Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

ORIGINAL CONTRIBUTION

Predictors of Failure of Empiric Outpatient Antibiotic Therapy in Emergency Department Patients With Uncomplicated Cellulitis

Daniel Peterson, MD, FRCP(C), PhD, Shelley McLeod, MSc, Karen Woolfrey, MD, FRCP(C), and Andrew McRae, MD, FRCP(C), PhD

Abstract

Background: Despite several expert panel recommendations and cellulitis treatment guidelines, there are currently no clinical decision rules to assist clinicians in deciding which emergency department (ED) patients should be treated with oral antibiotics and which patients require intravenous (IV) therapy at first presentation of cellulitis amenable to outpatient treatment.

Objectives: The objective was to determine risk factors associated with adult patients presenting to the ED with cellulitis who fail initial antibiotic therapy as outpatients and require a change of antibiotics or admission to hospital.

Methods: This was a prospective cohort study of patients 18 years of age or older presenting with cellulitis to one of two tertiary care EDs (combined annual census 140,000). Patients were excluded if they had been treated with antibiotics for the cellulitis before presenting to the ED, if they were admitted to the hospital, or if they had an abscess only. Trained research personnel administered a questionnaire at the initial ED visit with telephone follow-up 2 weeks later. Multivariable logistic regression models determined predictor variables independently associated with treatment failure (failed initial antibiotic therapy and required a change of antibiotics or admission to hospital).

Results: A total of 598 patients were enrolled, 52 were excluded, and 49 were lost to follow-up. The mean (±standard deviation [SD]) age was 53.1 (±18.4) years and 56.4% were male. A total of 185 patients (37.2%) were given oral antibiotics, 231 (46.5%) were given IV antibiotics, and 81 patients (16.3%) received both oral and IV antibiotics in the ED. A total of 102 (20.5%, 95% confidence [CI] = 17.2% to 24.2%) patients had treatment failures. Fever (temperature > 38°C) at triage (odds ratio [OR] = 4.3, 95% CI = 1.6 to 11.7), chronic leg ulcers (OR = 2.5, 95% CI = 1.1 to 5.2), chronic edema or lymphedema (OR = 2.5, 95% CI = 1.5 to 4.2), prior cellulitis in the same area (OR = 2.1, 95% CI = 1.3 to 3.5), and cellulitis at a wound site (OR = 1.9, 95% CI = 1.2 to 3.0) were independently associated with treatment failure.

Conclusions: These risk factors should be considered when initiating empiric antibiotic therapy for ED patients with cellulitis amenable to outpatient treatment.

ACADEMIC EMERGENCY MEDICINE 2014;21:526–531

Cellulitis is an acute or subacute infection of the dermis and subcutaneous tissue of presumed bacterial etiology characterized by warmth, erythema, swelling, and tenderness. Although cellulitis is a common emergency department (ED) presentation, there are few published studies documenting the actual

From the Division of Emergency Medicine, Department of Medicine, Schulich School of Medicine and Dentistry, The University of Western Ontario (DP, SL, KW), London, Ontario; and the Department of Emergency Medicine, University of Calgary (AM), Calgary, Alberta, Canada.

Received June 26, 2013; revision received December 2, 2013; accepted January 6, 2014.

Presented at the Society for Academic Emergency Medicine Annual Meeting, Chicago, IL, May 2012; and the Canadian Association of Emergency Physicians Conference, Niagara Falls, Ontario, Canada, June 2013.

The authors have no relevant financial information or potential conflicts of interest to disclose.

Supervising Editor: Sandy Bogucki, MD, PhD.

Address for correspondence and reprints: Daniel Peterson, FRCPC, MD, PhD; e-mail: dpeter6@uwo.ca.

