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ORIGINAL ARTICLE

Management and outcome of adults with skin and soft tissue infection caused by methicillin-resistant *Staphylococcus aureus* in a tertiary hospital in central Taiwan

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purulent skin and soft tissue infections

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) has been increasingly causing skin and soft tissue infections (SSTIs). Only limited studies have made comparisons between incision and drainage (I&D) alone and I&D with adjunctive antibiotic therapy for treatment effects, and most of the studies were conducted before the emergence of MRSA. This study was to evaluate whether antibiotics provide added benefit to I&D alone for purulent MRSA SSTIs.
Methods: This retrospective study collected data on SSTI patients, including patient demographics, treatment strategies, antibiotic susceptibilities of the infecting MRSA isolates, and clinical outcomes over the course of 24 months.
Results: Antimicrobial drug susceptibility rate were 100% for vancomycin, teicoplanin, and linezolid. Among the 211 patients, 7.6% were treated solely with I&D (Group A), 62.6% were treated via I&D with adjunctive antibiotic (Group B), and 29.8% patients received only antibiotics (Group C). The cure rate was highest in Group A (93.8%), followed by Group B (90.9%) and Group C (77.8%). Combining Group B and Group C, patients who were treated appropriately demonstrated a higher cute rate (91.3% vs. 75.4%, $p = 0.005$). Multivariate analysis showed that Group B was more likely to be successfully treated compared to Group C (odds ratio = 2.51, 95% confidence interval = 1.01–6.25, $p = 0.047$), whereas no difference between Group A and Group B was found (odds ratio = 2.09, 95% confidence interval = 0.20–22.34, $p = 0.542$, data not shown).

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Conclusion: Surgical intervention is the definitive therapy for purulent SSTIs. Adjunctive antibiotic therapy increased the cure rate and appropriateness of prescription is influential.

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) was first documented in the 1960s. Since then, this organism has become a major cause of serious nosocomial and community-associated infections.[1,2] Within Taiwan, MRSA was first detected in the early 1980s, with MRSA occurrence increasing swiftly in the 1990s.[3] MRSA infections can include sepsis, pneumonia, skin and soft tissue infections (SSTIs), bone and joint infections, bacteremia, and endocarditis.[4,5]

For SSTIs, surgical intervention is the favored therapy, notwithstanding the fact that cure rate versus failure rate for surgical intervention has been inconsistent in different studies.[6–8] Moreover, few studies have been carried out specifically on comparison of incision and drainage (I&D) alone and I&D plus antibiotic therapy, and most of the studies were conducted before the emergence of MRSA.[9–11] Adjunctive antibiotic therapy is controversial,[12,13] e.g., Rajendran et al[14] conducted a double-blind, randomized, placebo-controlled trial and concluded that adjunctive antibacterials do not add benefit to I&D for purulent MRSA SSTIs whereas Ruhe et al[8] conducted a retrospective, multicenter cohort study of patients with MRSA SSTIs and came to an opposite conclusion. Practice guidelines from the Infectious Diseases Society of America[15–17] as well as those from the Infectious Diseases Society of Taiwan.[18] recommend the use of specific antibiotics for treatment of MRSA SSTIs; however, in practice, many doctors follow their own prescription preferences.

In this study, we evaluated the success of surgical intervention upon SSTIs associated with MRSA, and compared cases that received I&D alone (Group A), I&D with adjunctive antibiotics (Group B), and antibiotics alone (Group C). We also evaluated whether adjunctive antibiotic therapy was significantly helpful. Lastly, we examined the choice of empirical antibiotic therapy in our hospital setting. In part, our goal is to provide doctors in different fields with feedback on their current practices so these doctors could reevaluate and adjust their treatment habits for consistency and moderation.

Materials and methods

Patients and data collection

This study was conducted retrospectively at China Medical University Hospital (CMUH), a 2000-bed tertiary hospital in central Taiwan, from July 1, 2011 to June 30, 2013. Patients were selected from various departments including out- and inpatients.

