ORIGINAL RESEARCH

Below-knee amputation under spinal anesthesia for osteomyelitis of the diabetic foot: Assessment of histopathology, microbial infection, and management

[1]Dr. Balendra Singh Sodhi, [2]Dr. (Lt Col) Shoba Srinivasan, [3]Dr. Vijay Kumar Sharma, [4]Dr. Hiren Vipinchandra Shah

[1]Associate Professor, Department of Pathology, Surabhi Institute of Medical Sciences, Siddipet, Telangana, India
[2]Classified Specialist Microbiology, Military Hospital, Kirkee, Pune, Maharashtra, India
[3]Associate Professor, Department of Anaesthesia, Adesh Medical College and Hospital, Shahbad, Haryana, India
[4]Associate Professor, Department of Orthopaedics, Ananta Institute of Medical Sciences and Research Centre, Udaipur, Rajasthan, India

Corresponding Author
Dr. Hiren Vipinchandra Shah
Associate Professor, Department of Orthopaedics, Ananta Institute of Medical Sciences and Research Centre, Udaipur, Rajasthan, India
Email: hirenvshah24@gmail.com

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ABSTRACT
Amputation may result from a common complication known as diabetic foot infection. Osteomyelitis outside of the context of the diabetic foot has a poor prognosis when it is present at the histopathologic margin of resection. In the prospective study design, we sought to evaluate clinical complications, healing, and microbiological evaluation of osteolyelitic and related amputations in patients with diabetes. We evaluated the frequency of amputation, the length of hospitalization, the causative organism's microbial culture, and histological parameters. Out of 18 patients, 12 had below-knee-above-ankle (major) amputations, and 6 had below-ankle (minor) amputations. The average age of the amputee patients was approximately 67.2 years. The length of hospitalization was longer in cases of major amputations. The pattern of microbial growth was similar in major vs. minor amputation osteomyelitis, and a similar range of microorganisms was reported in swabs, soft tissue, and bone cultures. Evaluation of osteomyelitis may help in planning for amputaions, which require the assessment of associated complications and related biochemical and histological parameters. We suggest that critical pathological evaluation of osteomyelitis may help in the determination of an antibiotic regimen post-amputation.

Keywords: Diabetes, Osteomyelitis, Amputation, Microbial assessment, Surgery

INTRODUCTION

A recent IDF diabetes atlas predicted that the global prevalence of diabetes among people aged 20 to 79 would be 10.5% (536.6 million) in 2021 and 12.2% (783.2 million) in 2045 [1]. Between 2021 and 2045, middle-income countries are predicted to experience the largest relative increase in the prevalence of diabetes (21.1%), followed by high-income (12.2%) and low-income (11.9%) nations. Diabetes-related medical expenses were projected to cost 966 billion USD globally in 2021 and 1 054 billion USD globally by 2045 [1]. The common complications of diabetes mellitus are well-known and continue to be a significant burden for millions of those who have the disease. Patients who have diabetes may develop a number of pathologies. The usual complications include microvascular conditions, including diabetic kidney disease, retinopathy, peripheral neuropathy, and diabetic foot infection and macrovascular conditions, such as coronary heart disease, stroke and peripheral arterial disease [2].

One of the most frequent complications of patients with poorly controlled diabetes mellitus is diabetic foot ulcers. Approximately 5% of people with diabetes mellitus experience foot ulcers, and 1% require an amputation [3]. It is usually the result of poor glycemic control, underlying neuropathy, peripheral vascular disease, or poor foot care. If left untreated, these wounds may develop into osteomyelitis, an infection that affects both soft tissue and bone. About 10%-15% of moderate and 50% of severe infectious cases of osteomyelitis are caused by non-healing ulcers [4]. Numerous of these cases necessitate hospitalization, and surgical amputation is 4 times more likely if the patient has osteomyelitis versus just a soft tissue infection [5].

Osteomyelitis is classified as either acute or chronic based on histopathological findings rather than the length of the illness [6]. Infiltrates of neutrophils, thrombosed or clogged blood vessels, and microorganisms are the main histopathological findings in acute osteomyelitis [6]. On the other hand, necrotic bone is the distinctive histopathological finding in chronic osteomyelitis. Other characteristics of chronic osteomyelitis include a predominance of mononuclear cells, granulation replacing osteoclast-resorbed bone, and fibrous tissue causing bone loss and the pathognomonic formation of sinus tracts [7]. Staphylococcus bacteria, which are frequently found on the skin or in the nose of even healthy people, are the primary cause of the majority of osteomyelitis cases. There are many ways in which germs can enter a bone, including through the bloodstream. Antibiotic resistance has been rising in the diabetic population recently, and multi-resistant organisms (MDRO) are frequent in such infections. Methicillin-resistant Staphylococcus aureus (MRSA) develops as a result of hospitalization, surgery, and protracted antibiotic therapy [8].