ISSN 1069-6563
PII ISSN 1069-6563583

doi: 10.1111/acem.12371

prevalence of this medical condition. Physician visits (physician offices, hospital outpatient departments, and EDs) for cellulitis increased from 32 to 48 visits per 1,000 patients from 1997 to 2005, with the largest relative increase occurring in EDs.[1]

There is no widely accepted classification system for grading the severity of cellulitis. This leads to considerable treatment variation among physicians based on their assessment of the severity of the infection and their preferred antibiotic regimens. Despite several expert panel recommendations and cellulitis treatment guidelines,[2–13] there are currently no clinical decision aides to assist clinicians when deciding which ED patients should be treated with oral antibiotics and which patients require intravenous (IV) therapy at first presentation.

The majority of publications reporting risk factors for cellulitis have been case-control studies of patients hospitalized with cellulitis.[14–17] These studies showed that disruption of the cutaneous barrier (leg ulcer, wound, fissurated toe-web intertrigo, pressure ulcer, or leg dermatosis), venous insufficiency, leg edema, being overweight, fungal infections, history of cellulitis, chronic venous insufficiency, prior saphenectomy, white race, and the presence of *Staphylococcus aureus* and/or B-hemolytic streptococci in the toe webs to be independently associated with cellulitis.[14–17] A retrospective study of admitted patients with cellulitis reported that lower extremity edema, body mass index (BMI), smoking, and homelessness were independently associated with recurrent cellulitis.[18]

Although these studies have reported potential risk factors associated with the development of cellulitis, there has only been one study describing univariate associations between factors associated with failure of standard ED treatment of cellulitis.[19] The small sample size of the study did not allow for multivariable analysis. Therefore, there are very little data on risk factors for treatment failure of cellulitis in the ED patient population.

The primary objective of this study was to determine risk factors independently associated with failure of empiric antibiotic therapy in ED patients with cellulitis initially treated as outpatients. The secondary objective was to describe the antibiotic prescribing practices for cellulitis at our institution.

METHODS

Study Design

This was a prospective cohort study. Approval for this research study was obtained from the Health Sciences Research Ethics Board at Western University, and the study was registered with ClinicalTrials.gov (NCT01972646).

Study Setting and Population

The study was conducted over an 18-month period (June 2010 to November 2011) at an academic tertiary care center consisting of two EDs with a combined annual census of 140,000 visits in London, Ontario, Canada. Adult patients (18 years or older) whose chief complaints were consistent with skin or soft tissue infections (key words included cellulitis, abscess, infection, bite, ulcer, or rash) were screened for eligibility by ED staff or trained research assistants and invited to participate in this study once an emergency physician (EP) confirmed a cellulitis infection.

Study Protocol

Our case definition of cellulitis was an acute or subacute infection of the dermis and subcutaneous tissue of presumed bacterial etiology characterized by warmth, erythema, swelling, and tenderness. The EPs in London, Ontario, operate a daily outpatient IV antibiotic clinic for conditions such as cellulitis that may require several days of IV therapy, including daily reassessment before switching to oral antibiotics. Therefore, when a patient presented to the ED with cellulitis during the study period, he or she followed one of three possible dispositions: 1) the cellulitis was severe enough to warrant admission to the hospital and the patient was excluded from the study, 2) the cellulitis was minor enough that the patient was discharged home with oral antibiotics, or 3) the patient was started on IV antibiotics and asked to follow up the following day in the IV antibiotics clinic for reassessment. The physicians had the option of starting their own preferred IV antibiotic regimens. If the chosen IV antibiotic regimen required more than once-daily dosing, then home care was arranged so the patients could receive the appropriate dosing. Each day in the clinic, the physicians would evaluate each patient and decide if the patient required continued IV administration of the same antibiotic, if the patient could be "stepped-down" to an oral antibiotic, or whether the physician deemed the situation a treatment failure and switched the IV antibiotics.