From an ethical perspective, a retrospective design (chart review) was adopted instead of a prospective design. For each patient, the medical record was collected for information regarding demographic data such as age, sex, and comorbid conditions such as cardiovascular disease, diabetes mellitus, end-stage renal disease, liver cirrhosis, cerebrovascular disease, and malignancy. Inclusion criteria were as follows: (1) age $>$ 18 years; (2) detection of MRSA in at least one patient pus culture; and (3) symptoms and signs consistent with SSTI, i.e., presence of at least three of the following: warmth, erythema, swelling, pain, tenderness, lymph node swelling/tenderness, drainage/discharge, or induration. Minor or superficial skin infections, such as folliculitis or impetigo, as well as those with rather complicated SSTIs (i.e., nonhealing skin ulcer or diabetic foot infection, postsurgical wound infection, or processes involving adjacent deep-tissue structures, including bone, fascia, or tendon sheaths), were excluded. Pus cultures that yielded mixed pathogens or pathogens other than MRSA were excluded from our study. Antibiotic susceptibility was recorded. Treatment data collected included surgical/bedside interventions (i.e., I&D) performed, as well as any additional antibiotics administered after determination of the organism identity and susceptibility, which result was released after 5 days of pus culture. Ultimately, we categorized patients' outcomes as either (1) cure or (2) failure, while also determining the appropriateness of the prescribed antibiotics in nonsurgical and postsurgical medical treatments. The study was approved by the institutional review board of China Medical University Hospital, Taichung, Taiwan (CMUH103-REC2-077).

Definitions

Purulent SSTIs, including furuncle, carbuncle, and abscess, are classified as severe, moderate, and mild infection.[17] Severe infection was applied to those patients who have failed incision and drainage plus oral antibiotics or those with systemic signs of infection such as temperature $>38^{\circ}C$, tachycardia (heart rate $>$ 90 beats/minute), tachypnea (respiratory rate $>$ 24 breaths/minute) or abnormal white blood cell count ($<12 \times 10^9$ cells/L or $<0.4 \times 10^9$ cells/L), or immunocompromised patients. Moderate SSTI was equivalent to purulent infection with systemic signs of infection. Mild infection was defined as purulent SSTI without signs of systemic involvement. Surgical interventions indicate incision and drainage, which were performed in the operating room or at the bedside. Regarding the clinical outcome, treatment failure was the primary outcome of interest and was categorized as no clinical improvement after $\geq$48 hours, plus one or more of the following: (1) new culture-proven MRSA SSTI while on

antibiotics; (2) microbiological failure in which MRSA was cultured from the original wound site after completion of antibiotic therapy; (3) further surgical intervention; or (4) subsequent hospitalization for the infection. Cases otherwise were categorized as cures.

One course of antibiotic administration was tantamount to 5 days of duration.

Appropriateness of antibiotic was defined as those prescription antibiotics that were in accord with the antimicrobial susceptibility of the MRSA isolates; such an antibiotic was designated as the appropriate antibiotic. The treatment otherwise was labeled as an inappropriate antibiotic.

Microbiology

The pus specimens were streaked on trypticase soy agar containing 5% sheep blood (TSA II), Levine EMB agar, Columbia CNA agar, chocolate agar, or thioglycollate broth (Becton, Dickinson and Company, Sparks, MA, USA). The plates were incubated at 35°C for appropriate time periods. Identification of bacteria and tests for susceptibility to various antimicrobial agents [i.e., vancomycin, teicoplanin, linezolid, levofloxacin, tetracycline, trimethoprim–sulfamethoxazole (TMP-SMX), clindamycin, and erythromycin] were performed with the BD Phoenix Automated Microbiology System (Becton, Dickinson and Company). Result of antimicrobial susceptibilities of the MRSA isolates take about 5 days to be released.

