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Original article

Diabetic foot infection in hospitalized adults

David E. Katz [a], N. Deborah Friedman [b], Evgenia Ostrovski [c], Dor Ravid [d], Nadav Amrami [d], Dori Avivi [d], Bethlehem Mengesha [d], Ronit Zaidenstein [d, e], Tsilia Lazarovitch [f], Mor Dadon [d], Dror Marchaim [d, e, *]

[a] Department of Internal Medicine D, Shaare Zedek Medical Center, Jerusalem, Israel
[b] Department of Infectious Diseases, Barwon Health, Victoria, Australia
[c] Department of Internal Medicine D, Assaf Harofeh Medical Center, Zerifin, Israel
[d] Unit of Infectious Diseases, Assaf Harofeh Medical Center, Zerifin, Israel
[e] Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel
[f] Clinical Microbiology Laboratory, Assaf Harofeh Medical Center, Zerifin, Israel

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ABSTRACT

Background: Acute infections of the diabetic foot (DFI) are a common and complex condition. Patients are generally managed in the ambulatory setting and epidemiological data pertaining to hospitalized patients is lacking. The aim of this study was to analyze the epidemiology, microbiology and outcomes of hospitalized patients with DFI, who are managed at a referral center equipped with hyperbaric oxygen (HBO) therapy.

Methods: A retrospective cohort study of adult patients admitted to a tertiary referral center with DFI over a six-month period in 2013 was undertaken. Predictors of clinical outcomes and efficacy of treatment modalities were analyzed by Cox regression.

Results: Sixty-one patients with DFI were identified. Most patients were elderly (67 ± 13 years), with long-standing (17 ± 9 years), poorly controlled (HbA1c 9 ± 3%) diabetes. Most patients had polymicrobial infection (80%); specifically, anaerobic (39%) and multi or extensively-drug resistant organisms (61%). Administration of appropriate antimicrobials was delayed for >48 h in 83%. Advanced age was associated with worse outcomes. Sicker patients with severe peripheral vascular disease were managed with HBO. The use of HBO was associated with higher costs and increased functional deterioration, and did not prevent future limb amputation.

Conclusions: Our study illustrates the descriptive epidemiology of hospitalized adults with DFI predominantly of polymicrobial etiology. MDROs and anaerobic organisms are common causative pathogens, and appropriate antibiotics were frequently delayed. HBO treatment may delay the need for limb amputation, but not obviate this eventual outcome.

1. Introduction

Diabetes mellitus affects 8–13% of the world population, and according to national data from the United States (US), has a prevalence of 27% in patients over 65 years [1]. Among patients with diabetes, diabetic foot infection (DFI) is one of the most common complications with up to 10% of diabetic patients developing a DFI [1,2]. DFI presents with a range of signs and symptoms, and the severity of the DFI can range from a superficial infection of the nail bed to deeper infections involving bone (osteomyelitis) [3]. Although DFI is predominantly managed in the outpatient setting, in the developed world, DFI is the most common admission diagnosis for diabetic patients [4], and management in these cases frequently involves partial or total amputation of the affected lower limb.

DFI is the most common reason for non-traumatic amputations in developed countries [2], with data from the US showing that up to 60% of all non-traumatic adult limb amputations in 2010 were related to DFI [1]. Survival following limb amputation for DFI is less

* Corresponding author. Unit of Infectious Diseases, AssafHarofeh Medical Center, Zerifin, 70300, Israel. Tel.: +972 8 977 9049; fax: +972 8 977 9043.
E-mail address: drormarchaim@gmail.com (D. Marchaim).

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than 50% within 3 years after surgery, and only 40% at 5 years after surgery [2]. Partial or total limb amputation for DFI predicts further amputation in 20% of patients within 2 years of the procedure, and also predicts development of another DFI in the initially unaffected limb in 50% of patients [2]. Therefore, amputation is both a marker for serious DFI and of an unfavorable outcome. Treatment with hyperbaric oxygen (HBO) is one of few existing modalities for treating DFI in order to avoid or delay amputation [5]. However, there is ongoing debate regarding the independent role of HBO treatment in effectively reducing amputation rates over time [6].

Although the clinical and microbiological diagnosis of DFI may be both challenging and complicated [7], early and precise diagnosis is important for both effective infection management and for reducing the need for subsequent amputation [3,6]. Microbiological diagnosis is critical as it allows the clinician to tailor antibiotic therapy to the causative organism [8]. However, in many cases, the antimicrobial management for DFI is empiric as there may be no appropriate site from which to obtain a culture, superficial skin cultures correlate with the 'true offending pathogen' less than 30% of the time, and patients may also present already taking long-term antibiotics, which further decreases the culture yield [6,9]. Importantly, inappropriate empiric broad-spectrum antimicrobial therapy can result in unfavorable outcomes for individual patients and contribute to the broader harmful ecological impact of antimicrobial therapy [10].

