The Journal of Foot & Ankle Surgery 58 (2019) 1055–1057

Contents lists available at ScienceDirect

The Journal of Foot & Ankle Surgery

journal homepage: www.jfas.org

Original Research

Do SIRS Criteria Predict Clinical Outcomes in Diabetic Skin and Soft Tissue Infections?

Easton C. Ryan, BS[1], Peter A. Crisologo, DPM, AACFAS[2], Orhan K. Oz, MD, PhD[3], Javier La Fontaine, DPM, MS, FACFAS[4], Dane K. Wukich, MD[5], Lawrence A. Lavery, DPM, MPH, FACFAS[2]

[1] *Student, University of Texas Southwestern Medical School, Dallas, Texas,*
[2] *Fellow, Department of Plastic Surgery, University of Texas Southwestern Medical Center, Dallas, Texas*
[3] *Professor, Department of Radiology, University of Texas Southwestern Medical Center, Dallas, Texas*
[4] *Professor, Department of Plastic Surgery, University of Texas Southwestern Medical Center, Dallas, Texas*
[5] *Professor, Department of Orthopaedic Surgery, University of Texas Southwestern Medical Center, Dallas, Texas*

ARTICLE INFO

Level of Clinical Evidence: 4

Keywords:
amputation
osteomyelitis
outcomes

ABSTRACT

The aim of this study was to assess whether systemic inflammatory response syndrome (SIRS) is correlated with outcomes in diabetic foot infections (DFIs). We retrospectively reviewed 137 diabetic patients admitted to the hospital with Infectious Diseases Society of America moderate and severe DFIs. We used SIRS criteria to define severe infection based on the presence of at least 2 of the following: heart rate >90 bpm, temperature >38°C or <36°C, respiratory rate >20 breaths per minute, and white blood cell count >12,000/mm^3 or <4,000/mm^3. Patients with severe DFI were significantly younger (median 49.6 versus 53.6 years, $p = .04$), less often had type 2 diabetes (88.6% versus 98.9%, $p = .01$), and less often had a history of previous amputation (15.9% versus 40.9%, $p < .01$). There were no differences in patients with severe infections defined by SIRS versus moderate infections in the need for surgery (47.7% versus 59.1%, $p = .27$), any amputation (20.5% versus 29.0%, $p = .29$), leg amputations (6.8% versus 7.5%, $p = .88$), duration of antibiotics (median ± standard deviation 34.1 ± 46.5 versus 31.9 ± 47.2 days, $p = .47$), or healing within 1 year (68.2% versus 66.7%, $p = 1.00$). Length of hospital stay was the only outcome variable that was significantly different in severe infections (median 12.7 ± 11.9 versus 7.8 ± 5.8 days, $p = .02$). Foot-related readmission was more common in moderate infections (46.2% versus 25.0%, $p = .02$). In conclusion, SIRS criteria for severe infections in diabetic patients with skin and soft tissue infections were not associated with a difference in outcomes other than longer hospital stay.

Diabetic foot infections (DFIs) are the most common component cause contributing to hospitalization and limb loss (1,2). Infection in a compromised host with diabetes, immunopathy, peripheral arterial disease, poor glucose control, and poor nutrition creates an ideal environment for the rapid spread of infection and destruction of the skin, fascia, tendon, and bones. Classification schemes to assess DFI severity can facilitate the development of algorithms for evaluation, testing, and treatment. Although systemic inflammatory response syndrome (SIRS) was initially introduced to assess severity of illness in the intensive care setting, it has been advocated to predict outcomes in patients with DFI (3–5). Our clinical observations led us to question the value of using SIRS in diabetic patients with soft tissue infections, because we did not see obvious differences in clinical outcomes. The purpose of this study was to evaluate clinical outcomes of DFI patients with skin and soft tissue infections based on SIRS criteria. We hypothesized that SIRS criteria would not be a strong predictor of outcomes or adverse events.

Patients and Methods

Patient Selection

After approval by the institutional review board, medical records of patients treated between June 2009 and February 2017 for DFI were reviewed. A soft tissue diagnosis was assigned if osteomyelitis was ruled out by a negative magnetic resonance imaging (MRI), single-positron emission computed tomography (SPECT CT), or bone biopsy for diabetic foot osteomyelitis. Patients with positive radiographs, MRI, SPECT CT, bone culture, or bone histopathology were considered to have diabetic foot osteomyelitis and were not included. Furthermore, patients who had additional sites of infection outside the affected foot or inflammatory disease processes were not included.