Research assistants enrolled eligible patients in the ED from 07:00 to 22:00 hours, 7 days a week. Patients were excluded from this study if they were admitted to the hospital, if they were currently taking or had been recently treated with antibiotics for the cellulitis prior to presenting to the ED, had abscesses with no concomitant cellulitis, were cognitively impaired, or did not read or speak English. If a patient had an abscess with a surrounding cellulitis, he or she was considered eligible for inclusion in the study if he or she received antibiotics in addition to incision and drainage (I&D) of the abscess with subsequent discharge from the ED. Patients with chronic wounds or ulcers were asked to continue their usual wound care practices during the study period.

During the initial ED visit, participants completed a health and lifestyle questionnaire that included a detailed assessment of demographic characteristics, past antibiotic use, alcohol/drug use habits, and past medical history. Survey questions were created by the investigators based on a review of relevant literature as well as consultation with emergency residents, physicians, and an epidemiologist. Prior to distribution, the questionnaire was peer-reviewed and tested for language and ease of comprehension. The research assistants screened for eligible patients and distributed and collected all questionnaires.

In conjunction with the treating physician, the research assistant completed a second data collection sheet that compiled data regarding the clinical

presentation, including triage vital signs, physical examination findings, and prescribed antibiotic regimen. Antibiotic treatment regimens were left to the discretion of the treating physicians. Participants were contacted by telephone by the research assistants 2 weeks after ED enrollment to evaluate response to antibiotics, unplanned return visits to the ED or another health care provider, subsequent need for hospitalization, subsequent need for I&D of the wound, and need for antibiotic adjustment.

Outcome Measures

The primary outcome was treatment failure, defined as subsequent hospitalization for the cellulitis or failed initial antibiotic therapy that required a change of antibiotics. A treatment failure for subsequent admission to the hospital had to be secondary to a worsening of the cellulitis or complication of the cellulitis and not due to another unrelated condition. A change in antibiotics was deemed a treatment failure if there was a switch from one oral or IV antibiotic to another or "stepping up" therapy from an oral to an IV antibiotic. "Step-down" therapy from an IV antibiotic to an oral antibiotic was not considered a treatment failure.

Data Analysis

To estimate the sample size required for the multivariable regression model, we used the formula by Peduzzi et al.,[20] $N = 10\ k/p$, where p is the estimated proportion of patients who would fail initial antibiotic treatment and k is the number of covariates (independent variables) to be included in the model. We estimated that 20% of patients would fail initial antibiotic treatment and expected to include 10 covariates in the model. We estimated that 500 patients needed to be enrolled and increased our sample size by an additional 20% to account for potential missing data.[20,21]As an estimate of precision, this sample size would permit a 95% confidence interval [CI] of 16.7% to 23.7% around a treatment failure incidence of 20%.

Data were entered directly into a study-specific Microsoft Excel database. Patient characteristics were summarized using descriptive statistics and 95% CIs using standard equations. Data elements were chosen with the intent of evaluating variables for model inclusion based on what is known about the epidemiology of the disease process as well as hypothesized relationships between potential independent variables and treatment failure. Univariable analyses of all potential patient risk factors were completed and clinically relevant variables with p-values of 0.10 or less in the univariable analysis were considered for the multivariable models. Multivariable logistic regression models were used to determine predictor variables independently associated with treatment failure. Likelihood ratio tests determined appropriate inclusion of variables in the multivariable logistic regression model. Backward, stepwise multivariable logistic regression (Wald removal criterion of 0.1) was used to determine predictor variables independently associated with treatment failure. The Hosmer-Lemeshow goodness-of-fit statistic measured how well the final model described the response variable. To test the robustness of the final multivariable model, a sensitivity analysis was planned to include all patients lost to follow-up. All analyses were performed using SPSS 21.0.

RESULTS

A total of 598 patients were enrolled in this study. Fifty-two were excluded, with the majority of these already on antibiotics when they presented to the ED and one patient sent directly to ophthalmology clinic for assessment of a postoperative facial cellulitis. Forty-nine patients were lost to follow-up, leaving 497 for final analysis. Figure 1 outlines the antibiotic prescribing pattern in terms of who received oral, IV, or both oral and IV therapy. Potential risk factors for failing antibiotic therapy for simple cellulitis were divided into patient historical characteristics (Table 1) and patient characteristics at ED presentation (Table 2).

