Internal and Emergency Medicine (2023) 18:185–191
https://doi.org/10.1007/s11739-022-03166-8

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Management patterns and outcomes of patients hospitalized with diabetic foot ulcers at one tertiary care hospital

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Received: 4 August 2022 / Accepted: 22 November 2022 / Published online: 6 December 2022
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Abstract

A diabetic foot ulcer is present in approximately 2.4% of hospitalized patients. Care for diabetic foot ulcers is highly variable. We sought to describe care practice patterns and risk factors for poor outcomes for patients hospitalized with a diabetic foot ulcer in our institution, an 894-bed tertiary care academic hospital located in downtown Chicago, IL. We conducted a retrospective cohort study of patients hospitalized with a diabetic foot ulcer between March 3rd, 2018 and December 31st, 2019. We categorized patients into having an uncomplicated ulcer or a complicated ulcer with cellulitis, wound infection, osteomyelitis, or gangrene. We evaluated rates of diagnostic resource utilization (imaging, cultures, biopsies, and antibiotics) and outcomes of osteomyelitis, amputation, and death. There were 305 patients of interest in the study cohort. A complicated lower extremity ulcer was found in 79% of patients. Amputation was required in 25% of patients, 21% were readmitted, and 13% died. Imaging was obtained in less than 50% of all patients, and in 60% or less of those with osteomyelitis. Bone biopsies were rarely acquired. Empiric antibiotics were prescribed in 77% of patients with osteomyelitis. Male, Black or African-American patients, and those with high Charlson score had the highest risk of poor outcomes. Care practices for patients hospitalized with diabetic foot ulcers were highly variable. Future interventions should target standardization to improve outcomes, with particular attention to health inequities as vulnerable populations have a higher risk of poor outcomes.

Keywords Diabetes · Foot ulcer · Infection · Musculoskeletal · Vascular · Orthopedics

Introduction

Approximately 11.3% of individuals in the United States have diabetes mellitus [1]. One major complication of long-standing diabetes is the development of a foot ulcer (DFU), with an annualized incidence of 6.3% in Medicare beneficiaries [2] and overall lifetime risk between 19 and 34% [3]. Moreover, DFUs can lead to further devastating complications, such as osteomyelitis, amputation, and death. In one managed care-based outpatient clinic, 9.1% of patients developed diabetic foot infections (DFI), of which 19.9% were biopsy-proven osteomyelitis [4]. Patients with DFU have a 31% incidence rate of lower extremity amputation [5], and relative to patients with diabetes and without DFU, DFU is associated with a 2.5-fold 5-year increased risk of death [6]. DFUs are expensive, adding an estimated $9 billion to $13 billion in additional healthcare costs per year [7]. The prevalence of DFUs among patients admitted to the hospital is 2.4% [8], presenting an opportunity to intervene with those with DFU. With proper management, the majority of DFUs will heal within a year, preventing need for amputation [9].

Assessment of a DFU should include classification of wound, evaluation for infection, and detection of peripheral vascular disease. Proper management often requires multidisciplinary care, which may include wound care, off-loading, glycemic control, smoking cessation, surgical debridement, and/or antimicrobial therapy. Bone biopsies

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are considered the gold standard to diagnose, identify, and treat microorganisms in the case of diabetic foot osteomyelitis [10]. Despite this recommendation, the frequency and methodology of bone biopsy in clinical practice varies greatly [11]. Arterial studies should be pursued to screen for candidates with reduced peripheral perfusion eligible for revascularization [12].

To better understand current variations in clinical practice of DFU in the inpatient setting that may impact care, we undertook a study to measure patient characteristics, clinical processes, and outcomes for DFU. The primary focus of this study was to characterize practice patterns at one single large, academic, tertiary care center. The secondary aim was to identify patient characteristics that may lead to poor outcomes.