Surgical resection followed by a protracted course of intravenous antibiotics is the standard course of treatment for osteomyelitis [9]. The majority of the evidence in favor of this strategy comes from case studies with relatively few diabetic foot cases. If surgery is chosen, it is common practice to examine the histopathologic margin for signs of osteomyelitis. To support suggestions for treating osteomyelitis of the diabetic foot, more proof is required. This study aims to evaluate the relationship between the histopathologic margin and the osteomyelitis outcome in the diabetic foot.

MATERIALS AND METHODS

STUDY DESIGN, INCLUSION, AND EXCLUSION CRITERIA

This was a prospective study carried out over a period from November 2021 to February 2023. This study included patients who were hospitalized with osteomyelitis, a severe diabetic foot infection, and it represented a single academic medical center. According to the criteria for admission, the patient had to have an osteomyelitis admitting diagnosis based on clinical and laboratory data. The infection was diagnosed according to the Infectious Diseases Society of America criteria and graded as moderate or severe [10]. According to the guidelines for systemic inflammatory response syndrome (SIRS), severe DFI is described as having two or more objective findings of systemic toxicity and/or metabolic instability at the time of initial assessment [11]. A mild DFI or being hospitalized for a foot infection while undiagnosed with diabetes were both exclusion criteria.

Positive bone culture and/or bone histopathology results that show the presence of an inflammatory response, bone necrosis, and/or bone fragmentation were used to confirm the diagnosis of osteomyelitis [12]. All patients with suspicion for DFO (ie, abnormal imaging study and/or positive probe to bone test) had a bone biopsy to confirm the presence of OM.

CLINICAL PARAMETERS

We evaluated the frequency of amputation, the length of hospitalization, the causative organism's microbial culture, and histological parameters. Major amputation was defined as an amputation at or proximal to the knee joint. A minor amputation was defined as amputation at or below the ankle joints or removal of a part of the foot at or distal to the transverse tarsal joint. After seeking advice from colleagues in infectious disease, plastic surgery, vascular surgery, anesthesiology, and pathology, the decision to proceed with the major amputation was made. Our infectious disease specialists assessed each participant in this study and discussed with the DFO patients the advantages and disadvantages of long-term antibiotic therapy. Plastic surgery examined the potential for local, regional, and distant flaps to cover large soft tissue wounds in patients with associated DFO. A vascular surgeon assessed the patient to determine whether open or endovascular reconstruction was necessary for those with peripheral arterial disease. An orthopaedic surgeon, determined whether osseous reconstruction was possible. Major amputations were ultimately only performed when the lower extremity was determined to be irreparably damaged due to significant bone defects, an inability to adequately cover soft tissue, or vascular disease that could not be repaired. All patients met with medical professionals from our physical medicine and rehabilitation service before having a major amputation. These doctors along with physical therapists and prosthetists, supervised our amputee clinic.

SPECIMEN COLLECTION

From each patient, three cultures were taken. Swab cultures from the base of the ulcer for each patient were taken at admission (without use of antibacterial drugs). The ulcer wound was flushed with saline solution, and the necrotic tissue and exudates on the surface were removed. Swabs were immediately scrubbed and rolled in a “Z” pattern onto the ulcer surface by nurses and then were placed in sterile test tubes. During an amputation, plastic surgeons collected samples of soft tissue and bone tissue. For the collection of bone specimens, if the patient with DFO had a fracture before the operation, the bone tissues on both sides of the broken ends were collected; in the absence of fracture, the bone tissue at the exposed area of the bone or near the proximal end of the ulcer was collected. The soft tissue at the boundary between necrotic and non-necrotic tissue was carefully extracted for soft tissue specimens. Within an hour, three cultures were delivered to the microbiology lab for pathogen culture.

MICROBIOLOGICAL ASSESSMENT

Utilizing a K-B (Kirby-Bauer) method and an automatic microbiological analyzer, bacteria isolates were identified at the species level. The Clinical and Laboratory Standards Institute protocol was followed to identify and test each strain that was cultured from the three specimens for antibiotic susceptibility. The standard definitions of multidrug-resistant, extensively drug-resistant, and pandrug-resistant bacteria were used to evaluate multi-drug resistant (MDR) strains [13].

