directly following surgery and at one year follow-up.[12] In patients in whom a secondary arthrodesis was deemed necessary, BA was measured prior to this procedure. All measurements were rounded to a full degree because of interobserver measurement reliability[3,15,16] and were made by an independent observer. A specialized trauma surgeon verified all measurements. In case of discrepancies, measurements were averaged.

Surgical procedure

The surgical procedure was performed via an ELA, in which the full-thickness flap was retracted according to the no-touch technique, with temporary K wires in the talus to facilitate operative exposure.[17] A nonlocking stainless steel AO/ synthes calcaneal plate with 3.5-mm stainless steel screws (Synthes, West Chester, PA, USA) was used.[17-19] The goal of surgery was restoration of articular surfaces, calcaneal height, width, length and correction of axis. No bone grafting or locking plates were used. Patients received a single administration of antibiotic prophylaxis preoperatively and thrombosis prophylaxis during their 12 weeks of non-weight bearing. No postoperative casting was used, and patients were instructed to perform flexion and extension exercises of the ankle.[20]

Clinical data

Data were obtained from the electronic and paper medical records. The Institutional Review Board approved the study. Patient characteristics collected were gender, age at time of operation, body mass index (BMI), presence of diabetes mellitus (DM), smoking habits, alcohol use, substance abuse and American Anesthesiologist Association (ASA) classification. Fracture-related characteristics were pre-operative BA, which was subdivided in three groups (<0°, 0–15° and >15°)[21] and fracture classification (Essex-Lopresti and Sanders). Treatment characteristics were peroperative increase in BA (postoperative BA minus pre-operative BA, subdivided into groups of <10°, 10–25° and >25°), postoperative decrease in BA and occurrence of postoperative wound infection (POWI), subdivided into superficial and deep according to criteria of the United States Centers for Disease Control and Prevention.[18,22]

Statistical analyses

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 19.0 (SPSS INC., Chicago, IL, USA). Descriptive analysis was performed to assess baseline characteristics. For continuous data, medians with interquartile ranges (IQR) of p75-p25 or Q3-Q1 in nonparametric data were calculated; the Mann–Whitney U test was used for analysis. Categorical data were compared using the $\chi 2$ test, and a p value <0.05 was set as statistically significant. Firstly, a univariate analysis was performed, followed by a multivariate logistic regression analysis to model the relationship between different covariates and calcaneal collapse. Covariates with a p value <0.05 were selected for multivariate logistic regression analysis.

RESULTS

A total of 262 patients with 276 calcaneal fractures over the 14-year study period were assessed. A postoperative calcaneal collapse of ≥10° occurred in 46 cases (17%). Median pre-operative BA was 2° (IQR = 13-10) (Figure 2): 42% of patients had a BA of <0° after trauma, followed by 38% with an initial BA between 0 and 15°, and 20% with a BA of >15°. Median peroperative increase in BA was 27° (IQR = 38-15) and median postoperative decrease in BA in 1 year was 4° (IQR = –2 - -7); 38 % of patients had a postoperative decrease in BA of >5° and 6% of >15°. Calcaneal collapse was seen more often following an increase of >25° in BA preoperatively, but no significant association was found (p=0.056).

Patient, fracture and treatment characteristics are shown in Table 1. Univariate analysis showed that patients who suffered from a POWI (N=70; 25.4%) and deep POWI (N=34; 12.3%) had a calcaneal collapse more frequently (respectively, p<0.001 and p=0.005). These findings remained following multivariate logistic regression analysis (respectively, p=0.035 and p=0.004). Also, patients with substance abuse (N=55) had

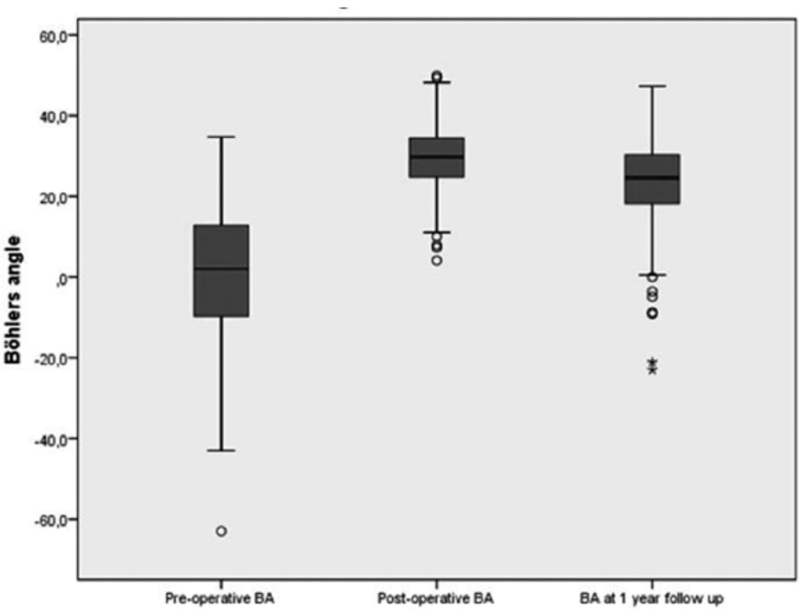

Figure 2. Böhler's angle (BA) at three time points: median pre-operative, postoperative and at one year follow-up.

a calcaneal collapse significantly more frequent (p=0.041). No association was found between substance abuse and the occurrence of POWI (p=0.293).

DISCUSSION

In nearly one in six surgically treated calcaneal fractures, a calcaneal of collapse ≥10° occurred within one year, which was associated with POWI and substance abuse. Importantly, no association was found between substance abuse and the occurrence of POWI. The reason calcaneal collapse was found frequently in this cohort at one year follow-up (17%) could be because no locking plates or bone-void fillers were used during

Table 1. Patient, fracture and treatment characteristics and incidence of calcaneal collapse in patients with calcaneal surgery.

	N of patients (%)	Collapse (%)	No collapse (%)	p value (2-sided)**
Patient characteristics	276	46 (17)	230 (83)	NA
Male	192 (71)	33 (72)	159 (69)	0.861
Age at time of surgery in years*	46 (35-55)	43 (34-54)	46 (35-56)	0.732
Diabetes mellitus	14 (5)	3 (2)	11 (5)	0.710
BMI*	24 (22-27)	24 (23-27)	24 (21-27)	0.168
ASA classification I	184 (67)	26 (58)	158 (69)	0.165
Smoking	108 (41)	17 (40)	91 (41)	1.000
Alcohol use	145 (56)	24 (59)	121 (56)	0.864
Substance abuse	55 (22)	15 (35)	40 (20)	0.041
Fracture characteristics				
Essex-Lopresti (Tongue Type)	125 (48)	16 (35)	109 (50)	0.073
Sanders (type 1 and 2)	205 (78)	37 (80)	168 (77)	0.700
Preoperative Böhler's angle				
< 0 degree	93 (42)	16 (40)	77 (42)	0.861
0 - 15 degree	86 (38)	19 (48)	67 (36)	0.212
> 15 degree	45 (20)	5 (13)	40 (184)	0.275
Treatment characteristics				
Surgical increase in Böhler's angle				
< 10 degree	29 (13)	4 (10)	25 (14)	0.795
10 - 25 degree	99 (44)	14 (35)	85 (46)	0.222
> 25 degree	126 (56)	28 (70)	98 (53)	0.056
POWI	70 (26)	24 (52)	47 (21)	<0.001
Deep POWI	34 (12)	12 (26)	22 (10)	0.005

* median with interquartile ranges
** $\chi 2$ or Mann Whitney U test on patients with a postoperative collapse and patients without a postoperative collapse
ASA; American Association of Anesthesiologists, NA; not applicable, N; number, POWI; postoperative wound infection, TT; tongue type

surgery. This is a limitation of our study. Locking plates may provide better stability and functional recovery[14,23] and less decrease of BA post-operatively.[10] Autologous bone grafting may aid in achieving and maintaining restoration of calcaneal height and anatomic reduction.[24] However, no objective radiographic or functional benefits of the use of bone-graft supplementation in the operative treatment of intra-articular calcaneal fractures was found.[6] A study by Johal et al. supports the use of an injectable in situ hardening calcium phosphate paste to fill the bone void after a displaced intra-articular calcaneal fracture, as it shows less reduction in BA during follow-up.[5]

It remains unclear how POWI is correlated with a postoperative decrease in BA. High rates of POWI were found, but numbers are in concordance with the literature on POWI following ORIF using the ELA.[18,25] The occurrence of POWI could be the result of decreased vascularization caused by the ELA and a calcaneal collapse due to subsequent delayed union. Shuler et al. found that patients with wound complications had a greater postoperative BA and a greater peroperative increase in BA than patients without wound complications.[26] This is likely a result of increased tension on the wound edges.[26,27] However, previous research by the investigators showed no correlation with the pre-operative BA or peroperative increase in BA and POWI.[18] In our study, calcaneal collapse occurred no more frequently if BA increased >25° during surgery, but no statistical significance was reached ($p=0.056$). Our standard recommendation is 12 weeks of non-weight bearing following ORIF via the ELA until fracture healing is seen on radiographs or, when in doubt, on a computed tomography (CT) scan. As calcaneal collapse is associated with the occurrence of POWI, our data might indicate that prolonged immobilization of these patients could be taken into consideration.

Importantly, in this study, we did not compare different surgical approaches. In current literature, a lower POWI rate of 6–14% is reported following the sinus tarsi approach.[28-31] This could be accompanied by a lower incidence of postoperative calcaneal collapse.

A calcaneal collapse in patients with substance abuse could be the result of limited compliance postoperatively, e.g. non-compliant weight bearing. However, as this was a retrospective study, we have no data to support this. Methods to increase fracture stability, such as primary arthrodesis, locking plates or bone-substitute materials, could be beneficial in patients in whom minimal compliance can be expected.

A general limitation of BA measurement is the risk of measurement errors due to interobserver variability or inability to correctly align the foot in standard radiographs; this misalignment can lead to errors in measurements.[33,34] Interobserver variability in BA was classified as moderate or good regarding agreement between independent observers.[3,16] Therefore, all radiographs were evaluated by two independent observers.

Radiographs of the contralateral calcaneus were not analyzed because pre-operative templating of the uninjured contralateral calcaneus does not allow for more anatomic reduction or restoration of pre-injury morphology of the calcaneus undergoing operative fixation based on BA and calcaneal length.[34]

Finally, we focused on radiographic analysis. Functional outcome, as measured using patient-reported outcome measures, was not used. Previous research showed that measurements on plain radiographs were not useful in determining outcome after intra-articular calcaneal fractures.[12] However, they are useful for determining fracture healing, alignment and surgical restoration of anatomy.

In conclusion, in nearly one in six patients with an intra-articular calcaneal fracture treated with ORIF through an ELA, a postoperative calcaneal collapse of ≥ 10° was found during follow-up. Collapse was correlated with the occurrence of POWI and substance abuse. A postoperative CT scan may be advisable following 12 weeks of non-weight bearing to evaluate bone healing prior to weight bearing in this group of patients.

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Chapter 7

SIMILAR ANATOMICAL REDUCTION AND LOWER COMPLICATION RATES WITH THE SINUS TARSI APPROACH COMPARED TO THE EXTENDED LATERAL APPROACH IN DISPLACED INTRA-ARTICULAR CALCANEAL FRACTURES

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ABSTRACT

Objectives

To investigate whether the sinus tarsi approach (STA) allows for a similar anatomical reduction of the posterior talocalcaneal facet as the extended lateral approach (ELA) and compare the rate of postoperative wound complications.

Design

Retrospective.

Setting

Level 1 Trauma Center.

Patients

All consecutive patients from 2012 to 2015 with a closed displaced intra-articular calcaneal fracture Sanders type II and III surgically treated with the ELA (N=60) and the STA (N=65).

Main Outcome

Wound complications, timing of surgery, operative time, length of postoperative hospitalization, and reduction of the posterior facet and calcaneal body.

Results

Incidence of wound complications, time to surgery, postoperative duration of hospital admission and number of hospital admissions because of wound complications were significantly different between the ELA group and STA group. There was no significant difference in restoration of calcaneal anatomy with either approach. Importantly, the STA was performed in a median duration of 105 minutes and the ELA in a median of 134 minutes, accounting for nearly half an hour difference in operating time ($p<0.001$).

Conclusions

The largest benefit of the STA was found in the significant reduction in wound complications and operative time, where time to closure may have accounted for the latter difference. This difference was without a compromise in reduction. Additional studies comparing functional outcome, especially rates of subtalar arthrosis, will be needed to determine the long-term benefits of the STA.

INTRODUCTION

Surgical restoration of anatomy in displaced intra-articular calcaneal fractures (DIACF) has improved outcome.[1–7] Since the 1990s the extended lateral approach (ELA) has been considered the standard approach for performing open reduction and internal fixation (ORIF) of a DIACF.1 Although in the past wound complications of 2% up to as high as 25% have been the main concern with the use of ELA,[5,7–12] authors have shown that it is possible to significantly lower these rates with increased experience.[4,5,7,11,13]

Despite these improvements in the standard technique, less invasive techniques have emerged in the last decade, which become more popular. The sinus tarsi approach (STA) originated from a direct approach over the peroneal tendons.[14] This incision was modified to an incision just above the peroneal tendons. The limited approach was popularized originally by Essex-Lopresti, Maxfield, Judet and others.[15–17] Soeur and Remy in 1975 and several others later are credited with developing and using the STA.[16,18–20]

A recent review article on the use of the STA identified 17 publications since 2000, mainly retrospective and noncomparative series. Functional outcome, obtained from 14 of these studies, showed promising results over a short follow-up period of approximately 2 years.[21] As a result of this analysis, we shifted our surgical technique from the standard ELA to the newer STA. Our hypothesis was that we could obtain similarly good reductions and less wound complications with the STA. We now report our results.

PATIENTS AND METHODS

This nonrandomized study included 125 consecutive fractures with a closed DIACF between January 2012 and March 2015. Sanders type I (fractures without displacement at the subtalar joint) and extra-articular fractures were excluded. Similarly, no Sanders type IV fractures were evaluated, as the majority went on to primary arthrodesis. The decision to perform an ELA of STA was left to the discretion of the 3 treating surgeons; all were experienced calcaneal fracture surgeons.

Patient characteristics collected were sex, age at the time of trauma, diabetes mellitus, use of nicotine, drug abuse, and American Society of Anesthesiologists (ASA) classification. Fracture characteristics were measurement of the pre-operative Böhler's angle (BA) on the lateral radiographic images and computed tomography (CT) classification (Sanders and Essex-Lopresti) based on lateral and axial CT in all patients (Fig. 1AB and Fig. 2AB).

Treatment characteristics included type of approach, time to surgery, duration of the procedure, duration of hospital admission after ORIF, surgical interventions due to wound complications with subsequent number of readmissions and total hospital stay. All patients were seen at regular intervals (2, 8, 26, and 52 weeks) postoperatively by a trauma surgeon specialized in foot and ankle surgery.

Postoperative wound complications were classified as minor or major complications according to the criteria of the US Center for Disease Control and Prevention.[22] Minor complications were wound edge necrosis and wound dehiscence. A superficial postoperative wound infection (POWI) was diagnosed if signs of infection were observed, confirmed with a positive culture but were amendable to nonoperative treatment methods including oral antibiotics. A major wound complication was defined as a deep POWI confirmed with both a positive culture and at least contiguous osteomyelitis, colonized implants, or a fistula requiring for implant removal or intravenous antibiotic treatment and/or wound debridement (with or without local gentamicin treatment or vacuum-assisted closure).

To assess the accuracy of the reduction of the posterior talocalcaneal facet, postoperative CTs were obtained (Fig. 1D and Fig. 2D).[23] The largest step-off seen on the semicoronal reconstructions was measured in millimeters (mm). A value of 0 to <1

Figure 1. Sanders type 3AB calcaneal fracture treated via sinus tarsi approach with screws only fixation. **A** pre-operative lateral view **B** pre-operative axial CT scan image **C** postoperative lateral view **D** postoperative axial CT scan.

mm indicated an anatomic reduction, 1 to <3 mm indicated a near anatomic reduction, 3–5 mm was considered an approximate reduction and > 5 mm was considered a failure of reduction.[1,4] The width of the calcaneus was measured on the axial CT just below the sustentaculum tali. Postoperative conventional radiographs were performed at 6 to 8 weeks consisting of a lateral view, axial view, and a 30–40 degree Brodén view. The postoperative BA was measured using the lateral view (Fig. 1C and Fig. 2C). The axis of the tuber was measured using the axial view and considered normal with a varus/ valgus angle of > 5 degree.