Statistical analysis

Clinical characteristics of the study patients are presented as mean ± standard deviation for continuous variable and number and percentage (*n*, %) for categorical variable. Comparison among groups was made by one-way analysis of variance (ANOVA) for continuous variable and by Fisher's exact test for categorical variable. The cure rate in the patients who were treated appropriately and inappropriately with antibiotics was compared by Fisher's exact test. To investigate the association of clinical characteristics with treatment outcome, univariate and multivariate logistic regression analyses were conducted. All the data analyses were performed using SPSS version 15 (SPSS Inc., Chicago, IL, USA).

Results

Antimicrobial drug susceptibility rates

Antimicrobial drug susceptibility rates across all 211 patients were as follows: vancomycin, 100%, teicoplanin, 100%; linezolid, 100%, TMP-SMX, 67.3%; tetracycline, 55.9%; levofloxacin, 55.0%; clindamycin, 19%; and erythromycin, 6.6% (Fig. 1).

Although there was no susceptibility test performed on daptomycin for MRSA isolate during the study period, this is considered to be an appropriate antibiotic against MRSA SSTI due to its low minimum inhibitory concentration. Daptomycin has been approved by the Food and Drug Administration (FDA), USA in 2003 for the treatment of complicated SSTIs. In various clinical trials, daptomycin proved to be as effective as vancomycin against MRSA.[19–22]

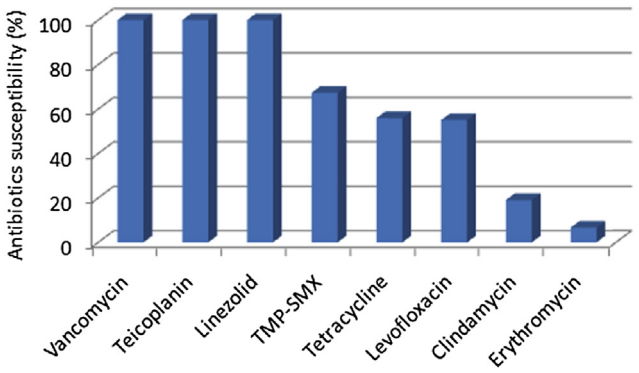

Figure 1. Antibiotic susceptibility of methicillin-resistant *Staphylococcus aureus*. Vancomycin, teicoplanin, and linezolid had 100% sensitivity, followed by trimethoprim–sulfamethoxazole (TMP-SMX; 67.3%), tetracycline (55.9%), and levofloxacin (55%). Daptomycin was not available so it was not tested during the study period.

Prescribed antibiotics by doctors from various fields prior to identification of the organism and susceptibility

We listed all the antibiotics prescribed for 195 patients (in Group B and Group C) with MRSA by doctors in various fields and found that the most frequently used antibiotic was vancomycin (86 courses given). The rest were as follows: teicoplanin (60 courses given), β-lactamase inhibitors such as ampicillin/sulbactam and amoxicillin/clavulanic acid (36 courses given), daptomycin (32 courses given), TMP-SMX (19 courses given), quinolones such as moxifloxacin/levofloxacin/ciprofloxacin (16 courses given), linezolid (12 courses given), tigecycline (12 courses given), and cefradine (11 courses given).

Clinical characteristics of the study patients

From July 1, 2011 to June 30, 2013, 211 patients with purulent SSTIs caused by MRSA were identified. Among all the patients, 16 (7.6%) underwent I&D alone (Group A), 132 (62.6%) had I&D with adjunctive antibiotics treatment (Group B), and 63 (29.8%) patients were treated merely with antibiotics (Group C). Their age ranged from 20 years to 94 years (mean 55.9 ± 19 years). There were 114 (54%) male and 97 (46%) female patients. Twenty-one (10%) patients had received antibiotics therapy before they came to the hospital. Eighty-five (40.3%) patients were classified as mild SSTI, 60 (28.4%) patients as moderate SSTI, and 66 (31.3%) patients as severe SSTI. Cardiovascular disease (35.5%) was the most common underlying disease, followed by diabetes mellitus (30.3%), and end-stage renal disease (11.8%). The overall cure rate was 87.2% (Table 1). Table 1 lists the clinical characteristics of each study group. The result clearly showed that the study groups differed