A total of 102 patients (20.5%, 95% CI = 17.2% to 24.3%) had treatment failures. The majority of treatment failures were a result of a change of antibiotic (78.4%, 95% CI = 69.5% to 85.3%) as opposed to subsequent need for hospital admission (21.6%, 95% CI = 14.7% to 30.5%). Treatment failures were similar in patients initially treated with IV antibiotics (40.2%, 95% CI = 31.2% to 49.9%) and those initially treated with oral antibiotics (38.2%, 95% CI = 29.4% to 47.9%), while those treated with both oral and IV antibiotics had a lower failure rate (21.6%, 95% CI = 14.7% to 30.5%; Table 3).

Fever (temperature > 38°C) at triage (odds ratio [OR] = 4.3, 95% CI = 1.6 to 11.7), chronic leg ulcers (OR = 2.5, 95% CI = 1.1 to 5.2), chronic edema or lymphedema (OR = 2.5, 95% CI = 1.5 to 4.2), prior cellulitis in the same area (OR = 2.1, 95% CI = 1.3 to 3.5), and

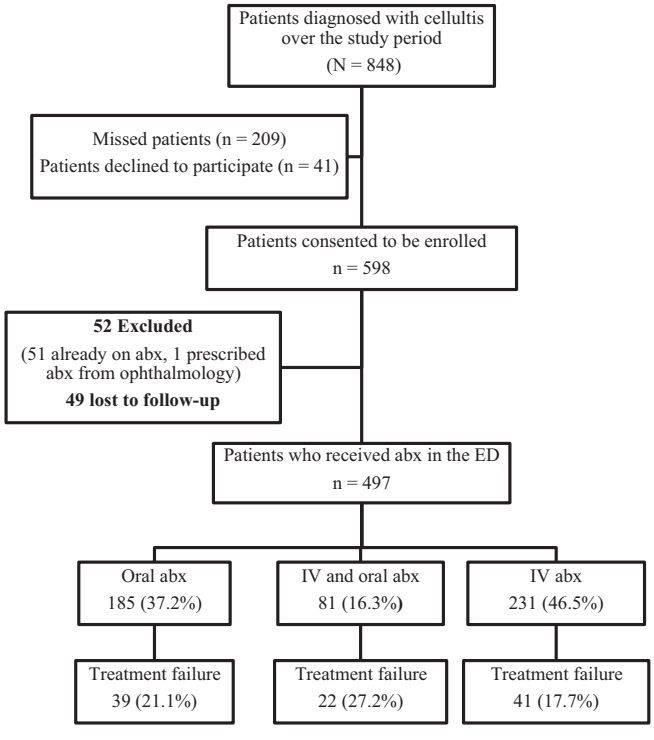

Figure 1. Flow diagram of enrolled patients in the study. Abx = antibiotics.

Table 1
Patient Characteristics Organized by Whether They Had Treatment Failure or Not