Figure 2. Sanders type 3BC calcaneal fracture treated via sinus tarsi approach with plate and screw fixation **A** pre-operative lateral view **B** pre-operative axial CT scan image **C** post-operative lateral view **D** postoperative axial CT scan.

Statistical Analysis

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS, Chicago, IL). Normality of continuous data was tested with the Kolmogorov–Smirnov test and by inspecting the frequency distributions. Descriptive analysis was performed to compare baseline characteristics between patients with the ELA and patients with the STA. For continuous data, the mean and standard deviation (parametric data) or medians and interquartile ranges (nonparametric) data were calculated. Differences were assessed using the Student's t test (parametric data) or the Mann–Whitney U test (nonparametric data). Categorical data were compared using the $\chi 2$ test. A p value of > 0.05 was taken as the threshold of statistical significance. All p values are 2 tailed.

RESULTS

The ELA was used in 60 patients (ELA group) and the STA in 65 patients (STA group). Patient demographics are shown in Table 1. The median follow-up was 22 months (IQR: 12–28). No patients were lost to follow-up and the minimum follow-up was 6 months. There were no significant differences between the groups regarding age, sex, diabetes mellitus, substance abuse, ASA type, or Sanders classification.

With respect to postoperative wound complications, in the STA group there were 4 minor and no major wound complications. In the ELA group 9 minor and 11 major complications were found (Table 2). This was a statistically significant difference (p<0.001). Rates of POWI per surgeon and per fracture type according to the Sanders classification are presented in Table 3 and Table 4.

Restoration of anatomy was comparable in both groups. There were 2 cases with a minimal step (<2 mm) in the ELA group (1 Sanders type II, 1 Sanders type III), with no steps in the STA group. The other anatomical variables; for example varus/valgus, postoperative BA, and postoperative width were similar in both groups (Table 2).

Of all baseline characteristics, time to surgery (median of 4 days earlier in STA group, p<0.001) and postoperative duration of hospital admission (median of 1 day shorter in STA group, p<0.001) were significantly different between the ELA group and STA group. Finally, the STA was performed in a median duration of 105 minutes and the ELA with a median of 134 minutes, accounting for nearly half an hour difference in operating time (p<0.001).

DISCUSSION

Our results indicate that when using the STA in Sanders type II and III fractures, we were able to obtain similar results in reduction with a significantly shorter operative time. Data regarding time to surgery were statistically significant; however, we are aware that a mean of 18 versus 14 days is minimal. This may indicate that we felt more comfortable operating sooner using a limited approach such as the STA. However, delay in surgery has

Table 1. Preoperative patient and fracture characteristics of 125 patients with displaced intra-articular calcaneal fractures with surgery via the extended lateral approach (N=60) and the sinus tarsi approach (N=65).

	Extended lateral approach	Sinus tarsi approach	p-value
Male gender (%)	43 (72)	43 (66)	0.565
Age, y*	48 (39-56)	46 (37-59)	0.890
Diabetes mellitus (%)	2 (3)	0	0.228
Nicotine use (%)	20 (33)	18 (28)	0.563
Drug abuse (%)	7 (12)	9 (14)	0.592
Alcohol abuse (%)	15 (25)	26 (40)	0.086
Isolated calcaneal fracture (%)	48 (80)	53 (82)	1.000
ASA classification			0.709†
I (%)	45 (71)	49 (69)	
II (%)	18 (29)	23 (32)	
III (%)	0	3 (4)	
Essex Lopresti Classification			
Joint depression (%)	33 (55)	20 (31)	
Tongue type (%)	27 (45)	39 (60)	
Combined (%)	0	6 (9)	
Sanders Classification			0.828
II (%)	48 (76)	50 (70)	
III (%)	12 (19)	15 (21)	
Preoperative BA, degree*	-5 (-15 to 7)	-2 (-14 to 9)	0.391
Time to surgery, d*	18 (14 to 23)	14 (11 to 18)	< 0.001

*Numbers in median (interquartile ranges)
†Difference between ASA 1 and 2+3 (χ^2)
ASA; American Association of Anesthesiologists, N=number; BA; Böhler's angle

been associated with an increased risk on postoperative wound complications.[24–26] With regard to postoperative hospitalization, although again statistically significant, this is probably a function of our medical system. We are aware that many countries perform this surgery in day-care or one overnight hospital stay. There were however significantly less readmissions because of wound complications, leading indirectly to lower immediate costs after the STA. Our results are in line with recent publications with smaller groups of patients comparing the STA and ELA regarding wound complications[27–29] and regarding similar reduction.[23,30,31]

As previously mentioned, the rate of wound complications after the ELA varies from 2 to approximately 25 percent in literature.[5,7–12] Our study shows a considerable rate of POWI. The policy at our facility is to treat the vast majority of displaced intra-articular calcaneus fracture patients operatively, irrespective of any unfavorable factors for wound healing, which could contribute to this high rate. In addition, there is a longer

Table 2. Treatment characteristics of 125 patients with displaced intra-articular calcaneal fractures with surgery via the extended lateral approach (N=60) and the sinus tarsi approach (N=65).

	Extended lateral approach	Sinus tarsi approach	p-value
Duration of procedure in minutes*	134 (118 - 149)	105 (90 - 127)	< 0.001
Total wound complications (%)	20 (31)	4 (7)	< 0.001
Major wound complications (%)	11 (17)	0	< 0.001
Postoperative hospital admission, in days*	4 (3-7)	3 (2 - 4)	< 0.001
Hospital readmission due to major complication (%)	7 (11)	0	0.028
Re-operation because of major complication (%)	14 (22)	0	< 0.001
Step-off posterior talocalcaneal joint in mm*	1 (0 - 2)	0 (0 - 1)	< 0.001
Varus/valgus >5 degree (%)	1 (2)	0	0.480
Postoperative BA in degree*	26 (20 - 30)	27 (24 - 32)	0.075
Postoperative width in mm*	36 (34 - 40)	36 (34 - 40)	0.694

*Numbers in median (interquartile ranges)
N; number, BA; Böhler's angle

Table 3. Surgeons performing the extended lateral approach (N=60) or sinus tarsi approach (N=65) in displaced intra-articular calcaneal fractures and POWI rates.

	Number (%)	Extended lateral approach (%)	Sinus tarsi approach (%)	p-value*
Surgeon A	27 (22)	17 (28)	10 (15)	0.244
Wound complication	9 (33)	7 (41)	2 (20)	
Minor	7 (32)	5 (29)	2 (20)	
Major	2 (7)	2 (12)	0	
Surgeon B	72 (58)	23 (38)	49 (75)	0.004
Wound complication	7 (10)	6 (26)	1 (2)	
Minor	4 (6)	3 (13)	1 (2)	
Major	3 (4)	3 (13)	0	
Surgeon C	26 (21)	20 (33)	6 (9)	0.628
Wound complication	8 (31)	7 (35)	1 (17)	
Minor	2 (8)	1 (15)	1 (17)	
Major	6 (23)	6 (30)	0	

*ELA vs. STA
N; Number

delay because many patients (>80%) are referred patients. In previous studies lower rates of POWI have been identified. When comparing these papers several differences may be observed: use of titanium versus RVS plate, use of tourniquet, standard versus

Table 4. Rates of POWI and step-off in posterior talocalcaneal joint in millimeters per intra-articular calcaneal fracture type according to the Sanders classification.

	Total number (%)	Extended lateral approach N (%)	Sinus tarsi approach N (%)	p-value
Sanders type 2	98	48 (49)	50 (51)	
POWI (%)	20 (20)	16 (34)	4 (8)	0.002
Step-off PTCJ (mm)*	0 (0 - 1)	1 (0 - 2)	0 (0 - 1)	0.002
Sanders type 3	27	12 (44)	15 (56)	
POWI (%)	4 (15)	4 (33)	0 (0)	0.028
Step-off PTCJ (mm)*	0 (0 - 1)	1 (0 - 2)	0 (0 - 0.5)	0.029

*Median (interquartile ranges)
N; Number, NA; Not available because 6 patients were treated with primary arthrodesis , PTCJ; posterior talocalcaneal joint

no use of closed suction drain, different closure techniques, and a significant difference in days to surgery (8 vs. 14 on average). Because of the lower number of patients (8 vs. 42 per year) and longer inclusion period there is a higher risk of patient selection bias in these studies.[32,33]

Surgical time for ORIF performed through the STA has been noted to be approximately 30 – 40 minutes shorter than that of the ELA in other publications.[29,34,35] Our results mirror this reduction in operative time. We believe this is because of the smaller incisional wound, requiring less time to open and close and because of better visualization of the subtalar joint with subsequent less time to achieve adequate reduction.

Although this is a nonrandomized study, we were able to monitor the occurrence of postoperative wound complications prospectively in a large cohort with an adequate follow-up. A weakness of our study is that it consists of 2 cohorts as a result of the quick transition from the ELA to the STA. This reduces, but does not rule out selection bias. In addition, this is a short-term follow-up study without Patient-Related Outcome Measures.

This study strengthens the available body of evidence on similar anatomical reduction, fewer wound complications, and a shorter surgical time using the STA. The STA is therefore now our preferred approach for Sanders type II and III DIACFs. This less invasive approach does not compromise reduction in relation to joint reduction, height, and axial alignment. We believe that reducing the rate of wound complications and the shorter operative time is a significant benefit of this less invasive approach. Whether or not this also results in a similar functional outcome needs to be investigated in a larger prospective study.

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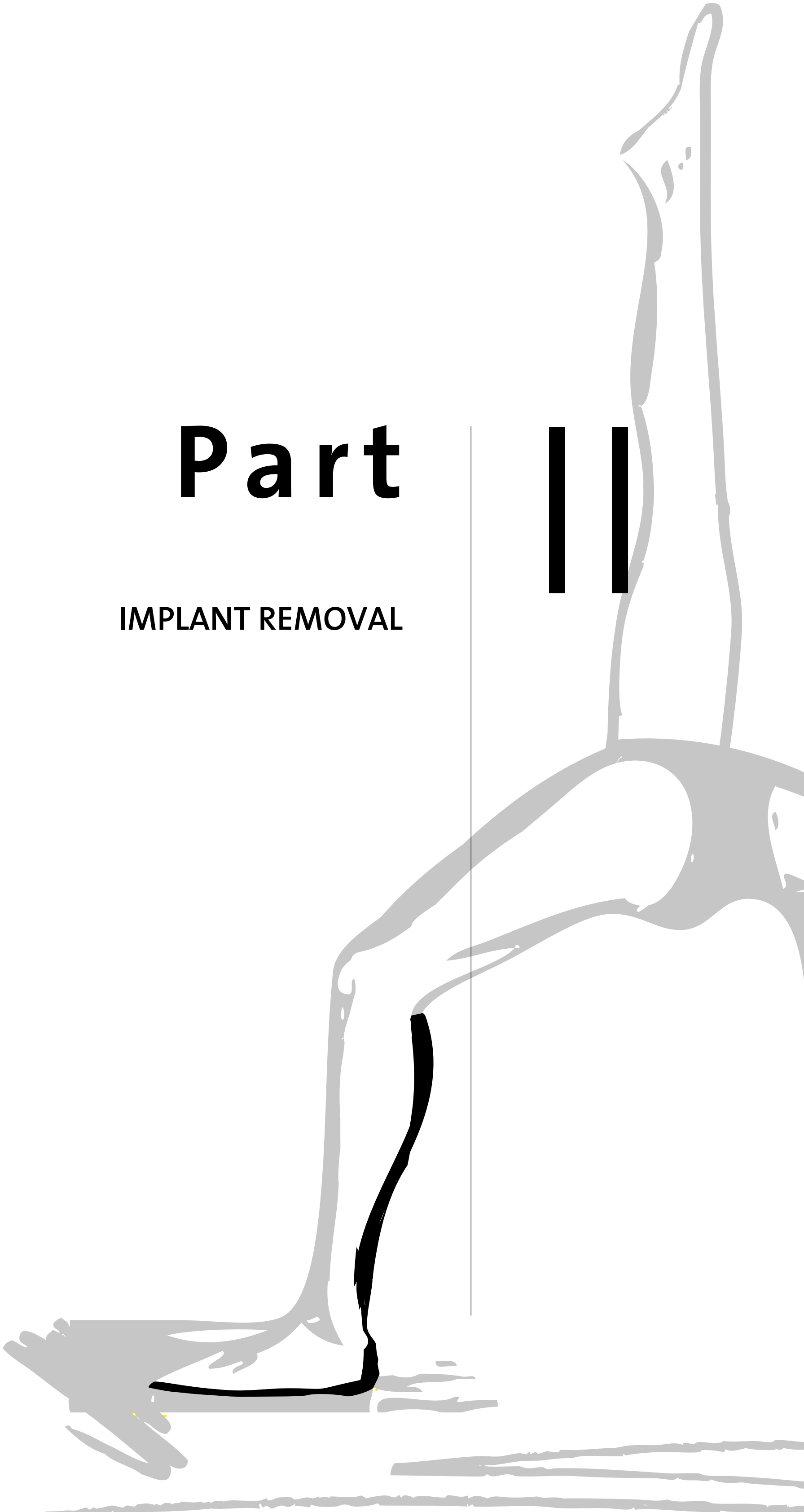
Part II

IMPLANT REMOVAL



Chapter 8

INDICATIONS FOR IMPLANT REMOVAL FOLLOWING INTRA-ARTICULAR CALCANEAL FRACTURES AND SUBSEQUENT COMPLICATIONS

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ABSTRACT

Introduction

Implant removal following operative calcaneal fracture treatment has received little attention in the literature. The aim of the current retrospective cohort study was to assess the indications and number of wound complications following calcaneal plate removal.

Methods

All consecutive adult patients who had their plate and screws removed following the operative treatment of a closed uni- or bilateral intra-articular calcaneal fracture using a stainless steel nonlocking calcaneal plate between 2000 and 2011 were included.

Results

In 102 patients (46% of the total number of operated calcaneal fractures) implants were removed. Implant removal was performed in 75 patients for symptomatic reasons, in 10 patients due to implant malposition and in 19 patients because of a persistent wound infection or fistula. Following implant removal 17 (16%) % behind patients had a wound complication (2 wound dehiscence, 15 culture positive wound infections). Six patients (9%) suffered from a wound complication following implant removal after uncomplicated fracture surgery. Implant removal for active infection or plate fistula displayed an infection rate of 8 out of 19 (42%).

Conclusion

Implant removal after an intra-articular calcaneal fracture treated with open reduction and internal fixation via an extended lateral approach was followed by a wound complication in 1 of every 10 patients without a pre-existing wound infection. Infection rates were especially high in patients in whom the implants were removed for an active wound problem.

INTRODUCTION

Routine implant removal can result in up to 15% of all operations performed with in a considerable burden on hospital budgets and the operating room schedule.[1] Implant removal on a routine basis has therefore been largely abandoned. Removal for specific complaints in different areas has been the subject of several investigations, but not yet in calcaneal fractures.[2-8] In foot and ankle surgery, the percentage of patients requiring implant removal is infrequently reported. For ankle fractures, implant removal is performed in 21% to 27% of patients.[2,9,10] Improvement in implant-related complaints following implant removal in ankle fracture patients ranges between 50% and 90%.[2,4,5,9,11]

Little information is available about implant removal following the operative treatment of a displaced intra-articular calcaneal fractures. The main reasons for implant removal following a calcaneal fracture are discomfort (pain, peroneal tendon irritation, or at patients' request), implant-related causes (malpositioned screws, implant breakage, planned removal in bridge plating) or because of a persistent infection (fistula or osteomyelitis). The percentage of implant removal following calcaneal fractures treated via an extended lateral approach (ELA) ranges between 10% and 40%.[12-16]

The aim of the current study was to assess the indications and incidence of wound complications following plate removal after a displaced intra-articular calcaneal fracture.