Table 1 Clinical characteristics of 211 patients with MRSA SSTI

Characteristics	All patients	Study group			*p*
		I&D alone (Group A)	I&D plus antibiotics (Group B)	Antibiotics alone (Group C)	
Number of patients	211	16	132	63	—
Age, y	55.9 ± 19.0	50.2 ± 17.7	55.4 ± 19.4	58.3 ± 18.3	0.282
Sex					0.290
Male	114 (54.0)	10 (62.5)	75 (56.8)	29 (46.0)	
Female	97 (46.0)	6 (37.5)	57 (43.2)	34 (54.0)	
Previous antibiotic therapy					0.871
No	190 (90.0)	14 (87.5)	119 (90.2)	57 (90.5)	
Yes	21 (10.0)	2 (12.5)	13 (9.8)	6 (9.5)	
SSTI severity					<0.001
Mild	85 (40.3)	15 (93.8)	11 (8.3)	59 (93.7)	
Moderate	60 (28.4)	1 (6.3)	55 (41.7)	4 (6.3)	
Severe	66 (31.3)	(0.0)	66 (50.0)	(0.0)	
Underlying condition					
Cardiovascular disease	75 (35.5)	5 (31.3)	46 (34.8)	24 (38.1)	0.872
Diabetes mellitus	64 (30.3)	4 (25.0)	38 (28.8)	22 (34.9)	0.662
ESRD	25 (11.8)	4 (25.0)	16 (12.1)	5 (7.9)	0.144
Liver cirrhosis	14 (6.6)	1 (6.3)	12 (9.1)	1 (1.6)	0.117
Cerebrovascular disease	16 (7.6)	(0.0)	5 (3.8)	11 (17.5)	0.004
Malignancy	16 (7.6)	2 (12.5)	7 (5.3)	7 (11.1)	0.200
Steroid using	2 (0.9)	1 (6.3)	(0.0)	1 (1.6)	0.051
HIV	1 (0.5)	(0.0)	1 (0.8)	(0.0)	> 0.99
Outcome of treatment					0.038
Failure	27 (12.8)	1 (6.3)	12 (9.1)	14 (22.2)	
Cure	184 (87.2)	15 (93.8)	120 (90.9)	49 (77.8)	

Data are presented as *n* (%) or mean ± SD.
ESRD = end-stage renal disease; HIV = human immunodeficiency virus; I&D = incision and drainage; MRSA = methicillin-resistant *Staphylococcus aureus*; SSTI = skin and soft tissue infection.

significantly in SSTI severity, cerebrovascular disease, and treatment outcome ($p < 0.05$). As to SSTI severity, a majority of the patients in Group A (93.8%) and in Group C (93.7%) were classified as mild SSTI, whereas approximately half of the patients in the Group B were classified as moderate (41.7%) and severe (50%) SSTI, respectively. The prevalence of cerebrovascular disease was apparently higher in the antibiotics alone group (17.5%) than the two other groups. The cure rate was substantially lower in Group C (77.8%) when compared to that of Group A (93.8%) and Group B (90.9%) before adjusting for other covariates.

Cure rate with and without appropriate antibiotic therapy

We reviewed the antibiotic treatment for 195 patients (in Group B and Group C); 138 (70.8%) patients were treated appropriately and 57 (29.2%) inappropriately. For the patients in Group B, the cure rate was significantly higher in the appropriately treated subgroup than in the inappropriately treated subgroup (94.6% vs. 82.1%, $p = 0.041$). In Group C, patients who were treated appropriately showed a higher but not significant cure rate than those were treated inappropriately (84.4% vs. 61.1%, $p = 0.090$). That was contributed to its smaller sample size in this group ($n = 63$) hence was not statistically significant. When combining Group B and Group C, the appropriately treated subgroup demonstrated a higher cure rate (91.3% vs. 75.4%, $p = 0.005$) compared to its counterpart (Table 2).