Methods

We conducted a retrospective cohort study of adults (age ≥ 18 years) with DFU hospitalized at Northwestern Memorial Hospital (NMH). NMH is an 894-bed academic medical center in Chicago, Illinois affiliated with the Northwestern University (NU) Feinberg School of Medicine. Using the NU Enterprise Data Warehouse (EDW), we identified the index encounter of eligible subjects who had active ICD-10 codes for diabetes and lower extremity ulcer and were discharged between March 3rd, 2018 and December 31st, 2019. March 3, 2018 was selected as start date for the cohort as this correlated with adoption of our current electronic medical record system. We then conducted manual chart review and excluded those with a non-foot ulcer or those without clear documentation of an ulcer. We included only patients with a known diagnosis of diabetes and clear documentation of a diabetic foot ulcer.

We utilized the EDW to collect baseline clinical, laboratory, and demographic data for patients. Laboratory data obtained was the erythrocyte sedimentation rate (ESR). Clinical data and comorbidities were obtained by International Classification of Diseases 10 (ICD-10) code. Outcome measures included length of stay, antibiotic prescriptions, type of imaging performed (x-ray (XR), magnetic resonance imaging (MRI) or lower extremity arterial duplex), physical therapy (PT) consultation, infectious diseases (ID) consultation, surgical revascularization, readmission, amputation, and death. Surgical revascularization, readmission, amputation, and death were evaluated and tallied if they occurred in the stated study period. We classified discharge antibiotics as PO-only if there was no IV antibiotic prescribed on discharge. Otherwise, antibiotics were classified as an IV-antibiotic-containing regimen. We grouped patients into complicated and uncomplicated DFU based on clinical adjudication and documentation from the primary service. We classified DFU as uncomplicated if an ulcer was documented as present with no other complications. We classified DFU as complicated if a DFU was documented as present with complications of cellulitis, wound infection, osteomyelitis, or gangrene. Patients with complicated DFU could concomitantly have multiple of the listed sub-diagnoses as can be evident in real-world practice, and was delineated by documentation and clinical adjudication of the primary service.

We summarized frequencies and counts of demographics, comorbidities, and outcome data by discharge diagnosis using descriptive statistics. We evaluated bivariate associations between clinical and demographic variables and outcomes using Chi-Square or Fisher's exact tests, based on counts. Missing data was labeled as "unknown" and retained for analysis in each category. We compared median length of stay using Kruskal–Wallis test. We used multivariable logistic regression to delineate likelihood of osteomyelitis, amputation, and death based on patient clinical and demographic factors decided a priori, and any that may have been found to be significant in bivariate Chi-Square associations. Only patients with complete data were included in the multivariate analysis and those with missing data were excluded by listwise deletion. R (4.1.1, Vienna, Austria) was used for analysis. The study was approved by the Northwestern University Institutional Review Board.

Results

Our study cohort included 305 patients with a diabetic foot ulcer on discharge. Patients were mostly male (69%) and had Medicare or Advantage insurance (69%). Black or African-American patients constituted 41% of the cohort. The median age was 66 years [IQR 57, 74] and median Charlson score was 8 [IQR 5, 11]. Most patients (79%) had a complicated lower extremity ulcer. Cellulitis was present in 28% of patients, wound infection was present in 16%, osteomyelitis was present in 49%, and 12% had gangrene. During the study period, 25% of patients required amputation, 21% of patients were re-admitted, and 13% of patients died. Additional baseline demographics of patients with uncomplicated ulcers and with osteomyelitis are displayed in Table 1. Supplementary table S1 displays baseline demographic data by all outcomes.

X-ray was obtained in 40% of all patients with an ulcer, MRI was obtained in 40%, and lower arterial extremity duplex was ordered in 48%. Blood cultures were obtained in 43% of all patients and were positive in 17% of those obtained. Surface swab wound cultures were ordered in 39% of all patients and positive in 92% of those obtained. Operating room (OR) tissue cultures were ordered in 14% of overall patients and positive in 81% of those obtained. OR bone cultures were ordered in 5% of all patients and

Table 1 Table demonstrating demographic data of cohort patients by uncomplicated ulcer and osteomyelitis

