Clinical Management of Skin and Soft Tissue Infections in the U.S. Emergency Departments

Rakesh D. Mistry, MD, MS*
Daniel J. Shapiro, BA†
Monika K. Goyal, MD‡
Theoklis E. Zaoutis§
Jeffrey S. Gerber, MD, PhD§
Catherine Liu, MD‖
Adam L. Hersh, MD, PhD¶

* University of Colorado School of Medicine, Department of Emergency Medicine, Aurora, Colorado
† University of California, San Francisco Medical Center, Department of Pediatrics, San Francisco, California
‡ George Washington University, Department of Emergency Medicine, Washington, District of Columbia
§ Perelman School of Medicine at the University of Pennsylvania, Division of Infectious Diseases, Philadelphia, Pennsylvania
‖ University of California, San Francisco School of Medicine, Division of Infectious Diseases, San Francisco, California
¶ University of Utah School of Medicine, Division of Infectious Diseases, Salt Lake City, Utah

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Introduction: Community-associated methicillin resistant *Staphylococcus aureus* (CA-MRSA) has emerged as the most common cause of skin and soft-tissue infections (SSTI) in the United States. A nearly three-fold increase in SSTI visit rates had been documented in the nation's emergency departments (ED). The objective of this study was to determine characteristics associated with ED performance of incision and drainage (I+D) and use of adjuvant antibiotics in the management of skin and soft tissue infections (SSTI).

Methods: Cross-sectional study of the National Hospital Ambulatory Medical Care Survey, a nationally representative database of ED visits from 2007-09. Demographics, rates of I+D, and adjuvant antibiotic therapy were described. We used multivariable regression to identify factors independently associated with use of I+D and adjuvant antibiotics.

Results: An estimated 6.8 million (95% CI: 5.9-7.8) ED visits for SSTI were derived from 1,806 sampled visits; 17% were for children <18 years of age and most visits were in the South (49%). I+D was performed in 27% (95% CI 24-31) of visits, and was less common in subjects <18 years compared to adults 19-49 years (p<0.001), and more common in the South. Antibiotics were prescribed for 85% of SSTI; there was no relationship to performance of I+D (p=0.72). MRSA-active agents were more frequently prescribed after I+D compared to non-drained lesions (70% versus 56%, p<0.001). After multivariable adjustment, I+D was associated with presentation in the South (OR 2.36; 95% CI 1.52-3.65 compared with Northeast), followed by West (OR 2.13; 1.31-3.45), and Midwest (OR 1.96; 1.96-3.22).

Conclusion: Clinical management of most SSTIs in the U.S. involves adjuvant antibiotics, regardless of I+D. Although not necessarily indicated, CA-MRSA effective therapy is being used for drained SSTI. [West J Emerg Med. 2014;15(4):491–498.]

INTRODUCTION

Background

Community-associated methicillin resistant *Staphylococcus aureus* (CA-MRSA) has emerged as the most common cause of skin and soft-tissue infections (SSTI) in the United States, especially in purulent skin abscess. In many areas of the country, MRSA prevalence is as high as 75-80% among cultured SSTI.[1–7] This epidemic has disproportionately

affected patients presenting to the emergency department (ED), where a nearly three-fold increase in SSTI visit rates had been documented in adults and children, and increases in both skin abscesses and cellulitis have been observed.[8–10] Although the rise in SSTIs due to MRSA has led to an increase in hospitalizations and, in some cases, invasive disease, the majority of skin infections are managed in ambulatory settings, including the ED.[8,9]