METHODS

We conducted a retrospective cohort study of all consecutive adult patients with a uni- or bilateral intra-articular calcaneal fracture treated operatively between 2000 and 2011 in a Level 1 (academic) Trauma Center. The electronic hospital database was searched from 2000 to 2011 for all calcaneal fractures using the appropriate surgical code. A patient was deemed eligible for study inclusion when the fracture(s) was approached via an ELA, stabilized using either a stainless steel nonlocking calcaneal plate with stainless steel 3.5 mm screws or in 2 cases with a 2.4/2.7 mm locking plate as bridging plate from calcaneus to the cuboid in comminuted anterior process fractures and the implant was removed in our hospital.

All hospital and operative records were checked for implant removal. Patient characteristics (gender, age, BMI, nicotine use, diabetes mellitus), injury-related characteristics (infection post fracture treatment, on-going infection) and surgical characteristics (time from injury, duration of operation, post removal wound complication, attending surgeon, and whether surgery was performed by a staff member or resident) were obtained. Open fractures and those treated percutaneously or via a sinus tarsi approach were excluded from this study. Included patients had a minimum follow-up of 2 years from fracture treatment.

Indications for removal were collected from the electronic charts (symptomatic, implant related, on-going infection). A symptomatic implant was defined as an implant causing symptoms such as pain, palpable screw head(s), stiffness of the subtalar joint, peroneal tendinitis, or at the request of the patient. In case of stiffness, the implant removal procedure was followed by a debridement of arthrofibrosis from the subtalar joint. A wound complication was defined as the occurrence of either a wound dehiscence (negative culture), minor (superficial) surgical wound infection treated with nonoperative treatment (e.g., oral antibiotics, local wound care), or a major (deep) infection treated with intravenous antibiotics, surgical wound debridement with or without vacuum assisted closure. In patients with implant removal due to a persistent infection of the index procedure, a secondary (new) wound complication was defined as deterioration in wound healing with a positive culture with a different (new) pathogen within 30 days following removal necessitating a change in treatment strategy.

Statistical Analysis

Data were analysed using SPSS version 19.0 (SPSS, Chicago, IL, USA). Normality of continuous data was tested with the Kolmogorov–Smirnov test and by inspecting the frequency distributions (histograms). The homogeneity of variances was tested using the Levene's test. Descriptive analysis was performed to compare baseline characteristics between patients with and without an infection. For continuous data, mean ± SD (parametric data) or medians and interquartile ranges (nonparametric data) were calculated. Differences were assessed using the Student's t test (parametric data) or the Mann–Whitney U test (nonparametric data). Categorical data were compared using the $\chi 2$ test. A p value <0.05 was taken as the threshold of statistical significance.

RESULTS

Of 214 patients with 228 operatively treated fractures, a total of 104 (46%) implants were removed in 102 patients, with 2 bilateral implant removals both in male patients (Table 1). Of these, most were middle-aged males. Of the 102 patients, 9 had a history of cardiac disease (9%), 1 had peripheral vascular disease (1%), 8 had pulmonary disease (8%), and 8 suffered from diabetes mellitus (8%). Nicotine use was recorded in 99 of 102 patients (97%), with 50 being active smokers (51%). These patient characteristics did not differ statistically from the total population of patients with a calcaneal fracture (23 patients with cardiac history, 13 pulmonary, and 14 diabetes mellitus). Removal was performed for symptomatic implants in 75 patients, for implant-related causes in 10 and as treatment for a persistent infection or fistula in 19 patients.

In 87 out of 104 procedures (83.7%) a staff surgeon was present (otherwise a senior resident). The total number of different surgeons was 14, of whom 3 performed calcaneal implant removal once in this group of patients.

Following implant removal 17 patients (16%) suffered from a wound complication: 2 wound dehiscences and 15 culture positive wound infections (Table 2). Of the 15 culture positive infections, 11 (73%) were caused by *Staphylococcus aureus*.

Table 1. Indications for implant removal after displaced intra-articular calcaneal fractures.

Removal indication	N	Male (%)	Age (years)	Time to Removal (months)	Duration surgery (minutes)	Wound complication (%)
Overall	104	64 (62)	44.6 (34.6-56.3)	32.8 (20.4-49.2)	64 (48-128)	17 (16.3)
Symptomatic	75	46 (61)	43.1 (30.9-51.8)	34.8 (26.3-54.4)	60 (45-122)	8 (10.7)
Pain	57					
Palpable screw	7					
Stiffness	7					
Peroneal tendinitis	2					
Request of patient	2					
Implant related	10	7 (70)	63.5 (37.2-69.1)	26.4 (16.1-37.6)	67 (58-95)	1 (10.0)
Implant breakage	5					
Malposition of screw	3					
Bridge plate	2					
Infection	19	11 (58)	44.9 (40.0-59,0)	17.6 (14.3-32.6)	87 (65-108)	8 (42.1)
Infection	10					
Fistula	9					

Values are medians with interquartile ranges (p25-p75) in parentheses.

A total of 69 patients had their implant removed following uncomplicated fracture treatment. In this group 6 wound complications occurred after implant removal (9%). The remaining 35 patients experienced a wound infection following the acute treatment of their calcaneal fracture, of which 16 (5 major, 11 minor) had resolved and 19 were on-going major infectious complications (9 fistulas, and 10 persistent infections). Eleven of these patients (31%) had a secondary (new) wound complication following implant removal. This difference was statistically significant ($p=0.0049$) when compared to the group with implant removal after uncomplicated fracture treatment.

Of the 19 cases in which the implant was removed for persistent infection or fistula, 8 patients (42%) suffered from a secondary post removal infection which was significantly higher than those removed for other indications ($p<0.001$).

Eventually all persistent infections for which implant removal was planned resolved. In 15 out of 19 cases (79%) the infection resolved by removal of the implant, and in 4 cases with additional treatment. No amputations were necessary due to an infectious complication of the primary procedure or implant removal.

When excluding patients with implant removal for an on-going infectious complication, the percentages change to 19% (3/16) following resolved infection after

Table 2. Demographics of patients with a wound complication following implant removal.

Patient	Gender	Age (y)	Smoking	Wound complication prior to IR	Indication for Removal	Time to Removal (m)	Additional Surgery	Wound complication type*	Culture
1	M	65	No	Major	Fistula	15.1	1	Major (surgery)	Coliform spp
2	F	49	NA	None	Symptomatic	26.9	0	Minor	Skin flora
3	M	37	No	None	Broken screw	38.4	0	Major (iv AB)	*Staphylococcus aureus*
4	F	67	Yes	Major	Infection	39.6	0	Minor	*Staphylococcus aureus*
5	M	29	Yes	None	Symptomatic	32.5	0	Minor	*Staphylococcus aureus*
6	F	59	No	Major	Fistula	13.0	0	Minor	*Staphylococcus aureus*
7	M	58	No	Minor	Symptomatic	33.1	0	Minor	*Staphylococcus aureus*
8	F	64	No	Major	Fistula	20.8	0	Minor	Insufficient swab
9	M	47	Yes	Minor	Symptomatic	38.2	1	Major (surgery)	*Staphylococcus aureus* and Coliform spp
10	M	45	Yes	Major	Infection	32.6	1	Major (surgery)	Coagulase-negative staphylococcus
11	M	29	No	None	Symptomatic	111.9	1	Major (surgery)	*Staphylococcus aureus*
12	M	57	Yes	Major	Infection	10.1	0	Minor	*M. Morganii*
13	M	43	NA	Major	Fistula	41.2	1	Major (surgery)	*Staphylococcus aureus*
14	M	31	No	None	Symptomatic	33.7	1	Major (surgery)	*Staphylococcus aureus*
15	M	24	No	Major	Symptomatic	20.9	0	Minor	*Staphylococcus aureus*
16	M	40	Yes	Major	Infection	14.3	9	Major (surgery)	*Pseudomonas aeruginosa*
17	F	15	No	None	Symptomatic	37.0	0	Minor	*Staphylococcus aureus*
Mean ± SD or N most common	Male (N = 12)	44.6 ±15.6	No (N = 9)	Major (N = 9)	Symptomatic (N = 8)	32.9 ± 22.8	0	Minor (N = 9)	*Staphylococcus aureus* (N = 11)

*Complications were classified as “minor” when resolved with local measures and oral antibiotics; “major” complications needed hospital admission with intravenous (iv) antibiotics or surgical debridement

F; female, IR; implant removal, M,; male, m; months NA; not available, SD; standard deviation, y; year.

initial fracture treatment versus 9% (6/69) after uncomplicated fracture treatment, which was not statistically significantly different given the current number of patients. In the univariate analysis, the other patient (gender, age, BMI, nicotine use, diabetes mellitus) and surgical characteristics (duration of surgery, surgery performed by staff member or resident) were not associated with a higher complication rate.

DISCUSSION

We report on a large series of implant removal following surgery with the ELA for displaced intra-articular calcaneal fractures. A total of 104 out of 228 (46%) of the calcanei required implant removal, with a 16% postoperative wound complication rate. This percentage of implant removal is in concordance with the literature.[12,14] The most common rationale for implant removal in this study was complaints related to the implant. Only 2 patients requested removal without a clear medical reason.

Previously, it was reported that half of the patients who had their implants removed because of implant-related complaints following an ankle fracture did not benefit from the procedure.[2] Furthermore, up to 25% of patients may present with new complaints following implant removal.[9] Even though the success rate of implant removal because of implant-related complaints is found to be high in foot and ankle trauma surgery,[6,9,11] there is a considerable number of patients that do not benefit from implant removal.[2,8,9] In our study the effect of the implant removal was documented in the medical charts in 80 out of 102 patients (78%). A total of 63 out of 80 (79%) patients reported improvement of complaints following implant removal. Even though we did not use an objective score, the number of patients with relief appears to be high enough to justify an additional surgical procedure.

Early studies on complications following implant removal report rates as high as 15-19%.[2,7] More recent studies on implant removal following ankle fracture surgery report wound complication rates of 3-20%.[4,9,17] In line with these findings, it has been postulated that implant removal might be accompanied with more risk than leaving implants in place.[18] The incidence of complications following removal of a stainless steel calcaneal plate has not been investigated in depth previously. We found a wound complication rate of 17% for the total population and 10% for patients with uncomplicated initial fracture treatment.

The incidence of wound complications following implant removal in this study was positively correlated with wound complications following initial fracture treatment. This finding is in concordance with results of other studies.[3,6,19] A high rate of (new) wound complications can be expected following implant removal because of an on-going infection. This is more likely the result of an on-going process of osteomyelitis or compromised soft tissue envelope, rather than a complication of the implant removal procedure itself. However, the high wound complication rate in patients with a fistula was unexpected. This might be because of a chronic low-grade infection due to bacterial colonization on the plate surface in a biofilm or in the peri-implant tissue.[20-22] No other patient or surgery-related factors were identified to predict the development of a postoperative wound complication.

We did not find similar studies on the indications, complications and effect of implant removal following displaced intra-articular calcaneal fracture treatment with the ELA. Even though the current study is retrospective, most data could be obtained from the medical records. In the Netherlands it is national and hospital policy to administer a first-generation cephalosporin prior to incision,[23] but not in short elective orthopaedic procedures like implant removal.[24,25] Also in elective foot and ankle surgery, the need for prophylactic antibiotics has been disputed.[25-27] Implant removal is considered a clean procedure, in which prophylactic antibiotics should not lower the postoperative wound infection rate. It is therefore uncommon in the Netherlands to administer antibiotics prior to implant removal. However, in light of the current study, we believe this policy should be reconsidered.

In conclusion, about half of all implants were removed following surgical treatment of a displaced intra-articular calcaneal fracture, mainly because they were symptomatic. Implant removal following ORIF via the ELA of a displaced intra-articular calcaneal fracture was affected by a relatively high rate of wound complications; 1 in every 10 patients without a pre-existing wound infection developed a wound complication. The wound complication rate was especially high in patients in whom the implants were removed for an active wound problem.

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Chapter 9

HIGH RATES OF POSTOPERATIVE WOUND INFECTION FOLLOWING ELECTIVE IMPLANT REMOVAL

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ABSTRACT

Introduction

Metal implants placed during fracture surgery are often removed for various reasons (i.e. pain, prominent material, patients request). The removal of implants is considered a 'clean' procedure and as low risk surgery. The incidence of wound infections following implant removal has received little attention in the literature. The aim of the current study was to assess the incidence and risk factors of postoperative wound infection (POWI) following implant removal.

Material and Methods

All consecutive adult patients in a Level 1 and Level 2 Trauma Center who had their implants removed during a 6.5 years period were included. Exclusion criteria were removal of implants because of an ongoing infection or fistula and removal followed by placement of new implants. Primary outcome measure was a POWI as defined by the US Centers for Disease Control and Prevention. Patient characteristics and peri-operative characteristics were collected from the medical charts.

Results

A total of 452 patients were included (512 procedures). The overall POWI rate was 11.6% (10% superficial, 1.6% deep). A total of 403 procedures (78.7%) comprised of implant removal below the knee joint with a 12.2% POWI rate. A wound infection following initial fracture treatment was associated with a higher rate of wound infection following implant removal (p=0.012). A POWI occurred more often in younger patients (median age 36 versus 43 years; p=0.004).

Conclusion

The overall incidence of postoperative wound infection was 11.6% with 10% superficial and 1.6% of deep infection in patients with elective implant removal. A risk factor for wound infection following implant removal was a previous wound infection.

INTRODUCTION

Implants are used to stabilize fractures and are often removed at a later stage for various reasons. Indications for implant removal mainly consist pain, functional impairment, prominent material or at patients request.[1] Removal can result in pain relief, improvement in function and a high rate of patient satisfaction.[2,3] Implant removal is a frequently performed procedure and it accounts for up to 29% of all elective surgery and 6.3% of orthopaedic surgical interventions.[4]

Antibiotic prophylaxis is administered prior to placement of implants in order to lower the rate of postoperative wound infection (POWI).[5] However, it is not common practice to administer antibiotic prophylaxis before implant removal. This is because, according to the Centers for Disease Control and Prevention classification of surgical wounds, implant removal is considered as a 'clean' procedure.[6] The effect of pre-operative antibiotics are disputed in clean wounds, as there is lack of evidence that they decrease the rate of POWI of 2%.[6]

Remarkably, in contrast with literature on infectious complications following elective fracture surgery such as open reduction and internal fixation, there is paucity in literature on rates of wound infection following implant removal (Table 1).[2,7-13]

The aim of the current study was to assess the incidence of postoperative wound infection following elective implant removal in a Level 1 and Level 2 Trauma Center and to evaluate possible risk factors.

MATERIAL AND METHODS

We conducted a retrospective cohort study of all consecutive adult orthopaedic trauma patients in two hospitals (Level 1 and Level 2 Trauma Center) who had their implants removed following fracture healing. The electronic hospital databases were searched from 2007 to 2012 for all procedures with implant removal using the appropriate surgical procedure coding reference. The start of the inclusion period coincided with

Table 1. Current literature on implant removal and the incidence of postoperative wound infection.

Study (year)	N of patients	N of POWI (%)
Raahave (1976)[7]	269	7 (3.2)
Richards (1992)[8]	88	0 (0)
Sanderson (1992)[9]	188	27 (14.4)
Minkowitz (2007)[10]	60	0 (0)
Pot (2011)[11]	80	16 (20)
Wadia (2012)[12]	27	0 (0)
Williams (2012)[2]	69	2 (2.9)
Vos (2013)[13]	284	23 (8)

N; Number, POWI; postoperative wound infection the introduction of electronic medical charts. We excluded patients from the analysis with implant removal because of an ongoing infectious complication (persistent infection or chronic plate fistula) and patients with removal as part of a new procedure (e.g. non-union).

Patient-characteristics (gender, age, BMI, ASA-classification, type of fracture) and peri-operative characteristics (time interval from index procedure to implant removal, surgical experience (senior or resident), duration of surgery, administration of antibiotic prophylaxis and type of wound closure (subdivided into intra- and transcutaneous) were obtained from the electronic charts.