Demographic	Total ($n=305$) (%*)	Uncomplicated ulcer ($n=63$) (%*)	$p^{\#}$	Osteomyelitis ($n=149$) (%*)	$p^{\#}$
Gender			0.42		0.18
Male	209 (69%)	40 (63%)		108 (72%)	
Female**	96 (31%)	23 (37%)		41 (28%)	
Age			0.65		0.43
< 50	38 (12%)	10 (16%)		21 (14%)	
50–70**	146 (48%)	29(46%)		74 (50%)	
> 70	121 (40%)	24 (38%)		54 (36%)	
Charlson score			0.36		0.35
< 6**	86 (28%)	16 (25%)		47 (31%)	
6–8	89 (29%)	23 (37%)		44 (30%)	
> = 9	130 (43%)	24 (38%)		58 (39%)	
BMI (kg/m^2)			0.32		0.04
< 18	8 (3%)	1 (1%)		5 (3%)	
18–24.9**	65 (21%)	10 (16%)		36 (24%)	
25–29.9	80 (26%)	14 (22%)		47 (32%)	
30–39.9	97 (32%)	22 (35%)		42 (28%)	
> = 40	39 (13%)	13 (21%)		12 (8%)	
Not reported	16 (5%)	3 (5%)		6 (5%)	
ESR (mm/hr)			0.01		< 0.001
< 41**	47 (15%)	13 (21%)		21 (14%)	
41–73.9	57 (19%)	9 (14%)		32 (21%)	
74–107.9	44 (15%)	4 (6%)		30 (20%)	
> = 108	50 (16%)	6 (10%)		34 (23%)	
Not measured	107 (35%)	31 (49%)		32 (22%)	
Race and Ethnicity			0.36		0.69
Non-Hispanic White**	118 (39%)	27 (43%)		57 (38%)	
Black or African-American	124 (41%)	28 (44%)		60 (40%)	
Hispanic or Latino	43 (14%)	6 (10%)		24 (16%)	
Other	20 (6%)	2 (3%)		8 (6%)	
Insurance			0.48		0.44
Medicare or Advantage	203 (67%)	45 (73%)		93 (62%)	
Medicaid or replacement	36 (12%)	8 (13%)		19 (13%)	
Commercial or Private**	52 (17%)	8 (13%)		30 (20%)	
Other	13 (4%)	1 (1%)		7 (5%)	
Length of Stay in Days (Median [IQR])[a]	7 [4, 13]	6 [4, 10]		8 [5, 15]	
Revascularization	22 (7%)	4 (6%)	0.79	10 (7%)	0.91
Amputation	77 (25%)	2 (3%)	< 0.001	48 (32%)	0.01
Readmission	64 (21%)	16 (25%)	0.42	32 (21%)	0.95
Death	41 (13%)	11 (17%)	0.40	17 (11%)	0.40

*All percentage values are relative to total column counts

**Reference categories for logistic regression

#p values by Chi Square to determine bivariate association between outcome and comorbidity or condition

[a]$p < 0.001$ by Kruskal–Wallis test for difference in median length of stay

positive in 73% of those obtained. Of note, all operative cultures were obtained at the time of amputation. Antibiotics were prescribed on discharge for 62% of all patients. Anti-pseudomonal antibiotics were prescribed for 25% of all patients, while anti-MRSA antibiotics were prescribed for 39% of all patients. An IV-antibiotic-containing regimen

was prescribed on discharge in 25% of patients while 36% of patients were discharged with a PO-only regimen. Of all patients, 53% had ID consultation, 55% had PT consultation, 25% underwent an amputation, and 7% underwent surgical revascularization.

Limiting evaluation to only those with a diagnosis of osteomyelitis ($n=149$), XR was ordered in 49% of patients, MRI was ordered in 59%, and lower extremity arterial duplex was ordered in 60%. Blood cultures were obtained in 49% of patients and were positive in 19% of those obtained. Surface swab wound cultures were ordered in 40% of patients and positive in 98% of those obtained. Operating room tissue cultures were ordered in 17% of patients in positive in 72% of those obtained. Antibiotics were prescribed on discharge for 77% of patients. Anti-pseudomonal antibiotics were prescribed on discharge for 39% of patients, while anti-MRSA antibiotics were prescribed for 48% of patients. An IV-antibiotic-containing regimen was prescribed on discharge in 40% of patients while 38% of patients were discharged with a PO-only regimen. ID was consulted in 75% of patients, 54% had PT consultation, 32% underwent an amputation, and revascularization was performed in 7% of patients. Additional process metrics for patients with uncomplicated ulcers and osteomyelitis are displayed in Table 2. Supplementary table S2 displays process metrics stratified by all outcomes.