Importance

The rise in SSTIs and CA-MRSA has led to significant changes in clinical ED practice. First, the determination of the presence of an abscess, as opposed to a cellulitis, is an increasingly frequent diagnostic challenge faced by emergency physicians (EP). As a result, many EPs are using formal or bedside ultrasonography for diagnostic evaluation of SSTI.[11–13] Also, due to the increasing number of patients presenting with purulent abscess, incision and drainage (I+D) procedures are more frequently indicated. I+D can be especially time consuming in children, as procedural sedation is often required, which also carries inherent risk to the patient.[14,15] Therapeutic decisions regarding use of antibiotic therapy are also changing. Soon after the emergence of CA-MRSA, use of agents "active" against this organism, such as clindamycin and trimethoprim-sulfamethoxazole (TMP-SMX) has increased, while ß-lactam antibiotics, which provide empiric therapy for methicillin-sensitive *S. aureus* (MSSA) and ß-hemolytic streptococcus (BHS) are prescribed less frequently.[8,14–16] The implications of this shift in antibiotic therapy, however, are uncertain. Despite a growing body of evidence suggesting that antibiotics may not be necessary for adequately drained skin abscesses,[17–19] studies have found that use of adjuvant antibiotics is common.[14,20] These various studies have reported changes in clinical practice with respect to treatment of SSTI, although many of these consist of single institution and survey studies, and isolated pediatric or adult data.

Goals of this Investigation

The objective of our study was to investigate national practice patterns of SSTI management in the ED. Specifically, we determined national rates of I+D use and patterns of antibiotic prescribing for ED patients with SSTIs.

METHODS

Study Design, Setting, and Subjects

We analyzed data from the National Hospital Ambulatory Medical Care Survey (NHAMCS), a cross-sectional survey conducted annually by the National Center for Health Statistics (NCHS).[21] The survey is used to collect information about patient demographics, diagnoses, medications prescribed, and procedures performed on a nationally representative sample of ED visits in the U.S. To collect data from a nationally representative sample of visits, the NCHS administers the survey at participating hospitals using a four-stage probability sampling design, after sampling geographic primary sampling units (PSUs), the NCHS samples hospitals within PSUs, emergency service areas and in-scope ambulatory surgery locations within hospitals, and visits within these settings. Data from sampled visits are collected by hospital staff, who were trained by and maintained contact with trained field representatives during the reporting period. The NCHS provides probability weights – equal to the inverse probability of any visit being sampled – that allow for the generation of nationally representative estimates using data collected in the NHAMCS. The study was granted exemption from the institutional review board review.

Methods and Measurements

In our analysis, we combined data collected in the NHAMCS between 2007 and 2009. The analysis was restricted to initial visits for an SSTI; we excluded visits for follow up. Methodology for identification of SSTI in NHAMCS mirrored that of previous published studies: we identified visits for SSTI using International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes for skin and soft issue infection (680.xx-682.xx), which includes carbuncle, folliculitis, cellulitis, and skin abscess.[8,9,22] Although the NHAMCS allows for up to three diagnosis codes to be assigned to a visit, we defined SSTI based upon the primary diagnosis listed. Study subjects included patients of all ages, and we analyzed participants' demographic data including race, gender, and insurance status. Location of ED care, in terms of geographic region, was also collected in the NHAMCS and described in our study. Geographic regions were defined using US Census Track Regions, including the Northeast, South, Midwest, and West.

Details of ED visits, including performance of drainage procedures, diagnostic testing, ED disposition, and prescription antibiotic use were recorded at each visit. Performance of diagnostic testing—including complete blood count, blood culture, or wound culture–was indicated via check box in the patient record form. We dichotomized ED disposition as outpatient management or hospitalization, which included admission to an inpatient ward or observation unit. Antibiotics were categorized using the Multum Lexicon Therapeutic Classification System. Starting with the 2006 surveys, the NHCS began to code drugs using the Multum system, which characterizes drugs using a three-tiered hierarchy. For example, beta-lactamase inhibitors are a "level 3" category of drugs within the "level 2" category that includes all penicillins. Penicillins, in turn, belong to a "level 1" category that includes all anti-infectives. In addition to broad categories, the Multum system allows for identification of specific drugs (e.g., clindamycin). For the purposes of our analysis, we grouped antibiotics into the following categories: anti-MRSA (trimethoprim-sulfamethoxazole, clindamycin, daptomycin, tetracyclines,

Table 1. Characteristics of initial emergency department (ED) visits for skin and soft tissue infections (SSTI) among study patients*†

