Diabetic Foot Infections: Truth in Numbers

SIRS is a method of distinguishing between moderate and severe DFI.

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Diabetic foot infections (DFI) are among the most serious and common complications encountered in patients with diabetes mellitus. According to the American Diabetes Association, diabetes affects 26 million people in the United States and more than 366 million people worldwide.[1] Up to 25% of those with diabetes will develop a foot ulcer, and more than half of all foot ulcers will become infected, with 20% of those requiring amputation.[2,3] Readmission rates for DFI patients are approximately 40% and nearly one in six patients dies within one year of infection.[4] Given these alarming statistics, DFIs remain a constant challenge facing healthcare providers across all medical disciplines.

The Diagnosis

Overall, 1.0 million cases of DFI presented to Emergency Departments (ED) in the U.S. from 2006-2010, constituting 1.9% of the 54.2 million total diabetes cases.[5] Therefore, it is important for the ED team to be aware of the severity of DFI, as more than half of diabetic foot ulcers (DFU) are clinically infected at the time of presentation.[6] Inflammatory lab markers, a complete metabolic panel (CMP) including albumin levels, hemoglobin A1c, and complete blood count (CBC) should be ordered upon admission. Acute phase reactants, including erythrocyte sedimentation rate (ESR) and C-reactive protein level (CRP), are markers of inflammation that are elevated during the presence of inflammation. Recent evidence supports the use of ESR and CRP for the evaluation of possible osteomyelitis.[7]

Akinci, et al. found that baseline and post-treatment CRP, ESR, and WBC were significantly elevated in patients who underwent amputation.[8] These results suggest that a prominent acute phase response after treatment, as demonstrated by post-treatment CRP levels, was a strong predictor of treatment failure and amputation risk in patients with DFI. However, Armstrong, et al. found that fewer than 50% of DFI patients mounted an elevated WBC greater than 12,000 in his study of 28 hospitalized DFI, validating that patients with diabetes do not always mount a robust immune response in the face of infection.[9] Approximately 20% of hospitalized patients exhibit hypoalbuminemia at the time of admission and hypoalbuminemia has been found to be associated with amputations in patients with DFI.[8,10]

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Basic radiographs should also be ordered to rule out medical emergencies such as gas gangrene that would require emergent surgical debridement. A proper neurovascular exam should be performed to assess the need for non-invasive vascular studies such as ankle brachial index (ABI), and early consultation to a vascular specialist as approximately 35% of patients develop a DFU secondary to inadequate arterial blood flow.[11] In a case control study of 112 hospitalized diabetic patients by Peters, et al., PAD was independently associated with a 5.5 fold increased risk for DFI.[12]

Initial antibiotic therapy should be started early, be empiric, and parenteral, covering the most common diabetic foot pathogens, staphylococci, streptococci and gram-negative bacteria.[13] In a study of 84 randomly selected hospitalized patients with severe DFI, 83% of cultures demonstrated polymicrobial flora at an average of 2.8 species per specimen and an aerobic to anaerobic bacteria ratio of 3:114.

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The Admission

Recently, a clinical guide has been developed for the inpatient management of diabetic foot disorders.[13] A team approach, consisting of medical specialists (infectious disease, hospital medicine, endocrinologists) and surgical specialists (podiatry, orthopedic surgery, plastic and vascular surgery) is recommended early on for the management of DFI in order to increase the likelihood of limb salvage. It is imperative that the treating clinician be capable of recognizing and properly classifying the DFI as mild, moderate, or severe. Following a classification scheme, such as the Infectious Diseases Society of America (IDSA) Clinical Classification Scheme, will guide the clinician in treatment protocol. According to the IDSA, the presence of infection is defined by two or greater classic findings of inflammation or purulence based on the size and depth of the infection.[15]