Factors associated with the diagnosis of osteomyelitis included male gender (aOR 2.1, 95% CI 1.0–4.1, $p=0.04$), ESR greater than 74 mm/hr (aOR 3.0, 95% CI 1.1–7.9, $p=0.03$), and ESR greater than 108 mm/hr (aOR 3.4, 95% CI 1.3–9.1, $p=0.01$). Male patients were more likely to have amputation (aOR 2.4, 95% CI 1.1–5.5, $p=0.04$). Patients with the highest odds for mortality were Black or African-American (aOR 3.8, 95% CI 1.1–13.2, $p=0.04$) and those with Charlson score ≥ 9 (aOR 5.9, 95% CI 1.2–29.5, $p=0.03$). Additional adjusted odds ratios are displayed in Table 3.

Discussion

Diabetic foot ulcers are associated with high rates of osteomyelitis, amputation, readmission, and death. During the almost 2-year study period, patients had an overall mortality

Table 2 Table demonstrating hospitalization processes (imaging, consultation, cultures, and prescription) by uncomplicated ulcer and osteomyelitis

Tests, consultations, and prescriptions	Total ($n=305$) (%*)	Uncomplicated Ulcer ($n=63$) (%*)	$p^{\#}$	Osteomyelitis ($n=149$) (%*)	$p^{\#}$
Imaging					
X-ray	123 (40%)	19 (30%)	0.09	73 (49%)	0.004
MRI	123 (40%)	9 (14%)	< 0.001	88 (59%)	< 0.001
Lower extremity arterial duplex / ABI	147 (48%)	17 (27%)	< 0.001	89 (60%)	< 0.001
Consultation					
Physical Therapy	167 (55%)	31 (49%)	0.39	80 (54%)	0.80
Infectious Disease	162 (53%)	15 (24%)	< 0.001	112 (75%)	< 0.001
Cultures					
Blood cultures ordered	131 (43%)	16 (25%)	0.003	73 (49%)	0.05
Blood cultures positive	22 (7%)	3 (5%)	0.46	14 (9%)	0.22
Wound swab ordered	118 (39%)	15 (24%)	0.01	60 (40%)	0.66
Wound swab positive	109 (36%)	11 (18%)	0.001	59 (40%)	0.21
OR Tissue culture ordered	42 (14%)	5 (8%)	0.19	25 (17%)	0.19
OR Tissue culture positive	34 (11%)	4 (6%)	0.26	18 (12%)	0.75
OR Bone culture ordered	15 (5%)	1 (2%)	0.22	12 (8%)	0.03
OR Bone culture positive	11 (4%)	0 (0%)	0.13	10 (7%)	0.01
Discharge antibiotics					
Any	187 (61%)	19 (30%)	0.29	115 (77%)	< 0.001
Anti-pseudomonal	76 (25%)	4 (6%)	< 0.001	58 (39%)	< 0.001
Anti-MRSA	118 (39%)	14 (22%)	0.004	72 (48%)	0.001
Regimen with IV antibiotic	76 (25%)	3 (5%)	< 0.001	59 (40%)	< 0.001
PO-only regimen	111 (36%)	16 (25%)	0.06	56 (38%)	0.76

*All percentage values are relative to total column counts

#p value generated by Chi square test between outcome and testing or treatment modality in question

Table 3 Table demonstrating adjusted odds ratios for osteomyelitis, amputation, and death by multivariable logistic regression