Patients were seen within four weeks postoperatively in the outpatient clinic where a wound inspection was performed. The primary outcome, POWI, was subdivided in superficial or deep by applying the criteria of the US Centers for Disease Control and Prevention.[6] A POWI was considered superficial if amendable for treatment with oral antibiotics and was considered as deep when treated with intravenous (IV) antibiotics or surgical wound debridement. Bacterial cultures were obtained postoperatively in the surgical ward or in the outpatient clinic and were recorded. They were collected upon suspicion of a POWI (dry swab). The occurrence of wound dehiscence was documented, which was diagnosed by wound inspection or a negative culture. Patient and peri-operative characteristics were compared between patients with and without POWI.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS, Chicago, Illinois, USA). Normality of continuous data was tested by inspecting the frequency distributions (histograms). Descriptive analyses were performed to compare baseline characteristics between patients with and without POWI. For continuous data mean SD (parametric data) or medians and interquartile ranges (non-parametric data) were calculated. Differences between the two groups of patients with and without POWI were assessed using the Student's T-test (parametric data) or the Mann-Whitney U-test (non-parametric data). Categorical data were compared using the $\chi 2$ test. A p-value $<$ 0.05 was taken as the threshold of statistical significance.

RESULTS

A total of 452 patients with 512 procedures were included. Patient- and perioperative characteristics are presented in Table 2.

Ten percent of patients (N=51) suffered from a superficial POWI and 1.6% (N=8) from a deep POWI. Of these eight patients one patient was treated with IV antibiotics. Seven patients were treated with IV antibiotics and surgical debridement. One of these patients was treated with surgical debridement three times. Forty-one of 51 patients with superficial POWI were treated with oral antibiotics (80.4%). A wound dehiscence occurred in 37 patients (7.2%).

Table 2. Patient- and perioperative characteristics with statistical association on postoperative wound infections following implant removal (N=512).

	N of implant removal (%)	N of POWI (%)	p-value (two-sided)
Patient characteristics			
Male	287 (56.1)	41 (14.3)	0.130
Age (years)*	42 (31-54)*	36 (25-49)*	0.004
BMI	25 (22-28)*	26 (22-30)*	0.336
ASA classification**			1.000
I	370 (72.3)	43 (11.6)	
II	130 (25.4)	14 (10.8)	
III	11 (2.1)	1 (9.1)	
Diabetes Mellitus	15 (2.9)	1 (6.7)	NA
POWI following index procedure	71 (13.9)	15 (21.1)	0.014
Peri-operative characteristics			
Weeks to implant removal	49 (25-78)	53 (34-85)	0.280
Resident performing procedure	299 (60.4)	43 (14.4)	0.551
Duration of surgery (minutes)*	40 (26-60)	46 (30-72)	0.070
Antibiotic prophylaxis	51 (13.6)	5 (9.8)	0.911
Transcutaneous wound closure	226 (69.1)	34 (15)	0.868

*Median with interquartile ranges
** ($\chi 2$) difference in between ASA I and II+III
N; Number, POWI; postoperative wound infection, NA; not available

In 51 patients (10.2%) IV antibiotic prophylaxis was administered prior to implant removal. Five of these patients (9.8%) developed a POWI, which were all superficial infections. Unfortunately, the reason for administration of antibiotic prophylaxis was not routinely documented.

Seventy-three procedures (14.3%) were performed in the upper extremity followed by four POWI (5.5%) versus 439 procedures in the lower extremity (85.7%) with 55 POWI (12.5%) (Figure 1).

Given the current number of patients, surgery performed in the lower extremity was not significantly associated with an increased risk of POWI (p=0.151). Fifteen of 71 patients (21.2%) with POWI following the index procedure developed POWI following implant removal versus 44 patients following 381 uncomplicated procedures (11.5%) (p=0.014).

Cultures were taken in 10 of these 15 patients, of which half showed the same microorganism; a *Staphylococcus aureus*.

A POWI occurred more often in younger patients with a median age of 36 against 43 without a POWI (p=0.004). No association was found with gender, BMI, ASA-classification, smoking, diabetes mellitus, duration to implant removal, surgical experience or type of wound closure (Table 2).

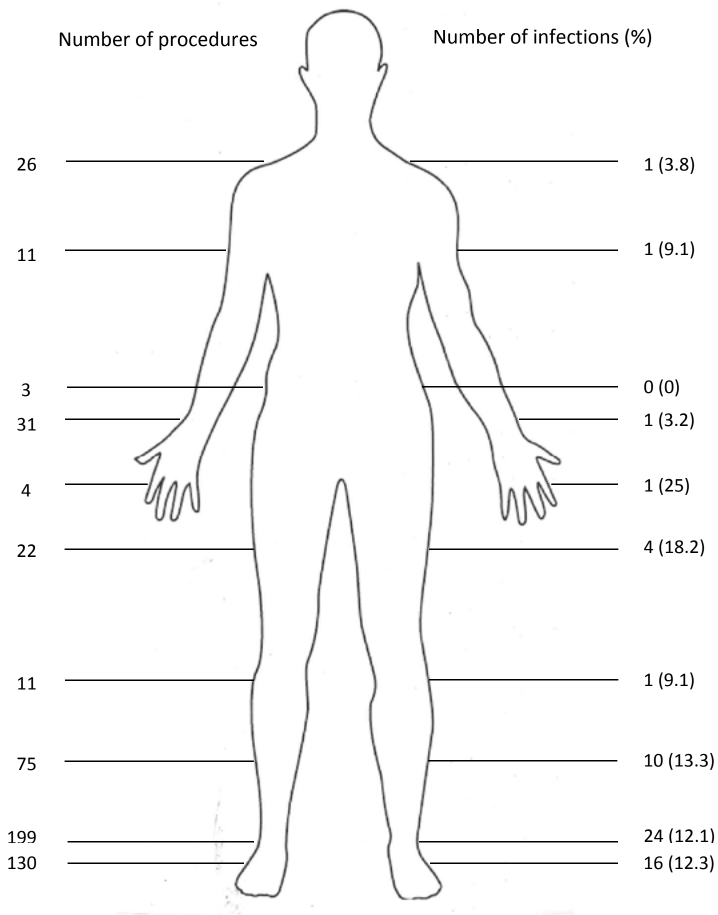

Figure 1. The number of implant removal procedures per body part (left) and the corresponding number of postoperative wound infection (%) (right).

DISCUSSION

Rates of POWI following implant removal from the upper and lower extremity in the current studies were 5.5% and 12.5%, respectively. These rates are consistent with rates in a recent prospective study of 6% and 10%.[13] Other retrospective studies show POWI rates of 9.2% following syndesmotic screw removal and 19% following calcaneal implant removal.[14,15] However, overall a lower POWI rate than 11.6% is reported in literature (Table 1).

The high rate in the current study might be the result of the relatively high number of lower extremity surgery (85.7%) compared to upper extremity surgery (14.3%). In the foot and ankle region the bones are more prominent because of limited soft tissue coverage (as compared to other bones with extensive muscle coverage). For example, after plating of the fibula in ankle fractures the plates are removed in about 27–36% of patients and following a calcaneal fracture almost 50% of patients have their implant removed.[11,16-18]

Remarkably, when looking at wound infection following elective orthopaedic surgery lower rates (0-5.4%) are found compared to implant removal.[5,19-28] This might be the result of instant use, full range of motion and weight bearing of a limb following implant removal compared to fracture surgery, when patients are asked to build up exercise. In addition, it is a secondary procedure through scar tissue.

Importantly, the occurrence of wound infection following fracture surgery was associated with the occurrence of wound infection following implant removal. This information might be of help to the clinician or patient in decision making on implant removal.

Our results show that relatively younger patients are more susceptible to develop a POWI. This could be a result of a higher level of activity or earlier motion of younger patients compared to older patients. Earlier motion is associated with an increased risk of POWI.[29]

Finally, in 10.2% of patients antibiotic prophylaxis was administered preoperatively. This was most likely the result of the surgeon's preference. This missing information is a drawback inherent to the retrospective character and the main limitation of the current study.

In conclusion, the incidence of wound infection following implant removal in a Level 1 and Level 2 Trauma Center is 11.6%. Risk factors for wound infection following implant removal are a previous infection after initial fracture management and younger age. The results of the current study will be used in a prospective study on the effects of antibiotic prophylaxis prior to implant removal on a POWI (www.clinicaltrials.gov).

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Chapter 10

STUDY PROTOCOL
WOUND INFECTIONS FOLLOWING IMPLANT REMOVAL BELOW THE KNEE: THE EFFECT OF ANTIBIOTIC PROPHYLAXIS; THE WIFI-TRIAL, A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background

In the Netherlands about 18,000 procedures with implant removal are performed annually following open or closed reduction and fixation of fractures, of which 30-80% concern the foot, ankle and lower leg region. For clean surgical procedures, the rate of postoperative wound infection (POWI) should be less than ~2%. However, rates of 10-12% following implant removal have been reported, specifically after foot, ankle and lower leg fractures. Currently, surgeons individually decide if antibiotics prophylaxis is given, since no guideline exists. This leads to undesirable practice variation. The aim of the study is to assess the (cost-) effectiveness of a single intravenous dose of cefazolin prior to implant removal following surgical fixation of foot, ankle and/or lower leg fractures.

Methods

This is a double-blind randomized controlled trial in patients scheduled for implant removal following a foot, ankle or lower leg fracture. Primary outcome is a POWI within 30 days after implant removal. Secondary outcomes are quality of life, functional outcome and costs at 30 days and 6 months after implant removal. With 2 x 250 patients a decrease in POWI rate from 10% to 3.3% (expected rate in clean-contaminated elective orthopaedic trauma procedures) can be detected (power=80%, 2-sided alpha=5%, including 15% lost to follow up).

Discussion

If administration of prophylactic antibiotics prior to implant removal reduces the infectious complication rate, this will offer a strong argument to adopt this as standard practice of care. This will consequently lead to less physical and social disabilities and health care use. A preliminary, conservative estimation suggests yearly cost savings in the Netherlands of € 3.5 million per year.

BACKGROUND

Open or closed reduction followed by internal fixation is a frequently performed operation for lower extremity fractures. Indications for implant removal in adult patients include symptomatic hardware (i.e. pain, thin overlying skin and restricted motion), implant failure (breakage, loosening) or a persistent infectious complication of the index procedure (infection or fistula). Following successful surgical procedures for extremity fractures, implant removal is not a routinely indicated procedure. However, removal of implants causing symptoms can result in pain relief and a high rate of patient satisfaction.[1,2]

In the Netherlands about 18,000 implant removals are performed annually, of which 30–80% in the foot, ankle and lower leg region.[3] Literature on implant removal is scarse, but studies show most of the implants removed are following lower extremity injuries, especially below the knee (Table 1).

In addition, there is only a small amount of literature available on the risk of postoperative wound infection (POWI) following implant removal (Table 2). For 'clean'

Table 1. Studies on implant removal and the portion of implant removal from the foot-ankle and lower leg region.

Study (year)	N of cases	N of IR FAL (%)
Raahave (1976)[4]	269	109 (41)
Richards (1992)[5]	88	25 (28)
Sanderson (1992)[6]	188	92 (49)
Minkowitz (2007)[7]	60	42 (70)
Vos (2013)[8]	284	89 (31)
Backes (2014)[9]	512	404 (79)

N; Number, IR; implant removal, FAL; foot- ankle or lower leg

Table 2. Implant removal and incidence postoperative wound infection.

Study (year)	N of cases	N of IR in FAL	N of POWI in FAL (%)
Raahave (1976)[4]	269	109	4 (3.7)
Richards (1992)[5]	88	25	0 (0)
Sanderson (1992)[6]	188	92	12 (13)
Minkowitz (2007)[7]	60	42	0 (0)
Schepers (2011)[10]	76	76	7 (9.2)
Backes (2013)[11]	228	69	6 (9)
Vos (2013)[8]	284	89	9 (11)
Backes (2014)[9]	512	403	49 (12.2)

N; Number, IR; implant removal, NA; not available, POWI; postoperative wound infection, FAL; foot-ankle and lower leg procedures the rate of POWI should be less than ~2%.[11] However, POWI rates of about 10-12%, specifically after foot, ankle and/or lower leg fractures, have been observed both by us and others in studies in which patients with implant removal due to an active wound infection were excluded.[2,8] In syndesmotic screw removal 9.2% of POWI were observed and in calcaneal implant removal following fracture surgery without postoperative complications in dislocated closed calcaneal fractures 19% of POWI were observed.[9,10] Preoperative prophylactic antibiotics might be beneficial to reduce the incidence of infectious complications following implant removal.

To date, only evidence exists on the effectiveness of prophylactic antibiotics in internal fixation with implants, but not in implant removal to prevent POWI.[12] In the Netherlands antibiotic prophylaxis is not routinely administered prior to implant removal as it is considered a clean procedure. Surgeons decide upon themselves if antibiotics are administered prior to implant removal, which is based on expert opinion as no evidence-based guideline exists. This results in an undesirable practice variation.

Our aim is to study the (cost-) effectiveness of a single intravenous dose of cefazolin prior to implant removal following surgical fixation of foot, ankle and/or lower leg fractures. The primary outcome is the incidence of POWI and secondary outcomes are health-related quality of life, functional outcome, health care utilization including trans mural care, and costs from a health care and societal perspective.

METHODS

This double blind randomised controlled trial will randomise between preoperative administration of a single dose of cefazolin or sodium chloride (NaCl) 0.9% in patients scheduled for elective implant removal below the knee. Twenty-one centers will participate, including two Level 1 trauma centers.

Participants

The eligible study population will consist of all consecutive adult patients who are planned for elective implant removal following fracture treatment of the foot, ankle and/or lower leg.

Inclusion criteria

- Patients ≥18 years and ≤75 years of all ethnic backgrounds
- Scheduled for implant removal following foot, ankle and/or lower leg surgery

Exclusion criteria

- Replacement of osteosynthesis material in the same procedure
- Active wound infection or (plate) fistula

- Antibiotic treatment at the time of implant removal for a concomitant disease or infection
- A medical history of an allergic reaction to a cephalosporin, penicillin, or any other β-lactam antibiotic
- Known kidney disease (or known eGFR<60 ml/min/1.73m^2)
- Pregnancy and lactation
- Immunosuppressant use in organ transplantation or rheumatoid joint disease

Interventions

After obtaining informed consent in the outpatient clinic, patients are contacted for a pre-operative assessment of functional status and health-related quality of life by way of self-administered questionnaires before surgery.

At the day of surgery, patients will be randomly assigned web-based in a 1:1 allocation ratio to one of the following study arms:

1. antibiotic prophylaxis: a single intravenous (IV) dose of 1000 mg cefazolin in 10 cc of NaCl 0.9% (intervention group) or
2. no antibiotic prophylaxis: a single IV dose of 10 cc NaCl 0.9%.

After implant removal, patients are routinely assessed within four weeks postoperatively at the outpatient clinic (Figure 1). They are instructed to visit the outpatient clinic sooner in case of any signs of POWI, including warmth, redness, pain, swelling, drainage or a fever above 38.5 degrees Celsius. In case of a POWI, appropriate treatment is started according to protocol. In addition to the one time visit, the patient is asked to return a surgical wound healing post-discharge questionnaire by mail filled in at thirty days postoperatively. At six months after implant removal, patients are contacted by telephone or mail to fill out web-based questionnaires to assess functional outcome, QOL measurement, patient satisfaction, health care resources utilization, costs evaluation and questions on late infections.

Randomization

Randomization will be stratified per center and will be blocked within strata. Randomization sequence is generated by a dedicated computer randomization software program and will be performed preoperatively by a theatre assistant and/or the anaesthesiologist using a dedicated, password protected, SSL–encrypted website, ensuring allocation concealment during the Time Out Procedure. Given the randomization result, the anaesthesiologist will prepare either a syringe with 1000 mg cefazolin or with NaCl 0.9% in the operating theatre or pre-operative holding area, which is administered thirty minutes prior to surgery through a peripheral IV catheter. The IV-catheter is used routinely for either sedatives, muscle relaxants and/or pain medication.