Patient Factors

Patients without diabetes mellitus (DM) were not included in the current study. Patient status regarding DM was assessed through patient history, glycated hemoglobin level,

Financial Disclosure: None reported.
Conflict of Interest: None reported.
Address correspondence to: Easton Ryan, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390
E-mail address: easton.ryan@utsouthwestern.edu (E.C. Ryan).

1067-2516/$ - see front matter © 2019 by the American College of Foot and Ankle Surgeons. All rights reserved.
https://doi.org/10.1053/j.jfas.2019.06.001

diabetes-related comorbidities, and glycemic control regimen. Presence of a severe soft tissue infection was identified according to the Infectious Diseases Society of America Classification of Diabetic Foot Infection (4), with clinical recognition of ≥2 of the following SIRS criteria: heart rate >90 bpm, temperature >38°C or <36°C, respiratory rate >20 breaths per minute or $PaCO_2$ <32 mmHg, and white blood cell count >12,000 cells/mm^3 or <4,000 cells/mm^3 or >10% immature bands. In addition, patient laboratory values including C-reactive protein, erythrocyte sedimentation rate, serum albumin, and hemoglobin were collected.

Patient Follow-Up and Outcomes

Patients included in the study were followed for at least 12 months or until they died; patients with <12 months of follow-up were excluded. The outcomes evaluated were the need for surgical intervention, lower-extremity amputation, hospital length of stay, wound healing, reinfection, readmission, and mortality.

Statistical Analysis

Patient data were summarized using descriptive statistics: median, mean, and standard deviation for continuous variables; frequency and percentage were used for categorical variables. Characteristics between patients with and without SIRS criteria were compared using parametric (Student's t, χ^2, multivariate regression) and nonparametric (Mann-Whitney U, Fisher's exact) tests as appropriate.

Results

Of 137 patients with DFI, 44 (32.1%) had clinically recognized severe soft tissue infection (meeting ≥2 SIRS criteria), whereas 93 (67.9%) had moderate infections (4). Demographics and patient characteristics are summarized in Table 1. Patients who presented with SIRS criteria for severe infection were significantly younger (median ± standard deviation 49.6 ± 11.4 versus 53.6 ± 10.4 years, $p = .04$), less likely to have type 2 DM (88.6% versus 98.9%, $p = .01$), less often had a history of previous amputation (15.9% versus 40.9%, $p < .01$), and had higher median white blood cell counts at the time of admission (8.6 ± 3.1 versus 11.3 ± 4.8, $p < .01$). There were no differences in patients with severe and moderate infections (Table 1) in the need for surgery (47.7% versus 59.1%, $p = .27$), the number of surgeries (median 1.0 ± 1.5 versus 1.2 ± 1.4, $p = .24$), any amputation (20.5% versus 29.0%, $p = .29$), minor amputations (13.6% versus 21.5%, $p = .27$), major amputations (6.8% versus 7.5%, $p = .34$), duration of antibiotics (median 34.1 ± 46.5 versus 31.9 ± 47 days, $p = .28$), wound healing within 1 year (68.2% versus 66.7%, $p = 1.00$), or time to heal (median 132.3 ± 102.0 versus 136.5 ± 103.3 days, $p = .74$). Foot-related readmissions to the hospital were more common in patients with moderate infections (46.2% versus 25.0%, $p = .02$). Length of hospital stay was the only outcome variable that was significantly higher in patients with severe infections (median 12.7 ± 11.9 versus 7.8 ± 5.8 days, $p < .01$).