Variable	Osteomyelitis		Amputation		Death	
	aOR (95% CI)	*p*	aOR (95% CI)	*p*	aOR (95% CI)	*p*
Gender						
Male	2.1 (1.0–4.1)	0.04	2.4 (1.1–5.5)	0.04	0.8 (0.3–2.1)	0.64
Female**	–	–	–	–	–	–
Age						
< 50	1.0 (0.3–3.1)	1	0.6 (0.2–2.1)	0.43	2.4 (0.3–16.9)	0.38
50–70**	–	–	–	–	–	–
> 70	0.9 (0.4–2.1)	0.87	0.6 (0.3–1.4)	0.25	0.8 (0.3–2.7)	0.78
Charlson						
< 6**	–	–	–	–	–	–
6–8	0.9 (0.4–2.2)	0.84	1.6 (0.6–4.2)	0.37	2.5 (0.5–13.2)	0.28
> = 9	0.7 (0.3–1.7)	0.41	1.6 (0.6–4.2)	0.36	5.9 (1.2–29.5)	0.03
BMI (kg/m^2)						
< 18	2.5 (0.2–31.5)	0.47	0.46 (0.03–7.01)	0.58	2.9 (0.2–45.8)	0.46
18–24.9**	–	–	–	–	–	–
25–29.9	1.0 (0.4–2.6)	0.98	0.5 (0.2–1.5)	0.23	1.4 (0.3–5.5)	0.67
30–39.9	0.4 (0.2–1.1)	0.07	0.6 (0.2–1.6)	0.29	1.2 (0.3–4.9)	0.81
> = 40	0.14 (0.04–0.47)	0.001	0.7 (0.2–2.5)	0.59	1.8 (0.3–9.8)	0.50
ESR (mm/hr)						
< 41**	–	–	–	–	–	–
41–73.9	1.4 (0.6–3.3)	0.48	1.5 (0.5–4.7)	0.45	0.5 (0.1–2.3)	0.37
74–107.9	3.0 (1.1–7.9)	0.03	1.9 (0.6–5.7)	0.28	0.3 (0.1–2.0)	0.23
> = 108	3.4 (1.3–9.1)	0.01	4.0 (1.3–12.1)	0.01	1.8 (0.5–6.5)	0.34
Race and Ethnicity						
Non–Hispanic White**	–	–	–	–	–	–
Black or African–American	1.4 (0.6–2.8)	0.42	1.5 (0.7–3.6)	0.31	3.8 (1.1–13.2)	0.04
Hispanic or Latino	1.7 (0.6–4.9)	0.35	1.7 (0.6–5.3)	0.35	2.3 (0.4–12.8)	0.35
Other	0.3 (0.1–1.5)	0.15	2.0 (0.4–10.3)	0.41	1.9 (0.1–25.5)	0.64
Insurance						
Medicare or advantage	0.8 (0.3–2.0)	0.60	0.5 (0.2–1.4)	0.19	0.7 (0.2–2.8)	0.64
Medicaid or replacement	0.8 (0.2–2.8)	0.76	0.18 (0.04–0.8)	0.03	0.27 (0.02–3.00)	0.29
Commercial or Private**	–	–	–	–	–	–
Other	0.3 (0.05–2.06)	0.23	2.0 (0.3–12.0)	0.47	1.6 (0.1–23.8)	0.74

**Reference category

of 13% (6.5% annually), consistent with rates previously described in the literature [13, 14].

Notably, care provided was quite variable. Imaging utilization was surprisingly low (less than 50% of all patients). Arterial studies were not commonly ordered despite societal recommendations and their notable benefit [12]. When considering patients with a diagnosis of osteomyelitis, imaging utilization increased slightly. Additionally, PT was also not commonly consulted despite a prominent role the discipline plays in gait training and wound healing [15–18]. Bone biopsy was rarely performed for the diagnosis of osteomyelitis in our institution as osteomyelitis was diagnosed predominantly by clinical examination, review of laboratory data, and imaging. Though bone biopsy is the gold standard for diagnosis of osteomyelitis, MRI has been shown to be non-inferior to bone biopsy [19], and may have reduced the number of obtained biopsies. Additionally, it is not clear if the physical exam at the time of hospitalization had grossly evident findings of osteomyelitis (probe-to-bone or purulence near bone), which may have further reduced imaging use.