	Enrollment	Allocation	Follow-up	
TIMEPOINT	**-t_1 *(Planning of surgery)***	**0**	***t_1 4(weeks)***	***t_2 (6 months)***
ENROLLMENT:	X	X		
Eligibility screen	X			
Informed consent	X			
Surgery		X		
INTERVENTION:		X		
Administration of AB prophylaxis		X		
ASSESSMENTS:	X		X	X
Incidence of POWI		◆—	—◆—	—◆
EQ-5D-5L	X			X
LEFS	X			X
Patient satisfaction			X	X
iMCQ and iPCQ	X		X	X

Figure 1. Schedule of the study procedures of the WIFI trial. AB; antibiotic, POWI; postoperative wound infection, EQ-5D; EuroQuality of Life-5D, LEFS; Lower extremity functional Scale, iMCQ; iMTA Medical Consumption Questionnaire, iPCQ; iMTA Productivity Cost Questionnaire

Blinding

Importantly, the anaesthesiologist prepares the study medication in the absence of the surgeon and administers the study medication or NaCl 0.9%. Neither the patient nor the surgeon will know if the patient receives prophylactic antibiotics. During the visit to the outpatient clinic the patient is seen by a physician other than the surgeon who performed the surgery. The attending physician will document signs of POWI and will determine its presence or any special findings on physical examination. In addition, a photograph of the wound(s) will be taken by the attending physician and kept in the medical charts. This will enable an independent outcome assessment committee to judge the clinical aspect of the surgical wound, blinded for the study intervention. If the local investigator or attending physician decides unblinding is essential, (s)he will make every effort to contact the coordinating investigator before unblinding to discuss options. Otherwise, the randomization code will be unblinded after analysis of the study results.

Primary Outcome

The primary outcome variable is a POWI within 30 days after implant removal as defined by the criteria applied by the CDC.[11]

Secondary Outcomes

The study will focus on the following secondary outcomes (Figure 1):

- Health-related quality of life as measured by the EQ-5D questionnaire. The EQ-5D-5L is a descriptive system of health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression.[13]
- Functional outcome as assessed with the Lower Extremity Functional Scale (LEFS). The LEFS is a questionnaire containing 20 questions about a person's ability to perform everyday tasks and can be used to monitor the patient over time and to evaluate the effectiveness of an intervention.[14,15]
- Patient satisfaction as measured by a ten-point Visual Analog Scale.
- Health care resources utilization (including amongst others, number of visits to the general practitioner and use of home care organizations) as measured by way of a combination of the Dutch iMTA Medical Consumption Questionnaire (iMCQ) and iMTA Productivity Cost Questionnaire (iPCQ).
- Costs (economic evaluation including budget impact analysis): the economic evaluation of antibiotic prophylaxis in patients scheduled for implant removal following a foot, ankle or lower leg fracture against no prophylaxis as its best alternative will be performed as a cost-effectiveness (CEA) as well as a cost-utility analysis (CUA). The primary economic outcome in the CEA will be the costs per patient without a POWI, which closely relates to the clinical outcome measure. The CUA outcome is the costs per quality adjusted life year (QALY), which is a suitable outcome measure for priority setting during health care policy making across interventions, patient populations, and health care settings.

Sample size

Since information from prospective studies is limited, there is uncertainty about the POWI rate in current medical practice. In recent Dutch prospective studies the incidence of POWI below the knee is 11%, 12.2%, 9.2% and 19%.[2,8-10]. To be on the safe side, a POWI rate of 10% is assumed for the control group. According to the expected rate in clean-contaminated elective orthopaedic procedures, a POWI rate of 3.3% for the antibiotic prophylaxis group is assumed.[11] At least 216 patients per study arm are necessary to detect this difference with a power of 80% and a two-sided alpha of 5%. An estimation of the POWI rate in the control group is planned midway, when 216 patients have been included and reached the primary outcome at 30 days post-surgery. Since only an estimation of the POWI rate of the control group is performed and no treatment effect is tested, the overall Type I error rate is maintained. This estimation will be performed by an independent statistician. To allow for an anticipated drop out of 10-15%, we will include a total of 250 patients per arm.

Based on our recent retrospective cohort studies in both an academic and non-academic hospital an annual number of 33–66 patients are expected to be included in our study for implant removal following lower leg injuries for each participating clinic.[8] With a number of 21 participating centers and an inclusion period of 1.5 years the number of study participants needed, is therefore highly feasible.

Statistical analysis

All analyses will be performed according to the intention-to-treat principle. In addition, protocol analyses will be done to check for robustness of results. A two-sided p-value < 0.05 will be considered statistically significant. In all analyses statistical uncertainties will be quantified using corresponding 95% two-sided confidence intervals. Descriptive analysis will be performed to compare baseline characteristics between patients with and without a POWI. Univariate analysis will be performed for primary and secondary outcomes, followed by a multivariate logistic regression analysis to eliminate confounders. All analyses will be done using the Statistical Package for the Social Sciences (SPSS) version 19.0. (SPSS, Chicago, Illinois, USA).

Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (version 10, 64th WMA General Assembly, Forteleza, Brazil, October 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO) and the Good Clinical Practice Guidelines (ICH-GCP).

Recruitment and consent

The patient will be informed about the WIFI trial when he or she visits the outpatient clinic and implant removal is discussed. Documents are handed to the patient and the patient is asked to read the patient information letter. In order to be able to prepare for the elective (day care) surgery the patient is asked to participate in the trial during this visit to the outpatient clinic and will be asked to sign the informed consent form. Surgeons are asked by the coordinating investigator to check whether patients are included in the pre-operative assessment a day prior to surgery.

Benefits and risks assessment, group relatedness

Patient risks in this study are minimal and acceptable, as cefazolin is currently used as prophylaxis in open reduction and internal fixation of fractures. Patients in both study groups will not be exposed to risks other than in current practice, since there is practice variation in the use of prophylactic antibiotics. As mentioned, currently surgeons decide upon themselves if antibiotics are administered preoperatively. We assume that the routine use of prophylactic antibiotics prior to implant removal following surgical fixation of foot, ankle and/or lower leg fractures will reduce the rate of POWI significantly (by two-thirds, from 10% to 3.3%). If our hypothesis is supported by the results of the proposed RCT, this will offer a strong argument to incorporate prophylactic use of a cefazolin as strategy of choice in (inter)national guidelines for implant removal following fixation of ankle, foot and lower leg fractures. This could lead to less morbidity and social adverse effects in patients like pain, physical discomfort, multiple outpatient clinic visits/less healthcare consumption, work absenteeism and decreased self-confidence.

Indemnities

The institutional review board at the AMC has waived liability insurance, because no additional risk can be attributed to participation in this study.

Publication plan

The principal investigator, the study designer and the study coordinator will be named author. There will be a limit of ten authors. All others will obtain group authorship in the study group. All authors including group members are allowed to present the results.

DISCUSSION

This RCT on wound infection following implant removal is performed in twenty-one different hospitals by a larger number of surgeons, which causes heterogeneity in patients and surgeons. However, we believe this also reflects normal practise in which antibiotic prophylaxis could be beneficial. If our assumption that prophylactic antibiotics prior to implant removal reduces the infectious complication rate is confirmed by this RCT, this will offer a strong argument to adopt a single dose of antibiotic prophylaxis as standard practice of care. This will reduce the incidence of POWI and consequently will lead to less physical and social disabilities and health care use. In addition, it will decrease the rate of use of empiric broad-spectrum antibiotics (and antibiotic resistance) prescribed upon suspicion or diagnosis of a POWI. A preliminary, conservative estimation suggests yearly cost savings in the Netherlands of € 3.5 million per year.

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Chapter 11

WOUND INFECTIONS FOLLOWING IMPLANT REMOVAL BELOW THE KNEE: THE EFFECT OF ANTIBIOTIC PROPHYLAXIS; A RANDOMIZED CONTROLLED TRIAL

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on behalf of the WIFI collaboration
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Submitted

ABSTRACT

Background

Following clean surgical procedures, the rate of postoperative wound infection (POWI) should be less than ~2%. However, a 12.2% infection rate has been reported following implant removal after foot, ankle and lower leg fractures. The aim of this study was to evaluate the effect of a single dose of antibiotic prophylaxis on the incidence of wound infection following implant removal below the knee.

Methods

We performed a double-blind randomized controlled trial with 500 patients in 20 hospitals during 22 months. Exclusion criteria were an active infection or fistula, antibiotic treatment, re-implantation of osteosynthesis material in the same session, allergy for cephalosporins, known kidney disease, immunosuppressant use and/or pregnancy. Patients were assigned to receive either 1000 mg of cefazolin (intervention group) or sodium chloride 0.9 % (control group) intravenously preoperatively. Primary outcome was POWI within 30 days. Patient- and surgical characteristics were collected.

Results

Four hundred seventy patients were available for analysis with 228 patients in the intervention group and 242 patients in the control group. Sixty-six patients developed a POWI (14.4%). In the intervention group 30 patients (13.2%) suffered from POWI versus 36 (14.9%) in the control group ($p=0.599$). The only factor significantly associated with the development of POWI was use of alcohol ($p=0.048$). No other possible risk factors were identified.

Conclusion

No evidence of treatment efficacy has been shown and we therefore believe there is no place for routine administration of a single dose of antibiotic prophylaxis prior to implant removal below the level of the knee.

BACKGROUND

Metal implants are often used in open reduction and internal fixation (ORIF) of fractures. With the use of antibiotic prophylaxis the postoperative wound infection (POWI) rate following ORIF declined from 8.3% to 3.6%, and therefore antibiotic prophylaxis is now routinely administered prior to fracture surgery.[1]

In most patients, removal of implants is not routinely indicated following fracture healing. Still, implant removal is one of the most frequently performed orthopedic procedures worldwide. For example, 28 to 79 percent of implants are removed following lower leg, ankle or foot fracture surgery.[2–8] Wound infection rates of 0-20% following implant removal have been reported, but in only one of these studies POWI was the primary outcome measure.[2–7,9,10] In this study the overall wound infection rate following implant removal was 11.6%, with the highest incidence in the foot, ankle and/or lower leg region (12.2%).[3]

As implant removal is considered a clean surgical procedure with an expected POWI rate of 2-3.3%, preoperative administration of antibiotic prophylaxis is not indicated according to the latest guidelines of the Centers for Disease Control and Prevention (CDC).[11–13] However, as mentioned before, higher rates of POWI than anticipated (compared to rates following ORIF) are reported following implant removal.[2–7,9,10,14] Due to these high rates some concluded that antibiotic prophylaxis should be administered prior to implant removal.[14] Considering the amount of implant removal procedures performed worldwide the lack of available evidence on this subject and the potential beneficial effect of antibiotic prophylaxis on POWI rates is striking.

The aim of this study was to evaluate the effect of a single dose of antibiotic prophylaxis on the incidence of postoperative wound infection following implant removal below the level of the knee, the area with highest rate of infection. Our hypothesis was that antibiotic prophylaxis lowers the incidence of POWI.

METHODS

Trial oversight and design

The WIFI trial was a multicenter, double blind, (placebo) controlled randomized trial in which patients with implant removal below the level of the knee were recruited. The trial was performed in 18 teaching hospitals and 2 academic hospitals in the Netherlands (see the Supplementary Appendix). The study protocol was approved by the medical ethics committee at the Academic Medical Center of the University of Amsterdam and published.[15] After publication of the study protocol diabetes mellitus was added as a second stratification factor and approved by the medical ethics committee. The study was conducted according to the principles of the Declaration of Helsinki (version 10, 64th WMA General Assembly, Forteleza, Brazil, October 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO). The first two authors and the last author had full access to all data and vouch for the accuracy and completeness of the reported data. Also, an independent monitoring board was appointed for assessment of performance of overall study operations and other relevant issues.

The trial was funded by the Netherlands Organization for Health Research and Development (ZonMw), which facilitated scientific peer and patient review prior to grant approval.

Participants

Patients between 18 and 75 years of age with implant removal of the foot, ankle, and/or lower leg following fracture treatment were eligible for inclusion. Exclusion criteria were an active wound infection or fistula, antibiotic treatment at the time of implant removal for a concomitant disease or infection, re-implantation of material in the same session, an allergy for cephalosporins, a known kidney disease, immunosuppressant use and/or pregnancy.

Intervention, randomization and blinding

After obtaining written informed consent eligible patients were randomly assigned to receive either 1000 mg of cefazolin in a bolus of sodium chloride 0.9% intravenously (intervention group) or a bolus of sodium chloride 0.9% intravenously (control group) preoperatively. This bolus, which was identical in appearance, was prepared and administered 60 to 15 minutes prior to incision in the holding or operation theatre by the anesthesiologist or nurse anesthetist in the absence of the surgeon. The dose of 1000 mg is in accordance with the current Dutch guidelines on antibiotic prophylaxis in orthopaedic trauma surgery.[16]

Participants were assigned to the intervention group or the control group in a 1:1 ratio. Randomization sequence was generated by a dedicated computer randomization software program (ALEA software, NKI-AVL, Amsterdam, The Netherlands) and was performed preoperatively by a theatre assistant and/or the anesthesiologist using a dedicated, password protected, SSL–encrypted website, ensuring allocation concealment for the patient and the surgeon.

Outcomes

Primary outcome was POWI within 30 days after implant removal as defined by the criteria applied by the Centers for Disease Control and Prevention.[12,13] Each POWI was classified as superficial or deep. A superficial POWI involves only skin or subcutaneous tissue of the incision and at least one of the following: 1) Purulent drainage from the incision with or without laboratory confirmation 2) Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision 3) At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and deliberately opening of superficial incision by surgeon unless incision is culture-negative 4) Diagnosis with subsequent treatment for superficial POWI by a (orthopedic) trauma surgeon. A deep POWI involves deep tissues and at least one of the following: 1) Purulent drainage from the incision 2) The incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: temperature >38 °C, localized pain or tenderness, unless site is culture-negative 3) An abscess or other evidence of infection involving the incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination 4) Diagnosis with subsequent treatment for deep POWI by an orthopedic trauma surgeon.[12] Secondary outcomes were treatment regimens (local wound care without antibiotics, oral antibiotics, intravenous antibiotics or surgical debridement), collection of a culture swab and subsequent growth of microorganisms. Patients were seen routinely at the outpatient clinic by a blinded physician (and not the surgeon) within four weeks postoperatively. Signs of POWI (warmth, redness, pain, swelling, wound dehiscence, purulent drainage, temperature >38.5 degree Celsius) were documented on a case report form. Patients were instructed to visit the emergency department or outpatient clinic sooner in case of any signs of POWI. In case of POWI, appropriate treatment was started according to local policy.

Data collection

Patient and surgical characteristics were collected. Patient characteristics were gender, age at the time of implant removal, location of index fracture, POWI following the index fracture, reason of implant removal, body mass index (BMI), diabetes mellitus and use of alcohol and/or drugs or nicotine.

The following surgical characteristics were documented: time to implant removal, location of implant removal, complete or partial removal of implants, duration of surgery, tourniquet use and resident or consultant performing surgery. If a wound or perioperative culture was collected the cultured microorganisms were documented.

Statistical analysis

For sample size calculation we assumed an incidence of 3.3% of POWI for the antibiotic prophylaxis group, as this is the expected rate in elective orthopedic procedures.[11,12] In recent studies the incidence of wound infection following implant removal was 9.2-19%[2,3,9,10], with an incidence of 12.2% in the foot, ankle and/or lower leg region. To be on the safe side, a POWI rate of 10% was assumed for the control group. We calculated that a sample size of 216 patients per study arm would provide 80% power to detect this difference with a two-group Chi-square= χ^2 test at a two-sided alpha level of 0.05.

An estimation of the POWI rate in the control group was planned midway (after inclusion of 216 patients) at 30 days postoperatively. Since only an estimation of the POWI rate in the control group was performed and no treatment effect was tested, the overall Type I error rate was maintained. To allow for an anticipated drop out of 10-15%, we included a total of 250 patients per study arm.

All analyses were performed according to plan described in the published protocol.[15] Descriptive analysis was performed to compare baseline characteristics between patients with and without a POWI. χ^2 testing was performed for the primary outcome measurement, followed by a generalized linear (binary logistic) regression model to control for confounding by center and diabetes mellitus as stratification factors. In all analyses statistical uncertainties were quantified using corresponding 95% two-sided confidence intervals. Patients who underwent randomization in error were excluded from analysis (i.e., they did not meet the inclusion criteria or did meet an exclusion criterion). All analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM, Chicago, Ill, USA).