Severe infections are distinguished from moderate infections by the presence of systemic toxicity or metabolic instability. A mild DFI, defined as <2cm of surrounding erythema, may be treated with oral antibiotic therapy in an outpatient setting, whereas a moderate to severe infection can be limb- or life-threatening, with the need for urgent intravenous inpatient antibiotic therapy, fluid resuscitation, surgical debridement, and control of metabolic derangements. A validation study of the IDSA classification observed a trend toward increased risk for amputation and lower extremity-related hospitalization with increasing infection severity.[15]

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Similarly, in a study by Wukich, Hobizal, and Brooks, the database of a single academic foot and ankle program was reviewed for 100 patients who were hospitalized for a DFI from 2006 to 2011. Severe DFI was defined as having two or more objective findings of systemic toxicity and/or metabolic instability at the time of initial assessment. Patients with severe DFI had a median hospital stay that was 60% longer than that of patients with moderate DFI; and 55% of patients with a severe DFI required some type of amputation compared with 42% of patients with a moderate DFI.[16]

SIRS

Recently, the IDSA updated their guidelines and recommended using SIRS as a method of distinguishing between moderate and severe DFI.[17] SIRS, or systemic inflammatory response syndrome, is a serious condition related to systemic inflammation, which can lead to possible organ dysfunction and failure. SIRS criteria includes a body temperature less than 36 degrees Celsius or greater than 38 degrees Celsius, heart rate greater than 90 beats per minute, respiratory rate greater than 20 breaths per minute and leukocytes (WBC) less than 4,000 or greater than 12,000 (Table 1).

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TABLE 1:

Systemic Inflammatory Response Syndrome (SIRS)

Criteria	Value
Temperature	<36°C or >38°C
Heart Rate	>90/min
Respiratory Rate	>20/min
White Blood Count (mm3)	<4,000 or >12,000

SIRS can be diagnosed when two or more of these criteria are met. SIRS has recently been validated as a method of discriminating between moderate and severe DFI in a group of hospitalized patients with diabetes. This study demonstrated that patients with DFI who manifest SIRS, or rather those with a severe infection, will have longer hospital stays and higher rates of major amputation than those patients who don't manifest SIRS, or rather those with a moderate infection.[18]

Treatment

Surgical management of some moderate and virtually all severe DFI is vital and should begin urgently with aggressive irrigation and debridement of non-viable infected or necrotic soft tissue and bone. Multiple serial debridements are often necessary to provide adequate drainage and control of infection. Emergent surgical treatment of DFI has been proven to reduce the

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need for major amputations. Tan, et al. retrospectively evaluated two groups of patients treated for DFI[19] In the first group, patients were solely treated with IV antibiotic therapy, while Group 2 received IV antibiotic therapy in addition to surgical management within the first three days of hospital admission. Patients in Group 2 were found to have fewer above ankle amputations and an overall six day shorter hospital course than those in Group 1. Empiric intravenous antibiotic therapy should be started initially upon presentation, but should be adjusted upon cultures obtained following surgical or bedside debridement.

Proper antibiotic management of lower extremity infections reduces complications and length of stay.[13] The infectious disease specialist should be involved for antibiotic management given the polymicrobial nature of most DFI. Furthermore, many patients with DFI will have complicated diabetes associated with renal impairment and may require dialysis, calling for specialized dosing of renal-based metabolized drugs. Nutritionists and diabetes educators should also be involved in the treatment of DFI to ensure tight glycemic control that is essential for wound healing once the infection is eradicated. This education should be carried forth in an outpatient setting in an effort to prevent further complication and optimize nutrition.

It is projected that by year 2030, at least 550 million people will have diabetes, which is 10% of the world's adult population. More than 60% of non-traumatic lower-limb amputations occur in people with diabetes.[1,20] These statistics speak volumes to health care providers dealing with the management and treatment of DFI. As the presence of diabetes continues to rise, the threat of DFI becomes more ominous worldwide. It is the responsibility of the treating clinician to be cognizant of the severity of DFI, and it is the responsibility of all healthcare providers who encounter patients with diabetes to be cognizant of these overwhelmingly negative statistics. **PM**

Proper antibiotic management of lower extremity infections reduces complications and length of stay.