Association of factors with treatment success

The result of univariate logistic analyses indicated that no clinical characteristics were associated with treatment outcome except for study group. Patients in Group B were more likely to be successfully treated than those in Group C [odds ratio (OR) = 2.86, 95% confidence interval (CI) = 1.23–6.62, $p = 0.014$]. By contrast, the difference in treatment success between Group A and Group C was not significant, despite the risk measure being even higher (OR = 4.29). The result of multivariate analysis remains unchanged as patients in Group B were more likely to be successfully treated compared to that in Group C (OR = 2.51, 95% CI = 1.01–6.25, $p = 0.047$). In addition, the likelihood of successful treatment in Group A and Group B was similar (OR = 2.09, 95% CI = 0.20–22.34, $p = 0.542$, data not shown). Notably, the SSTI severity was not included in the multivariate analysis because of serious multicollinearity involving the study group (Table 3).

Discussion

Incision and drainage has been the mainstay of therapy of purulent SSTI since the 1950s and should be performed

Table 2 Comparison of cure rate according to appropriateness of antibiotic administration

Group/status	Total	Appropriate therapy	Inappropriate therapy	p^a
I&D plus antibiotics (Group B)				0.041
Failure	12 (9.1)	5 (5.4)	7 (17.9)	
Cure	120 (90.9)	88 (94.6)	32 (82.1)	
Antibiotics alone (Group C)				0.090
Failure	14 (22.2)	7 (15.6)	7 (38.9)	
Cure	49 (77.8)	38 (84.4)	11 (61.1)	
Combined groups B+C				0.005
Failure	26 (13.3)	12 (8.7)	14 (24.6)	
Cure	169 (86.7)	126 (91.3)	43 (75.4)	

[a] Fisher's exact test.
Data are presented as *n* (%).
I&D = incision and drainage.

whenever feasible.[1,23] No study to date has evaluated the value of I&D versus no I&D in a prospective, controlled fashion.[24] Given the widespread use of I&D and high cure rates reported in the literature, such a trial is unlikely. Successful drainage is considered the standard of treatment for controlling the source of infection, thereby preventing the development of sepsis and septic shock.[25] Our study confirms this standard, with a demonstrated cure rate of 93.8% in the I&D alone group (Group A) and 90.9% in the I&D with adjunctive antibiotic group (Group B), values consistent with a number of previous studies.[6–8] However, the role of ancillary antibiotics is disputable. There are multiple trials evaluating adjunctive antibiotics for drained skin abscess, with different outcomes.[8,12–14,26–28]

In the present study, we found that the adjunctive use of antibiotics provided a key component of successful therapy, especially when an appropriate antibiotic was used. Hence, rectification of antibiotic administration is of paramount importance.

In fact, we detected that, for the patients in Group B, the cure rate was significantly higher in the appropriately treated subgroup than in the inappropriately treated subgroup (94.6% vs. 82.1%, $p = 0.041$). Due to the smaller sample size ($n = 63$) in Group C, the corresponding comparison turned out as statistically insignificant (84.4% vs. 61.1%, $p = 0.090$); however, when combining Group B and Group C, we found that the appropriately treated subgroup demonstrated a higher cute rate (91.3% vs. 75.4%, $p = 0.005$) compared to its counterpart.

Among our MRSA isolates, 100% were susceptible to vancomycin, teicoplanin, and linezolid, with susceptibility