RESULTS

Patients

From November 2014 until September 2016, 500 patients were included in 20 Dutch hospitals, of which two were university hospitals (See Supplementary Appendix). Two hundred thirty two patients received antibiotic prophylaxis intravenously (intervention group) and 245 patients sodium chloride only (control group). Eighty-eight patients were treated in an academic center. After randomization seven patients were lost to follow up. A total of 470 patients were available for analysis with 228 patients in the intervention group and 242 patients in the control group (Figure 1). Baseline characteristics are displayed in Table 1.

Outcomes

Sixty-six patients developed a POWI (14.4%). In the intervention group 30 patients (13.2%) suffered from a POWI versus 36 patients (14.9%) in the control group (p=0.599) (Table 2). Fifty-eight POWI were classified as superficial and eight as deep. Superficial and deep infections were equally distributed among the randomization groups.

In 6 of 8 patients (75%) with a deep POWI surgical debridement was performed and all patients were treated in hospital with intravenous antibiotics. In 49 of 58 patients (84.5%) with a superficial POWI antibiotics were started in the outpatient clinic, in two patients (3.4%) the wound was opened and eight patients (13.8%) were treated conservatively without antibiotics. A variety of microorganisms were cultured in patients with a POWI (Table 3). In 2.7% patients in whom a culture swab was obtained no growth was detected and in 45.5% of patients diagnosed with a POWI no culture swab was collected. Eighty-seven percent of the cultured microorganisms were sensitive to cefazolin.

Patients that reported use of alcohol had an infection more often following implant removal (p=0.048) (Table 4). This remained significant in multivariable logistic regression analysis and sensitivity analysis with possible risk factors from the baseline characteristics (implant removal from the ankle region, intramedullary nail removal and removal of plate and screws). Nicotine or drug abuse, diabetes mellitus, type of surgeon,

Table 1. Baseline characteristics of the patients in the WIFI trial*.

Characteristics	Intervention group∞ (N = 228)	Control group¶ (N = 242)
Male sex – no/total no. (%)	93/228 (40.8)	109/242 (45.0)
Age – yr	43.4±14.8	45.0±15.4
Body-mass index †	26.5±5.4	26.8±5.5
Diabetes mellitus – no/total no. (%)	5/228 (2.2)	7/242 (1.7)
Smoking – no/total no. (%)	56/218 (24.6)	62/231 (26.8)
Alcohol use – no/total no. (%)	57/211 (27.0)	65/224 (29.0)
Drug use – no/total no. (%)	6/228 (2.6)	10/242 (4.1)
POWI following ORIF – no/total no. (%)	15/222 (6.8)	12/238 (5.0)
Reason implant removal§ – no/total no. (%)		
Pain	163/228 (71.5)	182/242 (75.2)
Implant failure	7/228 (3.1)	8/242 (3.3)
Functional problem	15/228 (6.6)	12/242 (5.0)
Patients request	111/228 (48.9)	113/242 (46.7)
Planned procedure	30/228 (13.2)	30/242 (12.4)
Median time to implant removal – months (IQR)	11 (7-16)	11 (7-17)
Location implant removal – no/total no. (%)		
Fore/midfoot	15/228 (6.6)	12/242 (5.0)
Tarsus	30/228 (13.2)	29/242 (12.0)
Ankle ⌘	124/228 (54.4)	149/242 (61.6)
Lower leg	59/228 (25.9)	52/242 (21.5)
Type of implant removal § – no./total no. (%)		
Intramedullary nail ⌘	28/228 (12.3)	11/242 (4.4)
Syndesmotic screw	24/228 (10.5)	29/242 (12.0)
Screw only	52/228 (22.8)	49/242 (20.2)
Plate and screws ⌘	132/228 (57.9)	163/242 (67.4)
Kirschner wire	11/228 (4.8)	13/242 (5.4)

* Plus–minus values are means ±SD. ∞The intervention group was assigned to receive 1000mg of cefazolin intravenously. ¶ The control group was assigned to receive a bolus of sodium chloride intravenously. † The body-mass index is the weight in kilograms divided by the square of the height in meters. A body-mass index of 30 or higher indicates obesity. Data are missing for 20 patients in the treatment group and 25 patients in the control group. ⌘ p=<0.05. § more than one option possible N; Number, IQR; interquartile range, POWI; postoperative wound infection.

type of implant removal, use of a tourniquet and complete removal of implants were not associated with the occurrence of a POWI (Table 4). In the group of patients that had a wound infection following the index procedure a dose of antibiotic prophylaxis had no effect on the occurrence of a wound infection following implant removal. A POWI did not occur more frequently in an academic hospital (p=0.395).

Table 2. Postoperative wound infection outcomes in the WIFI trial.

	Intervention group (N = 228) ∞		Control group (N = 242) ¶			
	No. of patients	**in % (95% CI)**	**No. of patients**	**in % (95% CI)**	**Relative Risk (95% CI)**	**Absolute Risk Reduction (95% CI)**
POWI	30	13.2 (0.09 to 0.18)	36	14.9 (0.11 to 0.20)	0.88 (0.56 to 1.39)	0.02 (-0.05 to 0.08)
Superficial	29	12.7	29	12.0		
Deep	1	0.4	7	2.9		

∞The intervention group was assigned to receive 1000mg of cefazolin intravenously.
¶ The control group was assigned to receive a bolus of sodium chloride intravenously.
N; Number, CI; confidence interval, POWI; postoperative wound infection

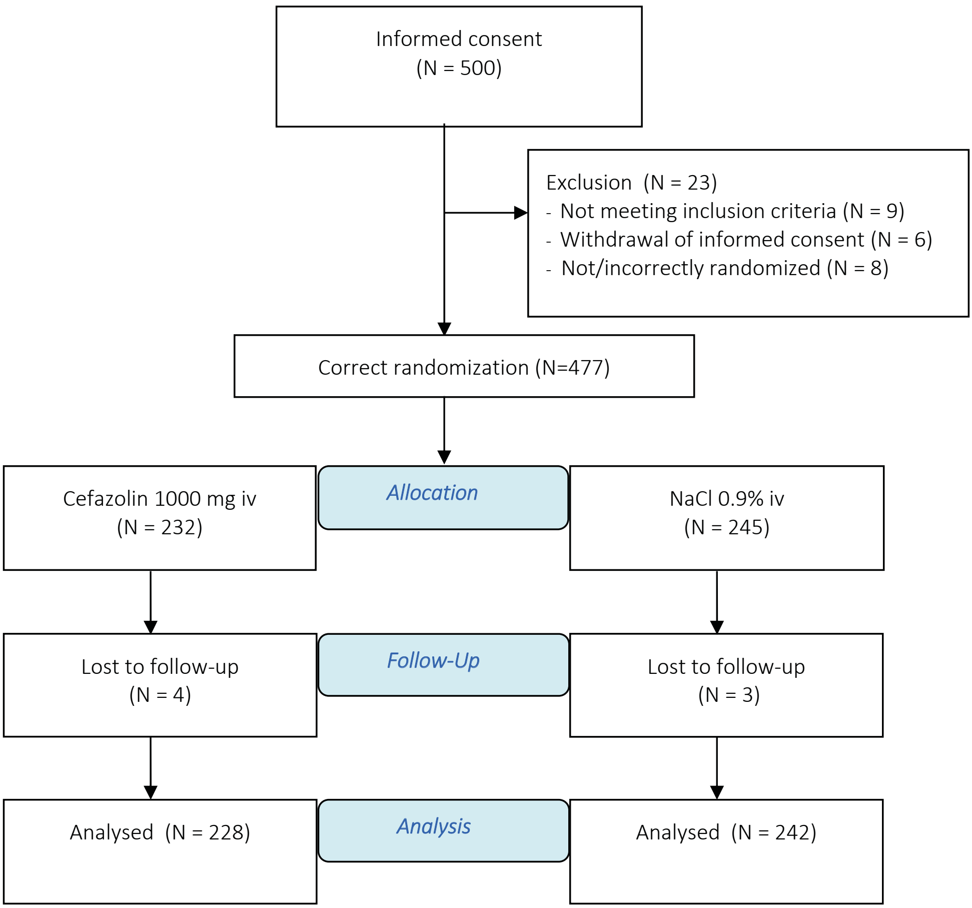

Figure 1. Inclusion flow diagram of the WIFI trial.

Table 3. Growth in culture swabs of patients with POWI§.

	POWI Intervention group (N = 30) ∞		POWI Control group (N = 36) ¶	
		No. of patients with growth of microorganism		**No. of patients with growth of microorganism**
No. of patients with culture swab – no./ total no. (%)	19/30 (63.3)		17/36 (47.2)	
Superficial POWI – no. with culture swab / no. with infection (%)	16/29 (55.2)*	Cocci 9 *Staphylococcus aureus* + 1 Coagulase-negative Staphylococci -/+ 2 Hemolytic Streptococcus + 1 *Peptoniphilus harei* + Rods 1 *Enterobacter cloacae* - 1 *Proteus mirabilis* + 1 *Pseudomonas putida* - Other 2 Skin flora ^ 2 Acinetobacter species -	13/29 (44.8)	Cocci 11*Staphylococcus aureus* + 2Hemolytic Streptococcus + Other 4 Skin flora ^
Deep POWI – no. with culture swab / no. with infection	1/1 (100)	Cocci 1 *Staphylococcus aureus* +	5/7 (71.4)	Cocci 4 Hemolytic Streptococcus + 3 *Staphylococcus aureus* + 1 No growth 1 $

∞The intervention group was assigned to receive 1000mg of cefazolin intravenously. ¶ The control group was assigned to receive a bolus of sodium chloride intravenously. § more than one option possible. * 2 missing data **2 no culture swab obtained. + sensitive for cefazolin. - not sensitive for cefazolin. -/+ majority not sensitive for cefazolin. ^ not applicable. $ Culture swab after start of antibiotic treatment. N; Number, CI; confidence interval, POWI; postoperative wound infection.

Table 4. Patient- and surgical characteristics and association with POWI in the WIFI trial*.

Possible confounder	POWI (N = 66)	No POWI (N = 404)	p-value
Duration of surgery – min∞	36.6±19.4	34.7±19.4	0.471
Substance abuse – no./total no. (%)			
Nicotine	19/62 (30.6)	99/375 (26.4)	0.537
Alcohol ⌘	24/62 (38.7)	98/373 (26.3)	0.048
Drugs	5/61 (8.2)	11/373 (2.9)	0.059
Diabetes mellitus – no./total no. (%)	2/66 (3.0)	10/404 (2.5)	0.680
Resident performing surgery – no./total no. (%)	49/66 (74.2)	291/403 (72.2)	0.882
Tourniquet use – no./total no. (%)	13/64 (20.3)	46/398 (11.6)	0.067
POWI following ORIF – no./total no. (%)	7/62 (11.3)	20/398 (5.0)	0.074
Median time to implant removal – months (IQR)	12 (8-17)	11 (7-16)	0.287
Location of implant removal § – no./total no. (%)			
Forefoot	6/66 (9.1)	44/404 (10.9)	0.830
Ankle	45/66 (68.2)	229/404 (56.7)	0.082
Hindfoot	5/66 (7.6)	32/404 (7.9)	1.000
Lower leg	10/66 (15.2)	103/404 (25.5)	0.087
Type of implant removal § – no./total no. (%)			
Intramedullary nail	2/66 (3.0)	37/404 (9.2)	0.144
Syndesmotic screw	4/66 (6.1)	49/404 (12.1)	0.206
Screw only	13/66 (19.7)	88/404 (21.8)	0.872
Plate and screws	48/66 (72.7)	247/404 (61.1)	0.075
Kirschner wire	4/66 (6.1)	20/404 (5.0)	0.761
Incomplete implant removal – no./total no. (%)	17/66 (25.8)	111/404 (27.5)	0.882

* Plus–minus values are means ±SD. ∞The duration of the surgery was from the time of incision to the time of wound closure. Data are missing for 7 patients. in the intervention group and 44 patients in the control group. ⌘ statistically significant ($p<0.05$). § more than one option possible
N; Number, ORIF; open reduction internal fixation, POWI; postoperative wound infection.

DISCUSSION

In this multicenter, double blind, controlled randomized trial we found that administration of a single dose of antibiotic prophylaxis prior to implant removal below the level of the knee does not result in a significantly lower rate of POWI than no administration of antibiotic prophylaxis.

We detected a high rate of POWI; higher than in most retrospective series.[2–7,9,10,14] Even though POWI rates are often higher in prospective studies as a result of more adequate registration, still the incidence is higher than expected. Importantly, the incidence of POWI following syndesmotic screw removal decreases from 12.1% to 6.1% and the incidence following intramedullary nail removal from 9.2% to 6.1% with administration of antibiotic prophylaxis. However, neither was significant by p-value and this study was not powered to look at the impact on specific procedures. So in contrast to our hypothesis, antibiotic prophylaxis did not statistically significantly influence POWI rate, which also exceed the rates observed following ORIF. The high rate of wound infection following implant removal could be the result of clinical and often pragmatic decision making in the outpatient clinic or in the emergency department by the attending physician. If a surgeon starts treatment upon suspicion of infection this is classified as a POWI, while another physician might have diagnosed wound dehiscence or wound edge necrosis without infection. This is reflected in the high number of patients that were diagnosed with POWI without collection of a wound culture swab.

Cefazolin was used in this study, a first generation cephalosporin, which is a broad spectrum antibiotic with good and rapid bone, soft-tissue and muscle concentrations.[17] Cephalosporins have proven to be effective as antibiotic prophylaxis in orthopedic trauma surgery.[1] It is widely used, as confirmed by a recent survey among US orthopedic surgeons in which 96% of the respondents reported to use cefazolin as the standard antibiotic prophylaxis.[18] Several microorganisms that were cultured in patients with POWI (12.8%) are not sensitive for cefazolin (Table 3), however the majority is sensitive (87.2%) and therefore cefazolin appears to be an adequate option for antibiotic prophylaxis.

We used a dose of 1000 mg of cefazolin. Some advocate administration of 2000 mg if a patient weights more than 86 kilogram.[17] However, a dosage of 1000 mg is recommended as the standard dose in the current guidelines.[16,19] Furthermore there are no RCT's available who show a beneficial effect of weight-adjusted dosing of antibiotic prophylaxis.[13] Some organizations now recommend a 2000 mg dose, but this is solely based on pharmacokinetic and observational studies.[13] Furthermore, as a large majority of the patients weighted less than 85 kilograms, inadequate dosage is an unlikely cause of failure of the primary outcome. Research on whether the biological availability of antibiotics to the lower extremity is adequate enough to prevent development of postoperative wound infection is needed.

Timing of administration of antibiotic prophylaxis has shown to be of importance; antibiotics should be administered within one hour prior to incision.[20] As randomization was performed on the holding or in the operation theatre we can be certain that the allocated treatment was administered within this timespan. Finally, some advocate repeated doses of antibiotic prophylaxis.[18] A Cochrane review has shown that a single dose of antibiotic prophylaxis is sufficient and multiple doses do not lower the POWI rate in surgical fixation of long bone fractures.[21] The guideline of the American Academy of Orthopedic Surgeons (AAOS) therefore only advises redosing if procedure time exceeds 1–2 times the half-life of the antibiotic (1.5–2 hours for cefazolin).[17] Implant removal lasted 36 minutes on average with a maximum of 109 minutes (Table 4), as a result not repeating prophylaxis will not have influenced our results. Thus, we feel that we have administered the correct type of antibiotic, in the correct dose, at the right time without need for redosing and still observe high infection rates following implant removal compared to ORIF procedures.

Other factors may contribute to the development of POWI. In literature obesity, smoking and diabetes mellitus are considered risk factors for the development of wound infection following fracture surgery.[22,23] Interestingly, none of these factors were significantly associated with the occurrence of POWI in uni- or multivariable analysis. The only factor significantly associated with the development of POWI was use of alcohol. An association with overuse of alcohol has been found previously.[23] It is known that stopping alcohol consumption one month preoperatively reduces complications following elective surgery.[24] However its specific role, particularly related to infection, remains scarsely studied.

In this study residents performed the procedure in the majority of patients, which was not associated with the development of POWI. This has also been reported in ankle fracture surgery.[25] We must remark that attribution bias may have played a role here as consultants may have performed more difficult/extensive procedures, which we could not correct for in this study.