Variables	No Treatment Failure (n = 395), n (%)	Treatment Failure (n = 102), n (%)	Total No. (n = 497)
Male	216 (54.7)	65 (63.7)	281
Age (yr), mean (±SD)	53.0 (±18.7)	53.5 (±17.4)	53.1
18–30	54 (13.7)	9 (8.8)	63
31–64	234 (59.2)	64 (62.7)	298
≥65	107 (27.1)	29 (28.4)	136
Income < $18,000	105 (26.6)	26 (25.5)	131
BMI			
<19	12 (3.0)	4 (3.9)	16
19–25	119 (30.1)	28 (27.5)	147
26–30	131 (33.2)	27 (26.5)	158
>30	133 (33.7)	43 (42.2)	176
Smoker	100 (25.3)	24 (23.5)	124
>15 alcoholic beverages per week	19 (4.8)	5 (4.9)	24
IV drug use	43 (10.9)	12 (11.8)	55
Steroid use	22 (5.6)	10 (9.8)	32
Diabetes mellitus*	67 (17.0)	27 (26.5)	94
Current liver disease	14 (3.5)	3 (2.9)	17
Current cancer	19 (4.8)	6 (5.9)	25
Current kidney disease	9 (2.3)	1 (1.0)	10
Current skin disease*	31 (7.8)	15 (14.7)	46
HIV	3 (0.5)	0 (0)	3
Known MRSA+ status	31 (7.8)	10 (9.8)	41
Prior antibiotic use within past 12 months	212 (53.7)	49 (48.0)	261
Cellulitis within past 12 months	219 (55.4)	60 (58.8)	279
Wound infection within past 12 months	165 (41.8)	51 (50.0)	216
Skin infection within past 12 months	128 (32.4)	35 (34.3)	163
History of cellulitis in same area*	91 (23.0)	41 (40.2)	132
History of surgery in same area	50 (12.7)	12 (11.8)	62

*Considered in the multivariable model.
BMI = body mass index; HIV = human immunodeficiency virus; MRSA = methicillin-resistant *S. aureus.*

Table 2
Patient Presenting Characteristics Organized by Whether They Had Treatment Failure or Not

Variables	No Treatment Failure (n = 395), n (%)	Treatment Failure (n = 102), n (%)	Total No. (n = 497)
Fever (T > 38°C at triage)*	9 (2.3)	13 (12.7)	22
Tachycardia (HR > 90 beats/min)*	109 (27.6)	37 (36.3)	146
Tachypnea (RR > 20/min)	9 (2.3)	2 (2.0)	11
Hypotension (sBP < 90) mm Hg	9 (2.3)	2 (2.0)	11
Hypoxia (O_2 saturation < 92%)	4 (1.0)	1 (1.0)	5
Chronic leg ulcers*	21 (5.3)	20 (19.6)	41
Wound*	137 (34.7)	48 (47.1)	185
Human, insect, or animal bite*	45 (11.4)	4 (3.9)	49
Intertrigo	7 (1.8)	1 (1.0)	8
Venous insufficiency	38 (9.6)	15 (14.7)	53
Chronic edema/ lymphedema*	56 (14.2)	36 (35.3)	92
Lymphangitic streaking	34 (8.6)	12 (11.8)	46
Cellulitis	343 (86.8)	85 (83.3)	428
Abscess with surrounding cellulitis	53 (13.4)	17 (16.7)	70
Location of infection			
Foot	59 (14.9)	18 (17.6)	77
Leg	135 (34.1)	39 (38.2)	174
Groin/hip/buttock	14 (3.5)	5 (4.9)	19
Trunk	14 (3.5)	6 (5.9)	20
Upper extremity	121 (30.6)	27 (26.5)	148
Head/neck*	38 (9.6)	4 (3.9)	42
Multiple sites	14 (3.5)	3 (2.9)	17
Size of infection (cm^2)			
<10	209 (52.9)	54 (52.9)	263
10–40	109 (27.6)	28 (27.5)	137
>40	74 (18.7)	20 (19.6)	94
Unknown	3 (0.8)	0 (0)	3

HR = heart rate; RR = respiratory rate; sBP = systolic blood pressure; T = temperature.
*Considered in the multivariable model.

cellulitis at a wound site (OR = 1.9, 95% CI = 1.2 to 3.0) were independently associated with failure of empiric antibiotic therapy in ED patients with cellulitis as determined by multivariable logistic regression analysis (Table 4).

Although fewer than 10% of the sample were lost to follow-up, it is still possible that exclusion of these patients introduced bias. To test the robustness of the final multivariable model, we performed a sensitivity analysis where we included all patients lost to follow-up and varied the proportion classified as having the outcome. We first classified all 52 patients as having had treatment failures and then again classified all 52 patients as having no treatment failures and repeated the analyses. The model parameters did not change substantially.