Table 3 Factors associated with treatment success

	Univariate analysis			Multivariate analysis		
Predictor	OR	95% CI	*p*	OR	95% CI	*p*
Age, per y	0.99	0.97–1.02	0.605	1.00	0.97–1.02	0.883
Male/female	1.55	0.69–3.51	0.287	1.33	0.54–3.29	0.534
Previous antibiotic therapy	1.44	0.32–6.56	0.638	1.36	0.28–6.58	0.698
SSTI severity[a]						
Mild	1	Reference	—			
Severe	2.20	0.74–6.53	0.154			
Moderate	1.02	0.41–2.57	0.961			
Cardiovascular disease	1.36	0.56–3.28	0.493	2.92	0.87–9.82	0.084
Diabetes mellitus	0.59	0.26–1.35	0.211	0.32	0.10–1.04	0.059
ESRD	0.74	0.23–2.35	0.611	0.88	0.22–3.55	0.860
Liver cirrhosis	NA	NA	NA	NA	NA	NA
Cerebrovascular disease	1.03	0.22–4.80	0.971	1.49	0.23–9.72	0.674
Malignancy	0.61	0.16–2.29	0.462	0.54	0.12–2.40	0.418
Steroid using	0.14	0.01–2.34	0.172	0.15	0.01–3.94	0.254
HIV	NA	NA	NA	NA	NA	NA
Study group						
I&D alone	4.29	0.52–35.33	0.176	5.25	0.49–55.69	0.169
I&D + antibiotics	2.86	1.23–6.62	0.014	2.51	1.01–6.25	0.047
Antibiotics alone	1	Reference	—	1	Reference	—

[a] SSTI severity was not included in the multivariate model due to apparent multicollinearity involving study group.
CI = confidence interval; ESRD = end-stage renal disease; HIV = human immunodeficiency virus; I&D = incision and drainage; NA = not applicable; OR = odds ratio; SSTI = skin and soft tissue infection.

also observed for TMP-SMX, tetracycline, and levofloxacin (in 67.3%, 55.9%, and 55% of isolates, respectively).

While there are existing guidelines to be followed in tackling MRSA related SSTIs, we found that many doctors in various fields in our hospital instead selected antibiotics according to their own taste or past experience. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America[17] has clearly suggested that, for mild purulent SSTI, I&D alone is indicated; for moderate purulent SSTI, it should be treated with I&D plus TMP-SMX or doxycycline as empiric antimicrobial therapy but remain or switch to TMP-SMX if MRSA is isolated. As for severe purulent SSTI, in addition to I&D, either vancomycin or daptomycin or linezolid or televancin or ceftaroline is recommended as empiric antimicrobial therapy and should remain unchanged when MRSA is suspected or confirmed. This guideline also stresses that clindamycin may be used if clindamycin resistance is $<$10—15% at the institution. In our study, β-lactam agents such as amoxicillin/clavulanic acid, ampicillin/sulbactam, and cefradine were actually being frequently prescribed. We attribute the inappropriate use of antibiotics to the lack of awareness that empiric treatment with β-lactam agents may no longer be appropriate to be prescribed in Taiwan, an area with a high prevalence of MRSA infection.[3,29]

To address the challenges noted in our study, further information regarding MRSA should be well disseminated among our doctors, possibly including the use of a local algorithm regarding treatment of SSTIs.

There are several limitations in the present study. First, this study was limited by its small sample size, so may not be an accurate representation of a wider population. Second, the study was limited to patients from whom a culture yielded MRSA; however, some milder SSTIs, from which culture samples were not obtained, but that might nonetheless have involved MRSA, would have been excluded from our study. Third, we were not able to assess antibiotic compliance of each patient, nor whether they had been receiving other treatments (such as hyperbaric oxygen therapy) outside of the hospital. Fourth, we may not have been informed about cases that included spontaneous drainage of abscesses. Fifth, we did not include body mass index as an assessment factor (due to the paucity of charting, especially in outpatient department and emergency room patients); obesity might have affected the pharmacokinetic profiles of antimicrobial drugs.[30] Sixth, cases might have been underestimated in terms of their underlying conditions, because related tests (such as oral glucose tolerance test to determine diabetic status) were not performed on all the participants. Seventh, we did not differentiate community-associated MRSA from hospital-associated MRSA due to lack of relevant facilities, and thereby could not offer a detailed analysis on this aspect. Eighth, I&D techniques were not standardized among the treating doctors. Differences in I&D techniques may have influenced SSTI outcomes. Ninth, there is to date no commonly agreed classification of the clinical presentation of SSTI, or a score for assessing the clinical severity of an SSTI validated by either prospective or retrospective clinical studies; despite several severity classification rules for SSTIs being proposed,[15—17,31] the best classification rule is yet unknown.[32] Our classification here may not be consistent with other studies/guidelines, and thereby may have affected treatment outcomes.