In a paper by Pocock et al. several causes for the failure of the primary outcome in the design of a RCT are identified: underpowering, inadequate primary outcome, inappropriate population, inappropriate treatment regimen and deficiencies in trial conduct.[26] We performed an adequate sample size calculation with conservative estimation of treatment effect, used an appropriate and unambiguous primary outcome measure and included the appropriate population and trial regimen. Also, the study was monitored ensuring its good trial conduct. When interpreting the result of a trial three possibilities are proposed; 1) the trial is positive, 2) improve the design of future trials or 3) declare the trial negative. Assessing our results we believe the results of our trial are negative and other actions should be taken to lower wound infection rates following implant removal.

In addition to the negative effects of POWI for the patient, wound infections incur a financial penalty to the health care system. In the current era of increasing burden of health care related costs on governmental spendings, prevention of POWI is of paramount importance. A superficial POWI may cost up to €1600 ($1700) per case and deep wound infections may cost up to €20000 ($21200) per case.[27]

This is the first published prospective study on (infection following) implant removal. It is striking that so little evidence is available on a procedure performed so often. We would like to create awareness on possible wound complications and emphasize that implant removal is not a straightforward procedure. Patients should be adequately counseled on the risks of wound infection following implant removal. The information provided by our study is helpful for shared decision making at the outpatient clinic in assessment of need for implant removal. We advise to leave implants in place if there is no indication for implant removal.

In conclusion, we show no evidence of treatment efficacy and therefore believe there is no place for routine administration of a single dose of antibiotic prophylaxis prior to implant removal below the knee.

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SUPPLEMENTARY APPENDIX

Participating study centers

Academic Medical Center
Alrijne Hospital
Amphia Hospital
BovenIJ Hospital
Catharina Hospital
Deventer Hospital
Flevo Hospitals
Gelre Hospitals
Medical Center Alkmaar
Medical Center Haaglanden Hospital
OLVG East
OLVG West
Red Cross Hospital
Reinier de Graaf Hospital
Spaarne Hospitals
Tergooi Hospitals
Vlietland Hospital
VU University Medical Center
Westfries Gasthuis Hospital

Chapter 12

THESIS SUMMARY AND FUTURE PERSPECTIVES

THESIS SUMMARY AND DISCUSSION

Studies enclosed in this thesis focus on wound complications in two specific areas of lower extremity trauma surgery; calcaneal fracture surgery and implant removal below the knee. There is a special focus on the effectiveness of antibiotic prophylaxis prior to implant removal on the incidence of postoperative wound infection (POWI). In this chapter our main findings are summarized and discussed. In addition, suggestions for future research are made.

PART I CALCANEAL FRACTURE SURGERY

In **Chapter 2** we described the results of a retrospective case series on the incidence and possible risk factors of postoperative wound complications in calcaneal fracture surgery with the extended lateral approach (ELA). This study is an addition to existing literature on risk factors of postoperative wound complications.[1–6] We found a high rate of POWI of 25%. Factors that were associated with an increased risk on development of POWI were: American Society of Anesthesiologists (ASA)-classification higher than 1 and not using a closed suction drain. No drainage had previously not been shown to reduce wound-healing complications in calcaneal fracture surgery. Our results were confirmed in a later study.[7] Placement of a closed suction drain might be a protective measure for development of POWI, since it reduces the likelihood of prolonged oozing from the wound and formation of hematoma. The rate of POWI between patients that stayed in hospital or at home prior to surgery was similar, so we conclude that preoperative outpatient management is acceptable.

As we found such a high rate of wound infection following calcaneal fracture surgery with the ELA in our clinic, we performed a systematic review of the literature in **Chapter 3** to evaluate and quantify geographical differences in the incidence of postoperative wound complications. Large differences were found between countries and continents: for example a median POWI rate of 4.5% in Asia versus 12.1% in Europe. It is possible that orthopaedic and trauma surgeons actually have less postoperative wound complications in Asia as a result of their expertise in this type of surgery. In China, for example, a very low percentage of wound complications was reported in combination with the highest amount of publications on calcaneal fracture surgery with the ELA. Also, the number of patients included in the published articles from China was substantially higher than numbers from other countries. However, a POWI rate of 0% in studies with a large cohort of patients remains extremely unlikely. We emphasize the need for transparent publication on this topic and avoidance of reporting bias and selection bias. For example, loss to follow up or exclusion of patients with high risk of postoperative wound complications (e.g. diabetes mellitus or severe fractures).[7] We strongly advise the use of a reliable postoperative complication registration system and the use of a standardized definition of wound complications for calcaneal fracture surgery. We suggest the criteria set by the US Centers for Disease Control and Prevention.[8,9]

We determined the type of causative pathogens of wound infection following calcaneal fracture surgery in **Chapter 4**, to investigate whether our prophylactic and therapeutic antibiotic regimen was adequate and because we noticed that literature on the pathogens responsible for deep infection of calcaneal fractures is scarce.[10] We found that infections in our hospital were mainly caused by Enterobacteriaceae or *S. aureus*. These findings resulted in a local change of the empiric treatment regimen for wound infection following calcaneal fracture surgery to intravenous flucloxacillin in combination with gentamicin. In addition, we showed that physicians cannot rely on results of superficially obtained cultures for adequate treatment of deep POWI, as many microorganisms are missed in a superficial culture. As the spectrum of sensitivity profiles varies greatly between hospitals and countries, we recommend empiric antibiotic treatment for both gram-positive and gram-negative microorganisms upon suspicion of deep POWI.

The clinical relevance of wound infections following calcaneal fracture surgery was discussed in **Chapter 5**. We evaluated the effect of POWI on functional outcome. We found better outcome scores in patients without POWI, but no statistically significant difference was detected. However, patients with POWI reported a poor and fair outcome significantly more often than patients without POWI. Importantly, almost one-third of patients required adjustment of their work environment following calcaneal fracture surgery. This emphasizes the impact a calcaneal fracture has on day-to-day life and supports the statement that a calcaneal fracture is a life-changing event.[11] Overall patient satisfaction measured by a visual analoge scale was significantly lower in case of POWI, also reflecting the burden a wound complication causes.

In **Chapter 6** we showed that the development of an infection following calcaneal fracture surgery is correlated with a collapse of the calcaneus postoperatively. A possible explanation is that a calcaneal collapse and a POWI are both result of compromised vascularization of the lateral side of the foot caused by the ELA.[12] The collapse could be an effect of delayed union due to this decreased vascularization, disruption of microcirculation or delayed healing due to the infection itself. A postoperative CT scan may be advisable following 12 weeks of non-weight bearing to evaluate bone healing prior to weight bearing in patients suffering from a POWI.

Recently, less invasive techniques emerged, like the sinus tarsi approach (STA). A lower POWI rate of 6-14% is reported following the STA.[13–15] In **Chapter 7** we performed a study to compare the incidence of infectious complications following the extended lateral incision and the sinus tarsi incision in our hospital. We found that the incidence of postoperative wound complications was significantly lower following the STA. No signifcant difference was observed in the restoration of calcaneal anatomy between these two approaches. Additionally, surgery with the STA lasted nearly half an hour shorter. The current study strengthens the available evidence on similar anatomical reduction, fewer wound complications and a shorter surgical time using the STA.[16] The STA is therefore now our preferred approach for displaced Sanders type II and III calcaneal fractures. A recent meta-analysis also showed that not only problems in wound healing can be reduced, but also similar functional outcomes can be achieved in calcaneal fracture surgery with the STA compared to the ELA.[17]

PART II IMPLANT REMOVAL

We found that half of the patients with calcaneal fracture surgery via the ELA had their implants removed (Chapter 5), which is in concordance with current literature.[20,21] In **Chapter 8** we reported that nearly 46% underwent implant removal due to symptomatic implants, implant malposition or a persistent wound infection or plate fistula. In total, 16% of patients suffered from a postoperative wound complication. Importantly, one in ten patients without previous wound problems suffered from an infection following implant removal. This information can be used for patient counseling and shared decision-making.

We investigated the incidence of wound complications following implant removal in general in **Chapter 9**, as we noted the high incidence of postoperative wound complications following implant removal after calcaneal fracture consolidation. In addition, we found it remarkable that this subject had received little attention in literature.[22–29] The overall incidence of POWI in an academic and teaching hospital was 11.6% in patients with elective implant removal and 12.2% following implant removal in the lower leg. This is higher than one might expect following elective orthopaedic trauma surgery. A risk factor for the occurrence of an infection following implant removal was an infection following the index procedure. This information is also beneficial for shared decision making in the need for implant removal and risk of POWI. These complication rates could not go unattended. In the Netherlands, it is policy to administer antibiotic prophylaxis prior to osteosynthesis, as lower rates of POWI have been found following preoperative administration of a single dose of antibiotic prophylaxis.[30] Until now, it was unclear whether administration of antibiotic prophylaxis prior to implant removal lowers the incidence of postoperative infectious complications as well, since no national or international guidelines exist. In **Chapter 10** we described the protocol of the study presented in **Chapter 11,** in which we evaluated the effect of a single dose of antibiotic prophylaxis on the incidence of wound infection following implant removal below the knee. Again, we found a high rate of POWI of 14.4%. Administration of a single preoperative dose of antibiotic prophylaxis did not decrease the incidence of POWI. We found a trend in effectiveness of prophylaxis in syndesmotic screw and intramedullary nail removal, but no statistical significance was reached and the study was not powered to look at the impact of specific procedures. This high rate of POWI might occur as implant removal is at least a second operation in the same area. It could also be the result of the, often pragmatic, decision making in the outpatient clinic or in the emergency department by the attending physician. If a surgeon starts treatment upon suspicion of infection this is classified as a POWI, while another physician might have diagnosed a wound dehiscence or wound edge necrosis without infection. This is reflected in the high number of patients that was diagnosed with POWI without collection of a wound culture swab. Again, we advise the use of a standardized definition of wound infection following trauma surgery and suggest the criteria set by the Centers for Disease Control and Prevention.[8,9] As we showed no evidence of efficacy we believe there is no place for routine administration of a single dose of antibiotic prophylaxis prior to implant removal below the level of the knee. In addition, we advise to leave implants in place if there is no indication for implant removal.

GENERAL CONCLUSION

In this thesis we show that the incidence of wound infection following lower extremity surgery is high. Use of a standardized definition of wound complications for (calcaneal) fracture surgery is of paramount importance, as well as transparent publication on wound complications. The preferred approach in operative treatment of displaced intra articular calcaneal fractures is the sinus tarsi approach, which has similar anatomical reduction, fewer wound complications and a shorter surgical time compared to the extended lateral approach. Implant removal of the lower extremity is not a straightforward procedure that is hampered by high postoperative wound infection rates. There is no place for routine administration of antibiotic prophylaxis prior to implant removal below the knee.

FUTURE PERSPECTIVES

In **Part I** we found that the extended lateral approach in calcaneal fracture surgery is accompanied with high rates of POWI. We stated that placement of a closed suction drain decreases the risk of POWI, because it most likely reduces prolonged oozing from the wound and formation of hematoma. Recently, the use of prophylactic negative wound pressure therapy on closed surgical incisions in high-risk lower extremity trauma has gained attention because it reduces POWI.[31] We will investigate the effect of a new portable single use negative pressure wound therapy device on the incidence of wound complications following calcaneal fracture surgery.

The learning curve of open reduction and internal fixation of intra-articular calcaneal fractures is estimated to be 35-50 fractures.[19] A Dutch survey showed that only 13% of trauma and surgery departments treat more than ten intra-articular calcaneal fractures per year.[32] Surgical experience and institutional fracture load have been correlated with occurrence of POWI and improved outcome in calcaneal fracture surgery.[2,6,18,19] We believe centralization of calcaneal fracture surgery will lower the incidence of postoperative wound complications, especially now the less invasive sinus tarsi approach has gained interest, an approach that is still performed less frequently compared to the extended lateral approach. We do not have data of the learning curve of the sinus tarsi approach yet. Studies on the effect of surgical experience with the sinus tarsi approach on the incidence of postoperative wound complications and studies on long-term functional outcome following the sinus tarsi approach are needed.

In **Part II** we showed that implant removal below below the level of the knee is accompanied with surprisingly high rates of postoperative wound infection and should not be considered a straightforward procedure. We will use the results of this study to set up an evidence-based guideline on antibiotic prophylaxis. Further research is necessary to investigate as to why infections occur frequently following this type of surgery.

Many patients have their implants removed if they are symptomatic and cause discomfort. In the RCT published in this thesis no culture swabs were taken from the implant during the implant removal procedure. It would be interesting to objectify bacterial colonization of implants, as an occult infection could cause pain. So the pain thought to be caused by the implant itself could be result of a low-grade infection. In arthroplasty revisions the use of implant sonicate cultures has proven to improve the diagnostic sensitivity for detection of presence of bacteria in both clinical and occult infections.[33] Use of (sonicate) cultures in a future study could gain insight in the development of infection following implant removal and subsequent treatment strategies.

In addition, it is not clear what the effect of tissue handling and tissue damage is during implant removal, as it is at least a secondary procedure in the same area. For example, it is unclear what the effect of scar incision versus scar excision is on the incidence of postoperative wound complications. We suggest a prospective study on the incidence of postoperative wound complications with and without scar excision following implant removal.

Furthermore, patients are often advised not to mobilize or are immobilized with a cast following fracture surgery. Following implant removal however, patients are never immobilized. Current evidence suggests that POWI and need for implant removal are more common after early ankle movement compared to ankle immobilization following ankle fracture surgery.[34] We believe immobilization until wound healing might lower the risk on development of a postoperative wound complication following implant removal as well. A well set up study is needed to analyze the effect of immobilization following implant removal.

Finally, we are currently investigating the effects of implant removal and postoperative wound complications following implant removal on functional outcome, patient satisfaction and cost-effectiveness.

My goal is to challenge trauma surgeons and researchers to publish their complications and their subsequent management. Sometimes you can learn more from the 10% of patients with postoperative complications than from the 90% of patients that heal without problems.

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Appendix &

DUTCH SUMMARY

Dit proefschrift is gericht op het optreden van complicaties na de operatieve behandeling van intra-articulair gedisloceerde calcaneus fracturen en na het verwijderen van osteosynthesemateriaal (VOSM) onder het niveau van de knie. **Hoofdstuk 1** is een algemene introductie. **Deel I** van dit proefschrift focust op complicaties na calcaneus chirurgie en **deel II** op complicaties na VOSM uit het onderbeen.

Het doel van Deel I is

- Het bepalen van de incidentie en risicofactoren van wondcomplicaties en functionele uitkomst na operatieve behandeling van gediscloceerde intra-articulaire calcaneus fracturen
- Identificeren van de verwekkers van postoperatieve wondinfecties na calcaneus chirurgie
- Het vergelijken van de incidentie van postoperatieve wondcomplicaties en de anatomische repositie van de extended laterale benadering met de sinus tarsi benadering

In **Hoofdstuk 2** wordt de incidentie van postoperatieve wondcomplicaties na operatieve behandeling van de calcaneus middels de extended laterale benadering (ELB) in een tertiair verwijscentrum beschreven en worden risicofactoren op het ontstaan van een postoperatieve wond infectie (POWI) geanalyseerd. Bij één op vier patiënten trad een POWI op. Risicofactoren op het ontstaan van een POWI zijn een American Society of Anaesthesiologists (ASA) classificatie >1 en het niet achterlaten van een redonse drain. Het niet plaatsen van een redonse drain is niet eerder geassocieerd met een verhoogd risico op het ontstaan van een POWI. Deze studie is een aanvulling op de huidige literatuur[1–6] en onze resultaten zijn in een latere studie bevestigd.[7] Het plaatsen van een redonse drain lijkt de kans op een POWI te verkleinen, omdat het wondlekkage en het risico op een postoperatief hematoom vermindert. Patiënten die preoperatief opgenomen zijn in het ziekenhuis blijken een even groot risico op een POWI te hebben als patiënten die voor de operatie thuis verblijven. Het lijkt dus veilig om patiënten met goede instructies thuis te laten verblijven tot de operatie plaats kan vinden.