Antibiotic treatment regimens were highly variable. Numerous oral, IV, and combination of oral and IV therapies were prescribed. Table 3 outlines the prescribed antibiotics by group according to treatment failure or not. Of the oral antibiotics, cephalexin was prescribed most frequently (66.5%), with cloxacillin the second most commonly prescribed (12.4%). Ceftriaxone (49.4%) and cefazolin (45.5%) were the most commonly prescribed IV therapies. The most common combination therapies were cefazolin/cephalexin (28.4%) and ceftriaxone/cephalexin (28.4%).

DISCUSSION

This is the largest prospective study of adult patients presenting to the ED with cellulitis that evaluates

Table 3
Common Antibiotics Prescribed According to Treatment Failure or Not

Type of Antibiotic	No Treatment Failure (n = 395), n (%)	Treatment Failure (n = 102), n (%)	Total No. (n = 497)
Oral antibiotics	146 (36.9)	39 (38.2)	185
Cephalexin	100 (25.3)	23 (22.5)	123
Cloxacillin	19 (4.8)	4 (3.9)	23
Amoxicillin-clavulanate	7 (1.8)	3 (2.9)	10
Trimethoprim/sulfamethoxazole	6 (1.5)	0 (0)	6
Clindamycin	5 (1.3)	3 (2.9)	8
Cefuroxime	2 (0.5)	1 (1.0)	3
Multiple oral antibiotics	7 (1.8)	5 (4.9)	12
IV antibiotics	190 (48.1)	41 (40.2)	231
Ceftriaxone	95 (24.0)	19 (18.6)	114
Cefazolin	85 (21.5)	20 (19.6)	105
Vancomycin	2 (0.5)	0 (0)	2
Cloxacillin	1 (0.2)	0 (0)	1
Multiple IV antibiotics	7 (1.8)	2 (2.0)	9
Both oral and IV antibiotics	59 (14.9)	22 (21.6)	81
Cefazolin + cephalexin	17 (4.3)	6 (5.9)	23
Ceftriaxone + cephalexin	19 (4.8)	4 (3.9)	23
Other combinations	23 (5.8)	12 (11.8)	35

IV = intravenous.

Table 4
Predictor Variables Associated With Failure of Empiric Outpatient Antibiotic Therapy in ED Patients With Cellulitis as Determined by Multivariable Logistic Regression Analysis

Predictor Variable	Adjusted OR	95% CI
Fever (T > 38°C) at triage	4.3	1.6–11.7
Chronic leg ulcers	2.5	1.1–5.2
Chronic edema or lymphedema	2.5	1.5–4.2
Prior cellulitis in the same area	2.1	1.3–3.5
Cellulitis at wound site	1.9	1.2–3.0

The Hosmer-Lemeshow chi-square test for the final model yields a p-value of 0.971 (χ^2 = 0.529, degrees of freedom = 4), thus suggesting a model with good predictive value.
T = temperature.

potential risk factors for failure of initial outpatient antibiotic therapy (i.e., a change of antibiotics or subsequent admission to the hospital). We found that fever, chronic leg ulcers, chronic edema or lymphedema, prior cellulitis in the same area, and cellulitis at a wound site were independently associated with failure of empiric antibiotic therapy in ED patients with cellulitis. Additionally, the variability in antibiotic prescribing regimens observed in this study reinforces the idea that despite many proposed treatment guidelines in the literature, there is little, if any, agreement among clinicians as to the optimal outpatient antibiotic regimen for cellulitis.