Discussion

DFI is a sentinel event that often necessitates multiple surgeries, amputation, and prolonged and repeated hospitalizations (6,7). Despite DFI's well documented contribution to limb loss and recidivism, there are relatively few studies on the topic. The classification schemes for DFIs are based mostly on consensus and not on evidence (3,6,7). Wukich et al (5) conducted the only study to evaluate SIRS criteria in DFIs and reported findings contradictory to our results. The differences might be explained by differences in the patient populations, selection bias, and culture bias; our concern was that the surgeon culture and the presence of osteomyelitis may have been underlying factors that could explain the difference in study results. The obvious difference in the patient population was that the majority of the patients in Wukich's study had osteomyelitis (~66%), and the current study included only patients with skin and soft tissue infections. It has been documented that patients with osteomyelitis have worse clinical outcomes than patients with soft tissue infections. In studies by Wukich et al (6) and

Table 1
Patient characteristics

Characteristic	All Soft Tissue Infections (N = 137)	Moderate Infection (n = 93)	Severe Infection (n = 44)	*p* Value
Age (yr)	53.0, 52.4 (10.9)	55.0, 53.6 (10.4)	49.0, 49.6 (11.4)	.04*
Male sex	102 (74.5)	69 (74.2)	33 (75.0)	1.00
BMI (kg/m^2)	29.8, 31.2 (7.7)	31.2, 32.9 (10.6)	28.9, 31.1 (8.8)	.22
Type 2 DM	131 (95.6)	92 (98.9)	39 (88.6)	.01*
History of ulceration	82 (59.9)	61 (65.6)	21 (47.7)	.06
History of amputation	45 (32.8)	38 (40.9)	7 (15.9)	<.01*
Ankle-brachial index	1.1, 1.3 (0.67)	1.2, 1.4 (0.70)	1.1, 1.2 (0.59)	.44
Neuropathy	123 (89.8)	86 (92.5)	37 (84.1)	.14
Retinopathy	34 (24.8)	24 (25.8)	10 (22.7)	.83
Chronic kidney disease	57 (41.6)	40 (43.0)	17 (38.6)	.62
Dialysis	15 (10.9)	13 (14.0)	2 (4.5)	.14
Glycated hemoglobin (%)	8.7, 8.9 (2.4)	8.4, 8.8 (2.7)	9.2, 9.3 (2.2)	.29
WBC (cells/mm^3)	9.0, 9.4 (4.1)	8.2, 8.6 (3.1)	10.2, 11.3 (4.8)	<.01*
Outcomes during admission				
Surgery during admission	76 (55.5)	55 (59.1)	21 (47.7)	.27
Number of surgeries	1.0, 1.1 (1.3)	1.0, 1.2 (1.4)	0, 1.0 (1.5)	.24
Amputation during admission	36 (26.3)	27 (29.0)	9 (20.5)	.29
Foot	26 (19.0)	20 (21.5)	6 (13.6)	.27
Leg	10 (7.3)	7 (7.5)	3 (6.8)	.88
Vascular intervention	12 (8.8)	10 (10.8)	2 (4.5)	.34
Antibiotic duration (d)	16.0, 25.2 (28.1)	17.0, 31.9 (47.2)	18.5, 34.1 (46.5)	.28
Index length of stay (d)	7.0, 8.6 (5.7)	6.0, 7.8 (5.8)	9.0, 12.7 (11.9)	<.01*
Outcomes after discharge				
Healed	92 (67.2)	62 (66.7)	30 (68.2)	1.00
Days to heal	91.0, 129.7 (99.7)	91.0, 136.5 (103.3)	131.5, 132.3 (102.0)	.74
Reinfection	52 (38.0)	40 (43.0)	12 (27.3)	.09
All-cause readmission	80 (58.4)	53 (57.0)	27 (61.4)	.71
Foot-related readmission	54 (39.4)	43 (46.2)	11 (25.0)	.02*
Mortality	4 (2.9)	3 (3.2)	1 (2.3)	1.00

Abbreviations: BMI, body mass index; DM, diabetes mellitus; WBC, white blood cell count.
Continuous factors such as age and BMI are represented as median, mean (standard deviation), and categorical factors such as sex and comorbidities are represented as frequency within the study population, n (%).
* Statistically significant.

Mutluoglu et al (8), patients with osteomyelitis had longer hospitalization, more overall amputations, more minor amputations, and more major amputations than patients with soft tissue infections.

The treatment of osteomyelitis may be different based on the cultural bias of the treating physician. Cultural bias is defined as making judgments based on one's training and beliefs (9–11). This can be applied within the field of medicine and can be affected by medical and surgical specialty training. We acknowledge that the ultimate decision for performing surgery or amputation was made by a team of surgeons. Some surgeons believe that medical treatment for osteomyelitis is not effective. Surgeons' training could bias them toward more aggressive surgery and perhaps more proximal amputations to completely remove the infected bone. Other subspecialties may favor less aggressive surgery and medical treatment in patients with osteomyelitis in the belief that limited bone resection or local amputation is often successful while maintaining function of the extremity.