	Estimated survey weighted ED visits (in millions)	All SSTI†† (n=1,806)	No I+D†† (n=1,311)	I+D†† (n=495)	p-value (X^2)
Year					
2007	2.03	30%	31%	27%	
2008	2.47	36%	35%	39%	0.51
2009	2.32	34%	34%	34%	
Age (years)					
<18	1.16	17%	18%	15%	
18-49	3.89	57%	53%	69%	<0.0001
>49	1.77	26%	29%	16%	
Race					
White	4.84	71%	77%	57%	<0.0001
Nonwhite	1.98	29%	23%	43%	
Gender					
Male	3.48	51%	50%	52%	0.64
Female	3.34	49%	50%	48%	
Insurance status					
Private	4.57	67%	67%	70%	0.23
Public/other	2.25	33%	33%	30%	
US census track region					
Northeast	1.09	16%	19%	9%	
Midwest	1.09	16%	17%	16%	
South	3.34	49%	45%	58%	<0.001
West	1.30	19%	19%	18%	

*Survey weights applied; †Totals may be >100%; ††Proportions represent total within each column; I+D, incision and drainage.

vancomycin, linezolid, and tigecycline), β-lactam (penicllins, cephalosporins, and carbapenems), and other (rifampin, macrolides, aminoglycosides, and quinolones).

Statistical Analysis

All statistical analyses took into account the complex sampling design of the NHAMCS, including sample weights, stratification, and clustering variables. Description of study subjects and ED visits were made using standard descriptive statistics. We made univariate comparisons using the $\chi 2$-test for proportions, and p-values were reported with a significance level of <0.05. Specifically, we compared patient characteristics, diagnostic testing, and adjuvant antibiotic prescription between patients with and without an incision and drainage procedure performed. To identify independent patient characteristics associated with clinical care of SSTI and to account for potential confounding, we performed multivariable logistic regression. Two regression models were created: one to identify factors independently associated with performance of I+D, and a second to assess factors associated with prescribing of adjuvant antibiotics among subjects that had a drainage procedure. We reported values as adjusted odds ratios (OR) with 95% confidence intervals (CI). We conducted all analyses using STATA 11 software (Stata Corp, College Station, TX).

RESULTS

Characteristics of Study Subjects

During the study period, based on a sample of 1,806 actual visits in the NHAMCS database, there were an estimated 6.82 (95% CI: 5.88-7.75) million initial ED visits for SSTI in the U.S. This corresponds to an average of 2.27 million visits annually. Survey weighted demographics of the study population are presented in Table 1. Most study subjects were above the age of 18 years, Caucasian, and privately insured. The largest number of SSTIs occurred among patients in the 18-49 year age group, while children (<18 years) had the fewest. The rate of ED visitation for SSTI was highest in the southern U.S., compared to other regions (Table 1).

Emergency Department Clinical Care for SSTI

Among visits for SSTI, an estimated 27% (95% CI:

Table 2. Antibiotics prescribed for study subjects.

Variable	Overall	No I+D	I+D	p-value[e]
Any antibiotic use[a]	85%	85%	84%	0.72
Anti-MRSA monotherapy[b]	43%	38%	57%	<0.0001
β-lactam monotherapy[c]	23%	27%	13%	<0.0001
Anti-MRSA + β-lactam combination	15%	16%	11%	0.08
Other antibiotics[d]	4%	5%	3%	0.18
No antibiotics	15%	15%	16%	0.72

[a] Values may not sum accurately as a result of rounding
[b] Includes sulfonamides, tetracyclines, clindamycin, vancomycin, linezolid, daptomycin, and tigecyclin.
[c] Includes cephalosporins, penicillins, and carbapenems.
[d] Includes macrolides, aminoglycosides, quinolones, and rifampin.
[e] Chi-square comparisons of No I+D with I+D
I+D, incision and drainage

24-31) had an I+D procedure performed. Performance of I+D occurred more often in patients who were 18-49 years of age (p<0.001), non-white, and when treated in the South (p<0.001). Wound cultures were performed in 16% of visits for SSTI, and they were performed more frequently when I+D was also performed (31%) than when I+D was not performed (11%) (p<0.001). Among the study population, ancillary diagnostic testing was obtained in many patients: 27% had a complete blood count and 12% had a blood culture obtained in the ED; each were more likely to be obtained in patients when an I+D was not performed (p<0.001). The majority of patients were cared for as outpatients, with only 15% of study subjects hospitalized after the ED visit. Hospitalization for SSTI was less common when I+D was performed during the ED visit (5%) than when I+D was not performed (19%) (p<0.001).