The epidemiology of DFI in Israel has not been comprehensively researched [9,11,12]. Moreover, internationally, the epidemiological features of patients with DFI managed as inpatients is also lacking [8]. The goals of this study were to perform a descriptive analysis of the epidemiological and microbiologic features of patients with DFI admitted to a referral acute-care facility, to determine risk factors for a worse clinical course (i.e., death, amputation, re-admission, and functional deterioration), and to analyze the controlled effect of HBO treatment on the clinical course of patients with DFI.

2. Materials and methods

2.1. Study setting

Assaf Harofeh Medical Center (AHMC) is an 815-bed tertiary care university-affiliated facility located in southern-central Israel. AHMC contains a state-of-the-art hyperbaric medicine centre (with dual chambers with capacity for 37 patients), and a multidisciplinary team with expertise in the management of DFI [13]. This study was approved by the institutional review board at AHMC according to the declaration of Helsinki statement of ethical principles for conducting human research.

A retrospective review of charts of patients consecutively admitted to AHMC from May through November 2013 was undertaken as part of a broader project on infectious syndromes among hospitalized patients. During this time period, 8132 charts were reviewed. Patients over 18 years of age with a diagnosis of DFI based on their discharge records and ICD-9 discharge codes, were included. The diagnosis of DFI was per accepted definitions [6] and in consultation with a senior infectious disease physician. Microbiology samples for culture were obtained by tissue biopsy or collected via sterile syringe in the case of direct pus draining from a deep sinus tract [9].

2.2. Definitions

Multidrug resistant organisms (MDR) included; extended-spectrum β-lactamase producing Enterobacteriaceae (ESBLs), methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenem-susceptible *Pseudomonas aeruginosa*, and carbapenem-susceptible *Acinetobacter baumannii*.

Extensively-drug resistant organisms (XDR) included; vancomycin-resistant enterococci (VRE), carbapenem-resistant Enterobacteriaceae (CRE), carbapenem-nonsusceptible *Pseudomonas aeruginosa*, and carbapenem-nonsusceptible *Acinetobacter baumannii*.

3. Data collection

The following data was extracted from patient medical records; patient demographics, details of the DFI, history and duration of diabetes, co-morbid illnesses (including Charlson's scores [14]), functional status, previous hospital admissions, surgical procedures and use of invasive devices (e.g. urinary catheters, feeding tubes) prior to admission, medications, hospital length of stay, details of HBO treatment, vital signs, physical examination findings, laboratory results including bacterial culture results, and the results of imaging of the affected foot. In addition, post-discharge follow-up data were collected on both surgical procedures, and microbiology results up to 6 months after the hospitalization. Mortality data was extracted from national records of the Israeli ministry of interior. The University of Texas (UT) diabetic wound classification incorporating wound stage and appearance was calculated for all patients to estimate the severity of the DFI [15].

3.1. Data management and analysis

The data was entered and processed using SPSS version 22.0 (2014). Both descriptive and univariable analyses were performed. Multivariable models were created for four outcomes: 1) decrease in functional status following the DFI index event, 2) re-admission to the acute care hospital within 6 months, 3) partial or total amputation of the limb affected resulting from the index DFI, and 4) increased cost (admissions costing in excess of 30,000 New Israeli Shekels [NIS], which equals ~$7700). Cost analyses were based on the total costs that were billed to insurance companies, based on the rates set by the Israeli ministry of health. These costs included; inpatient care, invasive procedures (including surgery), days of hospitalization (based on the type of unit), and imaging, set at fixed rates as determined by the Israeli ministry of health. HBO costs, if present, were deducted. An analysis was also performed comparing treatment groups (HBO versus no HBO).

All analyses were performed by accepted methods. Categorical variables were analyzed by the chi-square test or Fisher's exact test; continuous variables were analyzed by the student's t-Test or Mann–Whitney *U* test. Multivariable modeling was performed for each outcome, using Cox regression. Multivariable analysis of patient characteristics for those patients treated with HBO was performed using logistic regression. All parameters with a *P*-value less than or equal to 0.1 were incorporated to the multivariable analyses.

4. Results

Of the 8132 consecutive patient discharge notes reviewed during the 6-month study period, we identified 61 adult patients with DFI. All DFIs were present on admission. The study population was male predominant, of mean age 67 years and more than half were functionally impaired at baseline, with high Charlson's scores [14]. Most patients had long-term diabetes under poor control and had been diagnozed with diabetic microvascular disease (Table 1). Approximately one-third of patients were