In conclusion, surgical intervention, especially I&D, remains the cornerstone of therapy for purulent SSTIs. Adjunctive antibiotic use is determinative if an appropriate antimicrobial is being used. Our results suggest that vancomycin, teicoplanin, and linezolid (antibiotics to which 100% of our isolates were susceptible) are still the drug of choice in terms of antibiotic selection in our hospital setting; TMP-SMX, tetracycline, and levofloxacin (antibiotics to which 67.3%, 55.9%, and 55% of our isolates were susceptible, respectively) might be the next consideration. The establishment of a local use treatment algorithm to deal with SSTIs might be of help for doctors, because avoiding the prescription of inappropriate antibiotics would help to prevent the generation of resistant pathogens in this era of MRSA.

Conflicts of interest

All contributing authors declare no conflicts of interest.

References

1. Boucher H, Miller LG, Razonable RR. Serious infections caused by methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 2010;**51**(Suppl. 2):S183—97.
2. Awad SS, Elhabash SI, Lee L, Farrow B, Berger DH, Awad SS, et al. Increasing incidence of methicillin-resistant *Staphylococcus aureus* skin and soft-tissue infections: reconsideration of empiric antimicrobial therapy. *Am J Surg* 2007;**194**:606—10.
3. Huang YC, Chen CJ. Community-associated meticillin-resistant *Staphylococcus aureus* in children in Taiwan, 2000s. *Int J Antimicrob Agents* 2011;**38**:2—8.
4. Boucher HW, Corey GR. Epidemiology of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 2008;**46**(Suppl. 5): S344—9.
5. Yeh YC, Yeh KM, Lin TY, Chiu SK, Yang YS, Wang YC, et al. Impact of vancomycin MIC creep on patients with methicillin-resistant *Staphylococcus aureus* bacteremia. *J Microbiol Immunol Infect* 2012;**45**:214—20.
6. Labreche MJ, Lee GC, Attridge RT, Mortensen EM, Koeller J, Du LC, et al. Treatment failure and costs in patients with methicillin-resistant *Staphylococcus aureus* (MRSA) skin and soft tissue infections: a South Texas Ambulatory Research Network (STARNet) study. *J Am Board Fam Med* 2013;**26**: 508—17.
7. Duong M, Markwell S, Peter J, Barenkamp S. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. *Ann Emerg Med* 2010;**55**:401—7.
8. Ruhe JJ, Smith N, Bradsher RW, Menon A. Community-onset methicillin-resistant *Staphylococcus aureus* skin and soft-tissue infections: impact of antimicrobial therapy on outcome. *Clin Infect Dis* 2007;**44**:777—84.
9. Frei CR, Miller ML, Lewis 2nd JS, Lawson KA, Hunter JM, Oramasionwu CU, et al. Trimethoprim-sulfamethoxazole or clindamycin for community-associated MRSA (CA-MRSA) skin infections. *J Am Board Fam Med* 2010;**23**:714—9.
10. Macfie J, Harvey J. The treatment of acute superficial abscesses: a prospective clinical trial. *Br J Surg* 1977;**64**:264—6.
11. Llera JL, Levy RC. Treatment of cutaneous abscess: a double-blind clinical study. *Ann Emerg Med* 1985;**14**:15—9.