Overall, 85% of patients with SSTI received an antibiotic prescription. There was no difference in the rate of antibiotic use between those who did or did not receive an I+D (84% versus 85%, p=0.72). However, there were significant differences in antibiotic choices based on whether an I+D was performed. The majority (70%) of patients who had I+D were prescribed an anti-MRSA antibiotic, compared to 56% of those not receiving I+D (p<0.0001) (Table 2). Combination therapy, with prescription of anti-MRSA and beta-lactam antibiotics, was used in 15% of subjects; there was no association between the use of combination therapy and performance of a drainage procedure (p=0.08).

Multivariable Analysis

After adjusting for other potentially confounding factors, performance of I+D was significantly associated with patient age of 18-49 years, non-white race, and care in regions other than the U.S. Northeast, with the strongest association observed in the South. Among patients undergoing I+D, adjuvant antibiotic therapy was only associated with patients treated in the South (OR 3.23; 1.41-7.40 compared with the Northeast) (Table 3).

DISCUSSION

This study provides a nationally representative overview of ED management for patients with SSTIs. While I+D is considered the mainstay of therapy for purulent SSTI, it is performed in less than half of children presenting to the ED for an SSTI. Overall drainage procedure are less commonly performed for children <18 years compared to adults 18-48 years of age, and more commonly performed in non-white patients, and in those presenting outside of the Northeast. Furthermore, adjuvant antibiotic use for SSTIs is commonplace, regardless of whether or not I+D is performed. Though the majority of subjects are receiving CA-MRSA active therapy, consistent with current epidemiology, current evidence indicates that antibiotic therapy may be unnecessary for purulent abscesses that are adequately drained.

I+D remains the mainstay of treatment for purulent skin abscesses, irrespective of patient characteristics or site of care.[16,23,24] However, the results of our study demonstrate that for SSTIs presenting to the ED, I+D appears to be less likely to be performed in pediatric patients and white patients. While the ED is often the preferred site of care for potentially drainable SSTI, the pediatric population is less likely to receive an I+D. It is possible, though unlikely, that the prevalence of cellulitis is higher than abscess in the pediatric population; current administrative databases do not permit discrimination between ICD-9 codes for these infections. Factors such as reluctance to perform an empiric I+D procedure because of incurred pain or need for procedural sedation, or the limited use of bedside ultrasonography in children, may explain this finding, in part. For example, sedation possesses inherent logistical challenges in the ED setting, such as time required and associated risks; in addition, sedation is more likely to be employed in academic settings, which is not representative of the majority of ED visits across the U.S.15 In addition, bedside ultrasonography is underused in pediatric patients,[25,26] though it has proven benefit in adults; abscesses are often underdiagnosed compared with examination, and therefore may not receive I+D.[12,27] With respect to patient race and performance of I+D, there is suggestion that CA-MRSA and SSTI are more common in blacks, as compared to other races,[28–31] which accounts for differences in the performance of I+D; CA-MRSA infection is related to increased risk of abscess formation, and mirrors this epidemiologically.[2,6,29]

Several geographic differences with respect to SSTI management were elicited in our study, even after adjustment for multiple patient factors, including age, race, and insurance status. Patients with SSTI treated in EDs outside of the Northeast underwent I+D more frequently: compared with the

Table 3. Multivariable regression analyses of factors associated with performance of incision and drainage and with receipt of adjuvant antibiotics coupled with incision and drainage in patients with skin and soft-tissue infections.