SURGICAL AMPUTATION PROCEDURE

A tourniquet, fluoroscopy, large amputation blade, oscillating bone saw or manual saw, drill and bit set for myogenesis of muscle to bone ends, silk hand ties, rongeur, and a suction drain are all included in a standard orthopedic surgical set. The operation took place while the patient was in the supine position under spinal anesthesia with an antibiotic cover. In order to internally rotate the operative extremity so that the knee and ankle are vertically oriented, the patient was prepared and draped while lying on their side. The surgical team consisted of the operating surgeon, anesthesiologist, scrub tech, and circulator. The patient's nutritional status was evaluated. Physical examination and monofilament testing were used to identify the existence and proximal extent of any neuropathy.

RESULTS

PATIENT CHARACTERISTICS

The study cohort included 18 patients who underwent below-knee amputation due to diabetes at the medical center over a 16-month period. Out of 18 patients, 13 were men (72.2%). The patients with amputees were, on average, 67.2 years old. There was a high prevalence of comorbid medical conditions (Table 1). The most common comorbidities in these diabetic patients were hypertension (9, 50.0%), dyslipidemia (5, 27.7%), and chronic kidney disease (3, 16.6%). The average duration of diabetes was 15.6 ± 5.7 years, and the mean glycated hemoglobin level was 9.3% ± 1.3% and albumin 27.4 ± 2.6 mg/dL. A total of 14 patients had a wound duration of more than 30 days before admission, and the average duration of ulcers in patients was 42.6 ± 5.6 days (Table 1).

LEVEL OF AMPUTATION

The level of amputation did not significantly correlate with the patients' age or gender. Additionally, all comorbidities except for CKD did not significantly correlate with the level of amputation (Table 1).

LENGTH OF HOSPITAL STAY

After amputation surgery, the total number of days spent in the hospital was significantly correlated with the degree of amputation. In comparison to those who underwent below-ankle amputation, those who underwent below-knee above-ankle amputation had a significantly (P0.05) longer length of hospital stay (Table 2). The average hospital stay for below-knee-above-ankle amputations was 10.9±1.6 days and for ankle amputations, it was 7.7±0.9 days (P 0.05) (Table 2). But there was no statistically significant link between LOS and any comorbidity or aetiology (Table 1).

Table 1: Clinical and Functional assessment after proximal fibular osteotomy

Preoperative and postoperative variables	Number (Mean ± SE)	%
Sex		
Male	13	61.4
Female	5	38.6
Age (years)	62.9 ± 1.1	
The duration of diabetes (Years)	15.6±5.7	
Comorbidities		
Hypertension	9	50.0
Dyslipidaemia	5	27.7
Chronic kidney disease	3	16.6
Other	1	5.6
Laboratory values		
Albumin	27.4 ± 2.6	
HbA1c (%)	9.3 ± 1.3	
Duration of the ulcer (Days)	42.6 ± 5.6	
30 days or less	4	22.2
Over 30 days	14	77.7
Level of amputation		

Below knee-above ankle (Major) amputation	12	66.6
Below ankle (Minor) amputation	6	33.3
LOS (mean ± SE, days)		
Below knee-above ankle (Major) amputation	10.9±1.6	
Below ankle amputation (Minor)	7.7±0.9	
Side		
Right	8	44.4
Left	9	50.9

THE DISTRIBUTION OF BACTERIAL PATHOGENS FROM SWABS, SOFT TISSUE, AND BONE SPECIMENS ACCORDING TO CULTURE TECHNIQUE

According to Table 2, 15 patients (83.3%) had positive results for bone tissue, 14 patients (17.7%) had positive results for soft tissue, and 16 patients (88.8%) had positive results for swab cultures.

There were 46 different bacterial strains found in the swab specimens, of which 26 (56.5%) were Gram-positive, 15 (32.6%) were Gram-negative, and five (10.9%) were fungi. The mean number of isolates per swab specimen was 1.71 (range, 1–3).

Gram-positive bacteria made up 22 (45.2%) of the 42 strains of bacteria isolated from the soft tissue specimens, while Gram-negative bacteria made up 18 (42.8%) of the strains. Fungi made up two (4.7%) of the strains. The average number of isolates per specimen of soft tissue culture was 1.32 (range, 1–3).

The 43 bacteria strains that were isolated from the bone samples included two (4.6%) fungi, 18 (41.7% of them Gram-negative), 23 (53.5%) Gram-positive, and 43 (43.0%) gram-negative strains. The mean number of isolates per bone specimen was 1.14 (range, 1–3).