In their evaluation of SIRS criteria, Wukich et al (5) reported the results of 119 patients admitted to the hospital for moderate and severe DFIs; 66.4% had osteomyelitis. They reported a higher rate of amputation overall in people with SIRS criteria than in those with moderate infections (63% versus 40%) and a higher rate of leg amputation (25% versus 5%) (5). In patients that met SIRS criteria and patients that did not, we reported a lower rate of any amputation (20.5% versus 29.0%) and a lower rate of major amputation (6.8% versus 7.5%) compared with the rates in Wukich et al (5).

Selection bias in our series is likely for several reasons. Our study population may not be generalizable to the general population because our patients were from a safety-net hospital in which a large proportion of patients are uninsured or underinsured, with barriers that impede health care, including simple things such as available transportation to attend follow-up visits. Major barriers include the inability to receive outpatient parenteral antibiotic therapy, orthotics, and prosthetics and lack of a support system at home that promotes wellness. In additional, our study included a minority population that is disproportionately larger than the general population.

We defined soft tissue infection as a negative MRI, SPECT CT, bone culture, or histology because we wanted to reduce the risk that our cohort would have patients with misclassified osteomyelitis. We acknowledge that this could lead to selection bias, potentially including more severe soft tissue infections. In addition, measurement bias was likely because various operational definitions were used to define disease; however, the most important study criteria such as SIRS, peripheral arterial disease, amputation, and length of stay were objective. Finally, we recognize that the retrospective nature of this study is a major limitation.

In conclusion, based on our retrospective analysis of 137 hospitalized patients with DFIs, we found that patients that present with SIRS criteria for severe infection did not have significantly higher rates of surgery, amputation, duration of antibiotics, reinfection, or readmission for foot complications. Patients with SIRS experienced longer hospital stays. Consequently, the use of SIRS to assess outcomes in patients with soft tissue DFIs may be less predictive than previously reported.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1053/j.jfas.2019.06.001.

References

1. Lavery LA, Lavery DC, Hunt NA, La Fontaine J, Ndip A, Boulton AJ. Amputations and foot-related hospitalizations disproportionately affect dialysis patients. Int Wound J 2015;12:523–526.
2. Reiber GE, Pecoraro RE, Koepsell TD. Risk factors for amputation in patients with diabetes mellitus. A case-control study. Ann Intern Med 1992;117:97–105.
3. Lavery LA, Armstrong DG, Murdoch DP, Peters EJ, Lipsky BA. Validation of the Infectious Diseases Society of America's diabetic foot infection classification system. Clin Infect Dis 2007;44:562–565.
4. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, Deery HG, Embil JM, Joseph WS, Karchmer AW, Pinzur MS, Senneville E, Infectious Diseases Society of America. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54:e132–e173.
5. Wukich DK, Hobizal KB, Raspovic KM, Rosario BL. SIRS is valid in discriminating between severe and moderate diabetic foot infections. Diabetes Care 2013;36:3706–3711.
6. Wukich DK, Hobizal KB, Sambenedetto TL, Kirby K, Rosario BL. Outcomes of osteomyelitis in patients hospitalized with diabetic foot infections. Foot Ankle Int 2016;37:1285–1291.
7. Wukich DK, Hobizal KB, Brooks MM. Severity of diabetic foot infection and rate of limb salvage. Foot Ankle Int 2013;34:351–358.
8. Mutluoglu M, Sivrioglu AK, Eroglu M, Uzun G, Turhan V, Ay H, Lipsky BA. The implications of the presence of osteomyelitis on outcomes of infected diabetic foot wounds. Scand J Infect Dis 2013;45:497–503.
9. Douglas M. *In the active voice*. Routledge, Abingdon, UK, 2011.
10. PsycholoGenie. Understanding the phenomena of cultural bias with examples. Available at: https://psychologenie.com/understanding-cultural-bias-with-examples. Accessed June 27, 2018.
11. Mills AJ, Durepos G, Wiebe E. Cognitive biases. In: *Encyclopedia of case study research, volumes I and II*. Sage Publications, Thousand Oaks, CA, 2010.