An overall treatment failure rate of 20.5% was observed in this study. Although higher than expected, it is similar to the failure rate reported in a previous study of ED patients presenting with cellulitis (18.7%), where treatment failure was defined as hospital admission, specialist consultation, change in antibiotics, or surgical procedure.[19] A large retrospective epidemiologic study of cellulitis management reported a treatment failure rate of 13% and defined treatment failure as a change in or increased dose of antibiotics, addition of other agents, or relapse of infection.[22]

One Canadian study of ED patients with cellulitis identified older patients (mean age = 59 years vs. 46 years, p = 0.02), prior antibiotic treatment, and the initial size of the infection as risk factors for treatment failure.[19] However, their sample size was small (n = 75) and they were unable to perform a multivariable regression analysis. The majority of the remaining studies on risk factors for cellulitis were case-control studies of patients admitted with cellulitis and therefore represent a different population than our ED outpatient population.[14–17] Our large, prospective study identified one patient historical characteristic (prior cellulitis to the same area) and four patient presenting characteristics (temperature >38°C at triage, chronic leg ulcers, chronic edema/lymphedema, and cellulitis at a wound site) as independent predictors of failing empiric antibiotic therapy. Cellulitis at a wound site included scenarios where there was a break in the dermis and included postoperative incisions, lacerations, abrasions, bites, etc. These risk factors are easily obtained by history or readily apparent on physical examination and do not require fungal or bacterial skin cultures, blood tests, or imaging. Although commonly presumed to be risk factors for cellulitis, smoking, diabetes, obesity, and others were not found to be significant risk factors independently associated with treatment failure for cellulitis in our study.

There was a wide range of empiric antibiotic treatment regimens in our study. Eighteen different oral and IV antibiotics were used either alone or in various combinations. Another retrospective review of five urban centers found 25 different treatment regimens among 416 patients with cellulitis.[22] Under half (46.5%) of patients in this study were initially treated with IV antibiotics as opposed to oral antibiotics (37.2%). This perhaps reflects a local treatment practice where there is a morning clinic available 7 days/week where patients receive IV antibiotics with daily reassessment by EPs. This treatment variation indicates that despite many expert panel recommendations and guidelines, further work is required to develop evidence-based treatment strategies for cellulitis. Future studies should attempt to elucidate the optimal outpatient antibiotic regimen for ED patients with cellulitis.

Another recent study from our center showed that 13.2% of patients (27 out of 205) with skin and soft tissue infections were methicillin-resistant *S. aureus* (MRSA) positive.[23] Therefore, MRSA is not as pervasive in our community as others. In our study, patients were identified as MRSA positive if they had previous positive cultures, whether from infections or surveillance cultures. The likelihood that each subject's cellulitis was caused by MRSA was considered by the attending

physician at the time of assessment and treated accordingly.

LIMITATIONS

This study was conducted in two adult EDs within one medium-sized (approximately 350,000) city and as such the results may not be generalizable to other communities. Additionally, participants were contacted by telephone 2 weeks after ED enrollment; therefore, recall bias may have been a factor. Whenever possible, the electronic medical records were reviewed by research assistants to verify the information.

Similar to other EDs, if patients in this study required planned return visits for IV antibiotics or had unscheduled ED visits for reassessment, they were likely treated by more than one EP. Failure to respond to antibiotic therapy early in the course of antibiotics is highly subjective. The decision to change antibiotics, due to either a failure to respond or an antibiotic preference, was up to the discretion of the treating physician, which may have resulted in higher than actual failure rates due to clinician practice variability.

Finally, research assistants were only available from 07:00 to 22:00 hours, and therefore it is possible that some eligible patients may not have been enrolled if they presented outside these hours.

CONCLUSIONS

This is the largest prospective study to date evaluating potential risk factors for adult patients presenting to the ED with cellulitis who are initially treated as outpatients, who fail initial antibiotic therapy and require a change of antibiotics or admission to the hospital. Fever at triage, chronic leg ulcers, chronic edema or lymphedema, prior cellulitis in the same area, and cellulitis at wound site were independently associated with failure of empiric antibiotic therapy in ED patients with cellulitis. These risk factors should be considered when initiating empiric outpatient antibiotic therapy for patients with cellulitis.