Omdat de incidentie van POWI na calcaneus chirurgie met de ELB in ons ziekenhuis zo hoog blijkt en er in de literatuur uiteenlopende percentages beschreven zijn, verrichten wij een review in **Hoofdstuk 3**. Hierin worden de geografische verschillen in incidentie van postoperatieve wondcomplicaties na calcaneus chirurgie met de ELB geanalyseerd. Er worden grote verschillen tussen landen en continenten geïdentificeerd: bijvoorbeeld een mediaan infectiepercentage van 4.5% in Azië versus 12.1% in Europa. Dit kan een gevolg zijn van de expertise op dit gebied in Azië. In China wordt bijvoorbeeld een heel laag infectie percentage gerapporteerd in combinatie met de meeste publicaties op dit gebied. Ook het aantal patiënten per studie is hoger dan in andere landen. Een mediaan infectie percentage van 0% in een grote studie is echter zéér onwaarschijnlijk. We benadrukken het belang van transparantie in rapporteren en publiceren van wond complicaties en het vermijden van rapportage en selectie bias. Dit laatste door bijvoorbeeld patiënten zonder langdurige postoperatieve follow up of patiënten die een verhoogd risico hebben op het ontstaan van een POWI (bijvoorbeeld diabetes mellitus of een ernstige fractuur) te excluderen. We adviseren om een betrouwbaar registratie systeem en een gestandaardiseerde definitie te gebruiken voor het diagnosticeren of classificeren een postoperatieve wondcomplicatie, zoals de criteria van de US Centers for Disease Control and Prevention.[8,9]

De huidige literatuur over de micro-organismen die een diepe POWI veroorzaken of onderhouden is beperkt.[10] In **Hoofdstuk 4** ontdekken we wat de verwekkers zijn van een POWI na calcaneus chirurgie en onderzoeken we of ons profylactische en therapeutische antibiotica beleid adequaat is. In ons ziekenhuis worden POWI's vooral veroorzaakt door Enterobacteriaceae en *S. aureus*. Naar aanleiding van deze studie schrijven we nu flucloxacilline in combinatie met gentamycine voor bij de empirische behandeling van een POWI na calcaneus chirurgie. Daarnaast tonen we aan dat de behandelend arts niet op de resultaten van een oppervlakkige wondkweek kan vertrouwen om de juiste antibiotische behandeling bij een patiënt met een POWI te starten, omdat veel micro-organismen gemist worden in een oppervlakkige uitstrijk in vergelijking met een diepe kweek. Omdat de gevoeligheid van bacteriën op een antibioticum per centrum en land verschilt raden we aan bij verdenking op een diepe POWI empirische antibiotische behandeling met dekking voor zowel gram negatieve bacteriën als gram positieve bacteriën te starten na een debridement.

De klinische relevantie van het ontstaan van een POWI na calcaneus chirurgie wordt besproken in **Hoofdstuk 5**. In dit hoofdstuk evalueren we de gevolgen van een POWI op de functionele uitkomst. Hiervoor worden vragenlijsten gebruikt, waarbij patiënten zonder POWI beter scoren. Dit blijkt echter niet statistisch significant. We tonen wel aan dat patiënten met een POWI vaker een redelijk tot slechte functionele uitkomst rapporteren dan patiënten zonder een POWI. Het blijkt ook dat bijna één op de drie patiënten aanpassingen in zijn of haar werk nodig heeft na operatieve behandeling van een calcaneus fractuur. Dit toont aan dat calcaneus chirurgie een grote impact heeft op het dagelijks leven van een patiënt en dit ondersteunt de uitspraak dat een calcaneus fractuur een life-changing event is.[11] Tenslotte blijkt ook uit onderzoek naar patienttevredenheid dat patienten met een POWI significant minder tevreden zijn.

In **Hoofdstuk 6** tonen we aan dat het optreden van een POWI na calcaneus chirurgie geassocieerd is met een afname in de hoek van Böhler op postoperatieve Röntgenfoto's. Een POWI en een postoperatieve afname in de hoek van Böhler kunnen beiden het gevolg zijn van verminderde vascularisatie door de incisie (ELB).[12] Het inzakken van de hoek van Böhler kan ook een effect zijn van vertraagde fractuur consolidatie door de aanwezigheid van een infectie. Men kan overwegen om een CT scan te maken na een periode van 12 weken niet belasten bij patienten met een POWI, voordat met volledig belasten van het been gestart wordt.

Recent is een minder invasieve benadering van de calcaneus in populariteit toegenomen, mede vanwege het lagere risico op postoperatieve wondcomplicaties bij de sinus tarsi benadering (STB).[13–15] In **Hoofdstuk 7** wordt de incidentie van postoperatieve wondcomplicaties van de ELB en van de STB vergeleken en wordt onderzocht of de anatomische repositie net zo goed is. Bij de STB treden significant minder wondcomplicaties op in vergelijking met de ELB (7% versus 31%). De anatomische repositie (step, varus/valgus, postoperatieve hoek van Böhler, postoperatieve breedte van de calcaneus) is vergelijkbaar tussen beide benaderingen. De operatieduur bij de STB is echter wel bijna een half uur korter. Onze studie bekrachtigt de huidige literatuur over een vergelijkbare anatomische repositie, minder wondcomplicaties en een kortere operatieduur bij de STB.[16] Bij Sanders type II en III calcaneus fracturen heeft de STB voorkeur, zeker omdat een recente meta-analyse tevens laat zien dat dezelfde functionele uitkomsten behaald kunnen worden met de STB in vergelijking met de ELA.[17]

Het doel van Deel II is

- Het bepalen van de incidentie van verwijderen van osteosynthesemateriaal na calcaneus chirurgie
- Het bepalen van de incidentie van verwijderen van osteosynthesemateriaal in het algemeen en uit het onderbeen
- Het nut onderzoeken van antibioticaprofylaxe ter preventie van postoperatieve wondinfecties na het verwijderen van osteosynthesemateriaal uit het onderbeen

Bij bijna de helft van de patiënten met operatieve behandeling van van een calcaneus fractuur via met de ELB de wordt het osteosynthesemateriaal verwijderd (Hoofdstuk 5), wat overeen komt aantallen in de beperkt beschikbare literatuur over dit onderwerp beschreven worden.[20,21] In **Hoofdstuk 8** rapporteren we dat bijna 46% van de patiënten osteosynthesemateriaal uit de calcaneus laat verwijderen vanwege klachten, malpositie van osteosynthesemateriaal of vanwege een persisterende infectie of plaatfistel. Na VOSM trad er bij 16% van de patiënten een POWI op. Opvallend is dat bij één op tien patiënten waarbij geen wondinfectie optrad na de primaire behandeling van de calcaneus fractuur wel een POWI optrad na VOSM. Deze informatie kan gebruikt worden in de spreekkamer bij indicatie stelling voor VOSM, voorlichting en shared decision making.

Omdat zo'n hoog infectie percentage wordt aangetoond na VOSM uit de calcaneus, wordt de incidentie van wondcomplicaties na VOSM in het algemeen onderzocht in **Hoofdstuk 9.** Het is opvallend hoe weinig er gepubliceerd is over VOSM.[22–29] De incidentie van een POWI na het VOSM uit de bovenste en onderste extremiteit is 11.6% en 12.2% bij VOSM uit het onderbeen. Dit percentage is hoger dan men zou verwachten na electieve trauma chirurgie. Een risicofactor voor het optreden van een wondinfectie na VOSM is een infectie na de eerdere fractuur behandeling. Deze informatie kan ook in de spreekkamer gebruikt worden om de noodzaak en risicofactoren voor VOSM te bespreken met de patiënt.

De incidentie van POWI na VOSM uit het onderbeen is opvallend hoog. In Nederland is het gebruikelijk om antibioticaprofylaxe toe te dienen voor osteosynthese, omdat dit het risico op het ontstaan van een POWI verlaagt.[30] Tot op heden was het niet duidelijk of het toedienen van antibioticaprofylaxe voor VOSM ditzelfde effect heeft. De indicatie om wel of geen antibioticaprofylaxe toe te dienen wordt niet beschreven in (inter) nationale richtlijnen. In **Hoofdstuk 10** beschrijven we het protocol van de studie die we in **Hoofdstuk 11** presenteren. In dit hoofdstuk wordt het nut van een eenmalige gift antibioticaprofylaxe voor VOSM uit het onderbeen geëvalueerd. Opnieuw vonden we een hoog infectiepercentage van 14.4%. Het intraveneus toedienen van 1000 mg cefazoline blijkt echter het risico op het ontstaan van een POWI niet significant te verlagen. Er lijkt een effect te zijn bij het verwijderen van stelschroeven en intramedullaire pennen, maar dit is niet significant. Het hoge percentage van POWI na VOSM zou een gevolg kunnen zijn van een (tenminste) tweede ingreep in hetzelfde operatie gebied. Het kan ook komen door de vaak pragmatische besluitvorming van een (dienstdoend) arts bij het vermoeden op een POWI, omdat het starten van behandeling een criterium is voor een POWI volgens de classificatie van de Center for Disease Control and Prevention.[8,9] De ene arts kan een wond dehiscentie vaststellen, terwijl een andere arts een verdenking heeft op een POWI. Dit wordt ook gereflecteerd in het feit dat bij veel patiënten antibiotische behandeling gestart wordt zonder dat er eerst kweken zijn afgenomen.

We concluderen dat er geen indicatie is voor toedienen van antibioticaprofylaxe bij VOSM uit het onderbeen en adviseren osteosynthesemateriaal in situ te laten als er geen medische indicatie is voor het verwijderen hiervan.

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Wound infections following implant removal below the knee: the effect of antibiotic prophylaxis; a randomized controlled trial. *Submitted*

Dingemans SA, Birnie MF, Backes M, de Jong VM, Luits JSK, Goslings JC, Schepers T
Prophylactic negative pressure wound therapy after lower extremity fracture surgery: a matched case series *Submitted*

Appendix &

PHD PORTFOLIO

PhD period: 2013 –2017
PhD supervisor: Prof. dr. J.C. Goslings

PHD TRAINING	Year	Workload (ECTS)
ANIOS Chirurgie OLVG West	2013	
ANIOS Chirurgie Academisch Medisch Centrum	2014	
AIOS Chirurgie OLVG West	2014-2016	
AIOS Chirurgie Academisch Medisch Centrum	2016-2017	
General courses		
BROK (Basiscursus Regelgeving Klinisch Onderzoek)	2014	0.9
Evidence Based Surgery	2015	0.9
Scientific writing in English for publication	2016	1.5
Specific courses		
ABCDE for physicians	2012	
Advanced Trauma Life Support, Stichting ATLS	2013	
Basic Principles of Fracture management, Leeds	2015	0.5
Hip fragility fractures, Davos	2016	0.5
Seminars, workshops and master classes		
Weekly department seminars	2013-2017	3.75
Regionaal refereren region II	2013-2017	0.4
Monthly research meetings Trauma Unit	2013-2017	3.1
Medical Business Masterclass	2016-2017	1.5
(Inter)national conferences		
Assistentensymposium Traumachirurgie	2013	0.25
European Congress of Trauma & Emergency Surgery	2013-2017	2.5
Traumadagen NVT	2013-2017	2.5
NVvH Chirurgendagen	2013-2017	2.5
NVvH Najaarsdag	2013-2017	1.25
Surgical Infection Society-Europe	2016	0.5
Edinburgh Trauma Symposium	2016	0.5
4th Symposium Impaired mobility Amsterdam	2013	0.25
Oral presentations		
Preventie van wondcomplicaties na het verwijderen osteosynthesemateriaal na operatieve behandeling van fracturen in de enkel en/of voet. Advances Symposium AO Nederland, Zwolle.	2013	0.5
Wondcomplicaties bij open repositie en interne fixatie van calcaneus fracturen. NVvH Chirurgendagen, Veldhoven.	2013	0.5
Antibioticaprofylaxe bij het verwijderen van osteosynthesemateriaal, de eerste stap naar uniformiteit. 4th Symposium Impaired mobility Amsterdam, AMC Amsterdam.	2013	0.5

	Year	Workload (ECTS)
Antibiotica profylaxe en preventie van wondinfecties bij verwijderen van osteosynthesemateriaal onder de knie. Advances Symposium AO Nederland, Sint Michielsgestel.	2014	0.5
Functional outcome in patients with a wound infection following calcaneal fracture surgery. 15th European Congress of Trauma and Emergency Surgery & 2nd World Trauma Congress, Frankfurt.	2014	0.5
Wound infections following elective implant removal following fracture healing; incidence and risk factors. 15th European Congress of Trauma and Emergency Surgery & 2nd World Trauma Congress, Frankfurt.	2014	0.5
Determinatie van verwekkers van wondinfecties bij operatief behandelde calcaneus fracturen en hun behandeling. Traumadagen, Amsterdam.	2014	0.5
A study comparing the extended lateral and the sinus tarsi approach in displaced intra-articular calcaneal fractures; setting the new gold standard. Traumadagen, Amsterdam.	2014	0.5
High rate of postoperative wound infection following implant removal. Surgical Infection Society-Europe 2016, Amsterdam.	2015	0.5
Wound infections following implant removal below the knee; the effect of antibiotic prophylaxis; study protocol of the WIFI-trial, a multi center randomized controlled trial. Surgical Infection Society-Europe, Amsterdam.	2016	0.5
Determination of pathogens in postoperative wound infections in surgically reduced calcaneal fractures and implications for treatment. Surgical Infection Society-Europe, Amsterdam.	2016	0.5
Wound infection following implant removal; results of the WIFI trial, a multicenter RCT on the effect of antibiotic prophylaxis prior to implant removal. Traumadagen, Amsterdam.	2016	0.5
Poster presentations		
Is het verwijderen van osteosynthesemateriaal wel een schone operatie? Traumadagen, Amsterdam.	2013	0.5
Incidentie en risicofactoren van wondinfecties na verwijderen van osteosynthesemateriaal; bovenste versus onderste extremiteit. NVvH Najaarsdag, Den Bosch.	2013	0.5
Predicting loss of height in surgically treated displaced intra-articular fractures of the calcaneus. 16th European Congress of Trauma and Emergency Surgery & 3rd World Trauma Congress, Amsterdam.	2015	0.5
Determination of pathogens in postoperative wound infections in surgically treated calcaneal fractures. 16th European Congress of Trauma and Emergency Surgery & 3rd World Trauma Congress, Amsterdam.	2015	0.5

PhD Portfolio (continued)

TEACHING	Year	Workload (ECTS)
Lecturing		
Fasciitis necroticans, haast! *Invited speaker.* Amsterdam IC Symposium	2015	0.5
Acute buikpijn bij volwassenen. Hogeschool Inholland	2015 - 2017	1.5
Tutoring, Mentoring		
Supervising		
Student M.C. Dorr	2015	1
Student K.E. Spierings	2015, 2016	1
Other		
Reviewer for The Bone and Joint Journal	2016	1
PARAMETERS OF ESTEEM		
Grants		
Goed Gebruik Geneesmiddelen, ZonMw (€ 251.848)	2014	
Awards and Prizes		
AO Nederland Research Grant (€5000)	2013	
Best Oral Presentation Traumadagen (€250)	2016	

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PhD portfolio

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Appendix &

ABOUT THE AUTHOR

Manouk Backes was born on the 20th of November 1984 in Leiden. She attended the Stedelijk Gymnasium in Leiden and travelled for two years after graduating in 2003. She was admitted to medical school at the University of Amsterdam in 2005. After graduating in 2012 she started working as a non-training surgical resident in the Sint Lucas Andreas Hospital (OLVG West) under supervision of Dr. B.C. Vrouenraets. In addition, she started doing research projects under supervision of Prof. dr. J.C. Goslings, Dr. N.W.L. Schep and Dr. T. Schepers in the Academic Medical Center Amsterdam, which led to the writing of this thesis. After working as a non-training surgical resident in the Academic Medical Center Amsterdam under the supervision of Prof. dr. O.R.C. Busch, she started her training in General Surgery in 2014 at the Sint Lucas Andreas Hospital (OLVG West). Simultaneously, she continued conducting research on a parttime basis after securing a large government grant (ZonMW Goed Gebruik Geneesmiddelen) for the WIFI-trial (this thesis). From 2017 she will continue her surgical training fulltime in the Academic Medical Center and the Albert Schweitzer Hospital (Dr. P.W. Plaisier).