12. Hankin A, Everett WW. Are antibiotics necessary after incision and drainage of a cutaneous abscess? *Ann Emerg Med* 2007;**50**:49—51.
13. Talan DA. Lack of antibiotic efficacy for simple abscesses: have matters come to a head? *Ann Emerg Med* 2010;**55**:412—4.
14. Rajendran PM, Young D, Maurer T, Chambers H, Perdreau-Remington F, Ro P, et al. Randomized, double-blind, placebo-controlled trial of cephalexin for treatment of uncomplicated skin abscesses in a population at risk for community-acquired methicillin-resistant *Staphylococcus aureus* infection. *Antimicrob Agents Chemother* 2007;**51**:4044—8.
15. Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJ, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. *Clin Infect Dis* 2005;**41**:1373—406.
16. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children: executive summary. *Clin Infect Dis* 2011;**52**:285—92.
17. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2014;**59**:e10—52.
18. Chen YS. Guidelines for the treatment of methicillin-resistant *Staphylococcus aureus* infections in Taiwan. *J Microbiol Immunol Infect* 2013;**46**:147—50.
19. Gonzalez-Ruiz A, Beiras-Fernandez A, Lehmkuhl H, Dohmen PM, Loeffler J, Chaves RL. Effectiveness and safety of daptomycin in complicated skin and soft-tissue infections and bacteraemia in clinical practice: results of a large non-interventional study. *Int J Antimicrob Agents* 2013;**41**:372—8.
20. Aikawa N, Kusachi S, Mikamo H, Takesue Y, Watanabe S, Tanaka Y, et al. Efficacy and safety of intravenous daptomycin in Japanese patients with skin and soft tissue infections. *J Infect Chemother* 2013;**19**:447—55.
21. Sader HS, Watters AA, Fritsche TR, Jones RN. Daptomycin antimicrobial activity tested against methicillin-resistant staphylococci and vancomycin-resistant enterococci isolated in European medical centers (2005). *BMC Infect Dis* 2007;**7**:29.
22. Chen YH, Liu CY, Ko WC, Liao CH, Lu PL, Huang CH, et al. Trends in the susceptibility of methicillin-resistant *Staphylococcus aureus* to nine antimicrobial agents, including ceftobiprole, nemonoxacin, and tyrothricin: results from the Tigecycline *In Vitro* Surveillance in Taiwan (TIST) study, 2006—2010. *Eur J Clin Microbiol Infect Dis* 2014;**33**:233—9.
23. Grayson ML. The treatment triangle for staphylococcal infections. *N Engl J Med* 2006;**355**:724—7.
24. Ellis M. The use of penicillin and sulphonamides in the treatment of suppuration. *Lancet* 1951;**1**:774—5.
25. Marshall JC, Maier RV, Jimenez M, Dellinger EP. Source control in the management of severe sepsis and septic shock: an evidence-based review. *Crit Care Med* 2004;**32**:S513—26.
26. Chambers HF, Moellering Jr RC, Kamitsuka P. Clinical decisions. Management of skin and soft-tissue infection. *N Engl J Med* 2008;**359**:1063—7.
27. Schmitz GR, Bruner D, Pitotti R, Olderog C, Livengood T, Williams J, et al. Randomized controlled trial of trimethoprim—sulfamethoxazole for uncomplicated skin abscesses in patients at risk for community-associated methicillin-resistant *Staphylococcus aureus* infection. *Ann Emerg Med* 2010;**56**:283—7.
28. Singer AJ, Thode Jr HC. Systemic antibiotics after incision and drainage of simple abscesses: a meta-analysis. *Emerg Med J* 2014;**31**:576—8.
29. Chuang YY, Huang YC. Molecular epidemiology of community-associated meticillin-resistant *Staphylococcus aureus* in Asia. *Lancet Infect Dis* 2013;**13**:698—708.
30. Jain R, Chung SM, Jain L, Khurana M, Lau SW, Lee JE, et al. Implications of obesity for drug therapy: limitations and challenges. *Clin Pharmacol Ther* 2011;**90**:77—89.
31. 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 Chemother* 2003;**52**(Suppl. 1):i3—17.
32. Corey GR, Stryjewski ME. New rules for clinical trials of patients with acute bacterial skin and skin-structure infections: do not let the perfect be the enemy of the good. *Clin Infect Dis* 2011;**52**(Suppl. 7):S469—76.