References

1. Hersh AL, Chambers HF, Maselli JH, Gonzales R. National trends in ambulatory visits and antibiotic prescribing for skin and soft-tissue infections. Arch Intern Med 2008;168:1585–91.
2. Gunderson CG. Cellulitis: definition, etiology, and clinical features. Am J Med 2011;124:1113–22.
3. Bailey E, Kroshinsky D. Cellulitis: diagnosis and management. Dermatol Ther 2011;24:229–39.
4. Swartz MN. Cellulitis. N Engl J Med 2004;350:904–12.
5. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis 2005;41:1373–406.
6. Stevens DL, Eron LL. Cellulitis and soft-tissue infections. Ann Intern Med 2009;150:ITC11.
7. Anderson VL. Cellulitis. Lippincotts Prim Care Pract 1999;3:59–64.
8. Eron LJ, Lipsky BA, Low DE, Nathwani D, Tice AD, Volturo GA. Managing skin and soft tissue infections: expert panel recommendations on key decision points. J Antimicrob Chemoth 2003;52(Suppl 1): i3–17.
9. Gabillot-Carre M, Roujeua JC. Acute bacterial skin infections and cellulitis. Curr Opin Infect Dis 2007;20:118–23.
10. Bernard P. Management of common bacterial infections of the skin. Curr Opin Infect Dis 2008;21:122–8.
11. Guidelines and Audit Implementation Network. CREST Guidelines on the Management of Cellulitis in Adults. Available at: http://www.gain-ni.org/index.php/crest-cellulitis-guidelines. Accessed Feb 4, 2014.
12. Ki V, Rotstein C. Bacterial skin and soft tissue infections in adults: a review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. Can J Infect Dis Med Microbiol 2008;19:173–84.
13. Marwick C, Broomhall J, McCowan C, et al. Severity assessment of skin and soft tissue infections: cohort study of management and outcomes for hospitalized patients. J Antimicrob Chemoth 2011;66:387–97.
14. Dupuy A, Benchikhi H, Roujeau JC, et al. Risk factors for erysipelas of the leg (cellulitis); case-control study. BMJ 1999;318:1591–4.
15. Roujeau JC, Sigurgeirsson B, Korting HC, Kerl H, Paul C. Chronic dermatomycoses of the foot as risk factors for acute bacterial cellulitis of the leg: a case-control study. Dermatology 2004;209:301–7.
16. Björnsdóttir S, Gottfredsson M, Thórisdóttir AS. Risk factors for acute cellulitis of the lower limb: a prospective case-control study. Clin Infect Dis 2005;41:1416–22.
17. Halpern J, Holder R, Langford NJ. Ethnicity and other risk factors for acute lower limb cellulitis: a U.K.-based prospective case-control study. Br J Dermatol 2008;158:1288–92.
18. Doblecki Lewis S, Peter GS, Gómez-Marín O, Bisno AL. Risk factors for recurrent lower extremity cellulitis in a U.S. veterans medical center population. Am J Med Sci 2006;332:304–7.
19. Murray H, Stiell I, Wells G. Treatment failure in emergency department patients with cellulitis. Can J Emerg Med 2005;7:228–34.
20. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol 1996;49:1373–9.
21. Cohen J, Cohen P, West SG, Aiken LS. Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences. 3rd ed. Mahwah, NJ: Lawrence Erlbaum Associates, 2003.
22. Dong SL, Kelly KD, Oland RC, Holroyd BR, Rowe BH. ED management of cellulitis: a review of five urban centers. Am J Emerg Med 2001;19:535–40.
23. Achiam CC, Fernandes CM, McLeod SL, et al. Methicillin-resistant Staphylococcus aureus in skin and soft tissue infections presenting to the emergency department of a Canadian academic health care center. Eur J Emerg Med 2011;18:2–8.