References

[1] National diabetes fact sheet, 2011. US Department of Health and Human Services, Center for Disease Control and Prevention 2011: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf.

[2] Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA; 293:217-228, 2005.

[3] Lavery LA, Armstrong DG, Wunderlich RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. Diabetes Care;29:1288-93, 2006.

[4] Fincke BG, Miller DR, Turpin R. A classification of diabetic foot infections using ICD-9-CM codes: application to a large computerized medical database. BMC Health Serv Res; 10:192, 2010.

[5] Skrepnek GH, Mills JL, Armstrong DG. A Silent, Painless Emergency? The Burden of Diabetic Foot Infections and Emergency Department Admissions in the U.S. American Diabetes Association; 73rd Scientific Sessions (2013); Chicago.

[6] Frykberg RG, Armstrong JG, Edwards A, Kravette M, Kravitz S, Ross C, et al. Diabetic foot disorders: A clinical practice guideline. JFAS; 39: S1-60, 2000.

[7] Butalia S, Palda VA, Sargeant RJ, Detsky AS, Mourad O. Does this patient with diabetes have osteomyelitis of the lower extremity? JAMA;299:806-13, 2008.

[8] Akinci B, Yener S, Yesil S, Yapar N, Kucukyavas Y, Bayraktar F. Acute phase reactants predict the risk of amputation in diabetic foot infection. JAPMA;101:1-6, 2011.

[9] Armstrong DG, Lavery LA, Sariaya M, Ashry H. Leukocytosis is a poor indicator of acute osteomyelitis of the foot in diabetes mellitus. J Foot Ankle Surg;35:280-4, 1996.

[10] Vincent, J.L. Relevance of albumin in modern critical care medicine. Best Pract Res Clin Anaesthesiol;23:183-91,2009.

[11] Reiber GE, Vileikyte L, Boyko EJ, del Aguila M, Smith DG, Lavery LA, Boulton AJM. Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings. Diabetes Care; 22:157-162, 1999.

[12] Peter EJ, Lavery LA, Armstrong DG. Diabetic lower extremity infection influence of physical, psychological, and social factors. J Diabetes Complications; 19:107-112, 2005.

[13] Wukich DK, Armstrong DG Attinger CE, Boulton AJM et al. Inpatient Management of Diabetic Foot Disorders: A Clinical Guide. Diabetes Care; 36:2862-2871, 2013.

[14] Diamantopoulos EJ, Haritos D, Yfandi G, Grigoriadou M, Margariti G, Paniara O, et al. Management and outcome of severe diabetic foot infections. Exp Clin Endocrinol Diabetes;106:346-52, 1998.

[15] Lavery LA, Armstrong DG, Murdoch DP, Peters EJG, Lipsky BA. Validation of the Infectious Diseases Society of America's Diabetic Foot Infection Classification System. CID;44:562-5,2007.

[16] Wukich DK, Hobizal KB, Brooks MM. Severity of diabetic foot infection and rate of limb salvage. Foot Ankle Int.;34:351-8, 2013.

[17] Lipsky BA, Berendt AR, Comia PB, et al. Infectious Diseases Society of America. 2010 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis.;54:132-173, 2012.

[18] Wukich DK, Hobizal KB, Raspovic KM, Rosario BL. SIRS is valid in distinguishing between moderate and severe diabetic foot infections. Diabetes Care; 36:1-6, 2013. In press.

[19] Tan JS, Friedman NM, Hazelton-Miller C, Flanagan JP, File TM, Jr. Can aggressive treatment of diabetic foot infections reduce the need for above-ankle amputation? CID;23:286-91,1996.

[20] One Adult in Ten will have Diabetes by 2030. International Diabetes Federation. Services, 2011. http://www.idf.org/media-events/press-releases/2011/diabetes-atlas-5th-edition

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