Microbiologic data was of variable utility. Blood cultures rarely yielded organisms (17% of drawn, 7% of all patients). Surface wound cultures yielded organisms nearly 100% of the time, but the clinical significance of the organisms found is unclear. These two culture modalities do not seem to be particularly useful in patients hospitalized for DFU. In patients with osteomyelitis, operating room deep tissue cultures and bone biopsies demonstrated an organism in 18/25 patients and 10/12 patients, respectively. While

biopsies and deeper samples would be more likely to guide antibiotic choice, they did not constitute a large subset of patients in our cohort and were mostly performed at the time of amputation.

Most antibiotics were empirically prescribed. Antibiotic prescription occurred in 77% of patients with osteomyelitis and did not rely on culture. Anti-pseudomonal antibiotics were prescribed in 39% of patients with osteomyelitis, while anti-MRSA antibiotics were prescribed in 48%, which is slightly higher than prescription rates for these organisms than with the other diagnoses in the study. Anti-MRSA prescription rates were likely higher than necessary, given that MRSA seems to have detected in 17.5% [20], 4.3% [21], 9.6% [21], 12% [22], and 35% [23] of isolates in other case series. Similarly, anti-pseudomonal antibiotic prescriptions were likely higher than necessary, given that pseudomonas was detected in 9% of isolates in another case series [23]. Though bone biopsies were performed rarely in our institution, it is not clear if they would have changed management, as in one study, microbiologic diagnosis from percutaneous biopsy did not correlate with prescribed antibiotics [24]. Long-term outcomes are not known given the time-limited nature of our dataset. Further study should examine whether wounds heal more or less frequently or if outcomes improve with targeted versus empirically prescribed therapy.

Our secondary analysis demonstrates Black or African American patients are at highest risk for mortality, consistent with findings in the literature. Several studies have demonstrated Black or African American patients and rural patients are at high risk for amputation or death [25–28]. This suggests social determinants of health play a significant role and highlights the need to ensure parity of delivered care to optimize outcomes in a vulnerable population. Many patients in these communities do not have appropriate or adequate access to care, impairing ability of wounds to heal. Focus should be directed on expanding access to care and resources for these at-risk communities to improve healthcare equity and reduce risk of amputation or other deleterious outcomes.

Our study's strength lies in that it is a moderate to large sized retrospective cohort study of hospitalized patients with real-world data. Our study also has certain limitations. First, this study is single-site, and it is possible the trends elucidated in this study may be different at other institutions. Despite this, our reported findings are similar to those found in the literature. Second, it is possible that our institution had an underdiagnosis of osteomyelitis. Underdiagnosis of osteomyelitis may diminish some bivariate associations that could potentially inform future study. Despite this, the largest single outcome in our study was a diagnosis of osteomyelitis. Third, there is some overlap between the complicated ulcer outcome categories. This mirrors real-world findings where patients with complicated lower extremity ulcers often have multiple diagnoses (osteomyelitis and cellulitis, for example) and a principal diagnosis may be nebulous. Fourth, given that this was a retrospective cohort database study relying on a primary service's adjudication, there may have been some misdiagnosis or misclassification leading to bias. Finally, wound stages were frequently not documented and thus were not reported or analyzed. Outcomes may vary with wound stage, so this is a limitation of the data.

Despite guidelines on management, there seems to be significant deviation from standard care recommendations, reflecting the complex nature of these patients in real-world practice. Better adherence to guidelines would most likely improve outcomes but needs directed study. Blood and surface cultures seem to be low-yield and should likely be avoided. Increasing PT consultation may improve long-term outcomes through gait training, wound management, and footwear selection. Bone biopsies may facilitate microbiologic diagnosis and targeted therapy, but it is not clear if this would improve outcomes. Vulnerable populations seem to suffer the most and careful attention should be paid to increase access to care and ensure adherence to guidelines to maximize likelihood of good outcomes.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11739-022-03166-8.

Declarations

Conflict of interest To the best of our knowledge, no conflict of interest, financial or other, exists with regards to the information presented in this manuscript.

Ethical approval This study was approved through the Northwestern University Institutional Review Board (IRB).

Human and animal rights statement and informed consent This sudy complies with international, national, and/or institutional standards on research involving Human Participants and/or Animals and Informed Consent and was approved by the Northwestern University Institutional Review Board.

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