	% Receiving I+D	AOR (95% CI)	% Receiving antibiotics	AOR (95% CI)
Year				
2007	25%	1.00	91%	1.00
2008	29%	1.30 (0.90-1.90)	80%	0.57 (0.25-1.29)
2009	27%	1.34 (0.96-1.87)	83%	0.49 (0.23-1.04)
Age				
<18	24%	1.00	87%	1.00
18-49	32%	1.77 (1.23-2.55)	84%	0.46 (0.12-1.70)
>49	17%	0.94 (0.60-1.49)	81%	0.42 (0.10-1.66)
Race				
White	22%	1.00	85%	1.00
Nonwhite	41%	2.34 (1.71-3.19)	83%	0.77 (0.43-1.40)
Sex				
Male	28%	1.00	85%	1.00
Female	26%	0.86 (0.63-1.18)	83%	1.09 (0.58-2.03)
Insurance status				
Private	25%	0.96 (0.74-1.25)	84%	0.92 (0.47-1.80)
Public/other	28%	1.00	85%	1.00
US census region				
Northeast	15%	1.00	72%	1.00
Midwest	26%	1.96 (1.19-3.22)	78%	1.90 (0.62-5.81)
South	32%	2.36 (1.52-3.65)	89%	3.23 (1.41-7.40)
West	26%	2.13 (1.31-3.45)	78%	1.31 (0.49-3.52)

I+D, incision and drainage; *AOR*, Adjusted Odds Ratio

Northeast, patients treated in the South were twice as likely to have an I+D performed and three times as likely to receive adjuvant antibiotics after the I+D. However, it is unclear whether a true association exists between region and treatment strategies. It should be noted that the prevalence of CA-MRSA is highest in urban centers located in the South (Atlanta, Houston, Dallas), in the Midwest (Chicago, St. Louis), and in the West (San Francisco, Los Angeles), with rates as high 80-85% in many of these locations.[1,3,6,7,19,29,30] Meanwhile, many centers in the Northeast (New York, Philadelphia) documented rates of MRSA less than 70%.[29,32] Nonetheless, while the incidence of skin abscesses is related to CA-MRSA prevalence, it is unclear if this regional relationship purely reflects ED visitation, population demographic, or actual differences in clinical care. These findings should be interpreted in light of the fact that our ability to identify skin abscess was based on best literature-supported methods for administrative data; the true clinical scenario of abscess versus cellulitis cannot be assessed, and the prevalence of CA-MRSA in cellulitis is not known.

Our study confirms the frequent use of systemic antibiotics for SSTIs managed in the ED, which was not influenced by the performance of I+D: approximately 85% of all patients received adjuvant antibiotic therapy. This finding has important implications. For some patients, especially children among whom barriers to performing drainage exist, ED physicians may be using antibiotic therapy instead of performing a drainage procedure. It cannot be overemphasized that adjuvant antibiotics are not a substitute for I+D when treating purulent skin abscesses, and the assumption that antibiotic therapy alone will adequately treat a skin abscess might increase the possibility of treatment failure. Moreover, this high rate of adjuvant antibiotic use suggests that ED physicians are reluctant to withhold antibiotic therapy, despite recent evidence demonstrating a general lack of efficacy of this practice.[18,19] However, recent evidence suggests that I+D alone is sufficient for most ED patients with uncomplicated abscess. Chen et al demonstrated that failure rates between pediatric skin abscesses, in a study population with 70% CA-MRSA, did not differ when treated with adjuvant clindamycin compared to the non-MRSA active cephalexin (3 versus 6%, p=0.50).[17] The most salient of these was a methodologically sound, non-inferiority study of

TMP-SMX versus placebo in drained skin abscess, by Duong et al in 2010. Treatment failure in the placebo group was 5.3%, compared with 4.1% in the TMP-SMX group (mean difference 1.2% 95% CI: -∞ to 6.8).[19] These results, in conjunction with current evidence and national guideline recommendations, strongly suggest that adjuvant antibiotic therapy does not or only minimally improves cure rates compared with placebo or use of an agent that was inactive against the pathogen.[1,3,18,19,24,24,33] These findings support the need for knowledge dissemination of these studies and guideline recommendations, continued surveillance of ED prescribing practices, and more judicious use of adjuvant therapy.