Our findings showed that the pathogens (Gram-positive bacteria, Gram-negative bacteria, and fungi) cultured in the three types of specimens did not differ significantly from one another. The most prevalent Gram-positive bacterium was Staphylococcus aureus, which made up 55.5%, 44.4%, and 38.9% of the Gram-positive bacteria in swabs, soft tissues, and bone tissues, respectively. The most common type of Gram-negative bacteria was E. coli. The percentage of Gram-negative bacteria in the three specimens was 22.2%, 11.1%, and 16.6%, respectively.

Table 2: Distribution of Bacterial Pathogens Isolated in Ulcer Swab, Soft Tissue, and Bone Specimen Culture from Patients

Pathogens	**Swab Specimens (n=18)**	**Soft Tissue Specimens (n=18)**	**Bone Specimens (n=18)**
Positive specimens	16	14	15
No. of isolates	46	42	43
Mean no. of isolates per specimen	1.71	1.32	1.14
MDR	6 (33.3%)	3 (16.6%)	7 (38.9%)
Gram-positive bacteria	26	22	23
Staphylococcus aureus	10	8	7
Coagulase-negative staphylococci	2	2	2
Other *Staphylococcus*a	2	2	1
MRSA	3	1	3
Streptococcus	4	4	3
Enterococcus	3	3	5
Other Gram-positive bacteria	2	2	2
Gram-negative bacteria	15	18	18
Escherichia coli	4	2	3
Klebsiella pneumoniae	1	2	1
Enterobacter cloacae	1	1	2
Klebsiella aerogenes	1	1	1
Proteusbacillus vulgarisb	3	2	3
Citrobacter freundii	1	2	2
Serratia marcescens	1	2	1
Morganella morganii	1	2	3
Pseudomonas aeruginosa	1	1	1
Acinetobacter baumannii	0	2	1
Other Gram-negative bacteria	0	1	1
Fungus	2	2	2
Candida albicans	1	1	0
Candida parapsilosis	0	1	1

Candida tropicalis	1	0	1
Trichosporon asahii	0	0	0

DISCUSSION

Major lower extremity amputations have a greater impact in developing countries because of poverty, a lack of health insurance, and cost-control measures [14]. Additionally, the indications reported vary greatly for major lower extremity amputation. In the present study, major lower extremity amputation due to diabetic foot infection was studied for microbiological, histopathological, and clinical assessment. Infection of the diabetic foot is the most common indication for major lower extremity amputation [15,16]. Given that diabetes causes peripheral arterial disease and that diabetic patients account for 75 percent of major lower extremity amputation procedures, this is not unexpected [17].

In our sample, 72.2% of the participants were men, which is consistent with other reports [17–19]. The population in this study had a mean age of 67.2 years, which is similar to other study populations in the literature [17,18]. The reason for this finding is that diabetes is affecting the population at an early age and gradually causing complications that lead to the risk of amputation at a geriatric age. The length of hospital stays still has a big impact on how effective healthcare is, how much it costs overall, how happy patients are, and how well-off they are [20]. The level of amputation had a significant impact on how long patients stayed in the hospital. For below-ankle amputations, the mean acute postoperative length of hospital stay in our study was 7.7 ± 0.9 days, which was comparable to that reported by Wise et al. [21]. Major amputations (below the knee, above the ankle) require a stay that is significantly longer (10.9 ± 1.6 days) than minor amputations (below the ankle). The length of our hospital stay overall was shorter than that described in recent reports from developed nations. This is a result of our hospital not having rehabilitation services. When the patient's pain is under control and the wound is beginning to heal, the hospital releases them to go home.

This study also examined the antimicrobial susceptibility of bone samples to offer recommendations for the care of patients who have had an amputation due to osteomyelitis. According to previously published findings [22], the distribution of pathogenic bacteria cultured in three specimens was dominated by Gram-positive bacteria. Gram-negative bacteria were alsocounted among the pathogenic bacteria cultured from three specimens. Therefore, the results suggest that empirical antibacterial treatment decisions for treating osteomyelitis-related amputations should consider both Gram-positive and Gram-negative bacterial infections. Our findings also confirmed that Staphylococcus aureus was the most prevalent bacterium isolated from matching swab, soft tissue, and bone tissue cultures, as previously reported in the studies [23].

CONCLUSION

Our results indicate that osteomyelitis is associated with the significant development of a microbial organism that worsens the infection. This infection is present at the soft tissue level as well as in the bones. When infection cannot be controlled by antibiotic therapy, amputations are necessary. Amputations are not linked with the associated comorbidity but with the level of infection, and surgical implications are associated with the level of amputations, viz., below the ankle or below the ankle amputations. Postoperative complications are also based on this. The study may aid in determining initial empirical clinical antibacterial therapies and subsequent targeted antibacterial treatments for patients with amputation due to osteomyelitis in diabetic patients.

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