On the other hand, our findings suggest that EPs do appear to be tailoring their antibiotic selection patterns based on the epidemiology of the infection. Use of anti-MRSA therapy, including clindamycin and TMP-SMX, was higher for patient visits where I+D was performed. This is consistent with the likely differences in pathogens between purulent and nonpurulent SSTI: purulent SSTI such as abscesses are more likely to be caused by *S. aureus*, whereas nonpurulent cellulitis and erysipelas are more likely to be caused by BHS.[29,34,35] Therefore, if antibiotics are deemed necessary for the management of purulent SSTI, an antibiotic with activity against MRSA is generally recommended, typically clindamycin or TMP-SMX, based on local resistance patterns.[16,24] With respect to non-purulent SSTI, a recent study of inpatients residing in a high-MRSA prevalence community demonstrated that BHS was the causative agent in 73% of cases of non-purulent cellulitis.[34] Therefore, use of therapy with activity against BHS for cellulitis, especially beta-lactams or clindamycin is prudent, as TMP-SMX alone is not considered adequate and has been associated with treatment failure when used as monotherapy for non-drained SSTIs.[10]

Differences exist with respect to ancillary testing and ED disposition for SSTIs, based on performance of I+D. In the setting of a known abscess, clinicians will be more likely to perform drainage without additional testing. Diagnosis of and treatment of skin abscess is more straightforward as compared to non-drained lesions, where cellulitis, or even deeper skin lesions may be a consideration. As a result, it is logical that patients with non-drained SSTI were more likely to receive laboratory testing, including complete blood counts and blood cultures. While there may be an effect from institutional differences, these findings seem justified, as patients with non-drained SSTIs were also four-times as likely to be admitted to the hospital for continued therapy. Although many physicians continue to favor use of serum testing in SSTI management.[14] It should be noted that serum testing adds little to the management of SSTI, and rates of bacteremia in cellulitis and skin abscess remain quite low.[36] Notably, wound cultures were not obtained in the majority of SSTI even after drainage. This is incongruent with current recommendations from the IDSA and CDC, which recommend wound culture in the management of SSTI to monitor for therapeutic failure, and track current *S. aureus* epidemiolgy.[16,24]

LIMITATIONS

Among the limitations to our findings is the use of large-scale administrative data from NHAMCS, as has been well documented.[37] Specifically, the NHAMCS survey does not include some potentially important clinical information that could influence treatment decisions around I+D or antibiotic use, including lesion size or prior history of MRSA or SSTI. As a result, we are not able to fully evaluate the appropriateness of clinical management. NHAMCS is also limited by its use of ICD-9 codes for diagnosis. In the case of SSTI, ICD-9 does not distinguish between cellulitis and abscess, and use of ICD-9 codes for SSTI and procedure codes of I+D to identify abscesses is limited and prone to misclassification. Additionally, the limited sample of patients did not permit sub-analysis of our study population by smaller increments of age, and it is possible that further differences exist in management of younger pediatric patients compared to older adolescents. In addition, regional differences found in our study may not be accurate, as NHAMCS coding and Census Track Regions results in overrepresentation of the South in terms of ED visits. Since our data source did not contain results or microbiologic testing for ED patients with SSTI, we could not confirm this relationship between CA-MRSA prevalence and the need for incision and drainage. Although relatively unlikely, particularly because we restricted our analysis to initial ED visits, some patients may have undergone I+D previously in an office setting, which would not have been captured by the NHAMCS dataset. Finally, although we found differences in clinical care across the large geographic areas of U.S. Census Track Region, we could not comment on actual care provided, or account for potentially important differences across smaller geographic areas.

CONCLUSION

In spite of current literature disputing the need for adjuvant antibiotic therapy for uncomplicated SSTI that has undergone I+D, this practice remains common in adults and children presenting to the ED for skin abscesses. While CA-MRSA active therapy for drained SSTI has increased concomitant with the rise in CA-MRSA, prescribing practices for non-drained SSTIs such as cellulitis reflect increased use of CA-MRSA active therapy, which may not be appropriate, as Group A Streptococcus remains prevalent. Meanwhile, the practice of serum testing for non-drained SSTI remains common, despite uncertainty in the diagnostic and therapeutic utility. Nationally representative studies are essential for evaluating current practice for SSTI, and continued assessments of antibiotic therapy will be necessary to evaluate dissemination of evidence regarding appropriate use of diagnostics and adjuvant antibiotics for SSTIs.

Address for Correspondence: Rakesh Mistry, MD, MS, Children's Hospital Colorado, Department of Emergency Medicine, 13123 E. 16th Avenue B251, Aurora, CO, 80045. Email: mistryr@email.chop.edu.

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