Enferm Infecc Microbiol Clin. 2017;35(2):76–81

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Original article

Skin and soft-tissue infections: Factors associated with mortality and re-admissions

Cristina Macía-Rodríguez, Vanesa Alende-Castro, Lourdes Vazquez-Ledo, Ignacio Novo-Veleiro*, Arturo González-Quintela

Servicio de Medicina Interna, Hospital Universitario de Santiago de Compostela, A Coruña, Spain

ARTICLE INFO

Article history:
Received 12 November 2015
Accepted 29 February 2016
Available online 6 April 2016

Keywords:
Skin and soft-tissue infections
Healthcare-associated infections
ESBL-producing bacteria
Mortality
Readmission

ABSTRACT

Introduction: Skin and soft-tissue infections (SSTIs) are common and are linked to a wide variety of clinical conditions. Few studies have analysed the factors associated with mortality and re-admissions in medical patients with SSTIs. Accordingly, this study sought to describe the clinical and microbiological characteristics of patients diagnosed with SSTIs, and identify mortality and re-admission related factors.
Patients and methods: A total of 308 patients were included in the study. Clinical, socio-demographic and microbiological characteristics were collected. Univariate and logistic regression multivariate analyses were performed in order to identify factors associated with mortality and re-admission.
Results: The bacteria responsible were identified in 95 (30.8%) patients, with gram-positive bacteria being isolated in 67.4% and gram-negative in 55.8% of cases. Multi-resistant bacteria were frequent (39%), and the initial empirical treatment proved inadequate in 25.3% of all cases. In-hospital mortality was 14.9%; the related variables were heart failure (OR = 5.96; 95%CI: 1.93–18.47), chronic renal disease (OR = 6.04; 95%CI: 1.80–20.22), necrotic infection (OR = 4.33; 95%CI: 1.26–14.95), and inadequate empirical treatment (OR = 44.74; 95%CI: 5.40–370.73). Six-month mortality was 8%, with the main related factors being chronic renal disease (OR: 3.03; 95%CI: 1.06–8.66), and a Barthel Index score of under 20 (OR: 3.62; 95%CI: 1.17–11.21). Re-admission was necessary in 26.3% of cases, with the readmission-related variables being male gender (OR: 2.12; 95%CI: 1.14–3.94), peripheral vascular disease (OR: 3.05; 95%CI: 1.25–7.41), and an age-adjusted Charlson Comorbidity Index score of over 3 (OR: 3.27; 95%CI: 1.40–7.63).
Conclusions: Clinical variables such as heart failure, chronic renal disease, peripheral vascular disease, and necrotic infection could help identify high-risk patients. The main factor associated with higher mortality was inadequate initial empirical treatment. Physicians should consider gram-negative, and even extended-spectrum beta-lactamase-producing bacteria when assigning initial empirical treatment for SSTIs, especially in healthcare-associated cases.

© 2016 Elsevier España, S.L.U. and Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. All rights reserved.

Infecciones de piel y partes blandas: factores asociados a mortalidad y reingreso

Palabras clave:
Infecciones de piel y partes blandas
Infecciones asociadas a los cuidados sanitarios
Bacterias productoras de BLEE
Mortalidad
Reingreso

RESUMEN

Introducción: Las infecciones de piel y partes blandas (IPPB) son frecuentes y se asocian a una amplia variedad de presentaciones clínicas. Los factores asociados a mortalidad y reingreso en pacientes con IPPB han sido poco estudiados hasta ahora. En este sentido, el objetivo del presente trabajo es describir las características clínicas y microbiológicas de pacientes diagnosticados de IPPB e identificar factores asociados a mortalidad y reingreso en ellos.
Pacientes y métodos: Fueron incluidos un total de 308 pacientes. Se realizó una descripción de las características clínicas, sociodemográficas y microbiológicas. Se llevaron a cabo análisis uni y multivariantes de regresión logística para identificar factores asociados a mortalidad y reingreso en pacientes con IPPB.

* Corresponding author.
E-mail address: ignacio.novo.veleiro@gmail.com (I. Novo-Veleiro).

http://dx.doi.org/10.1016/j.eimc.2016.02.030
0213-005X/© 2016 Elsevier España, S.L.U. and Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. All rights reserved.

Resultados: Los microorganismos responsables fueron identificados en 95 (30,8%) pacientes, de ellos el 67,4% presentaban bacterias grampositivas y el 55,8%, gramnegativas. La presencia de bacterias multirresistentes fue frecuente (39%) y el tratamiento empírico fue inadecuado en el 25,3% de los casos. La mortalidad intrahospitalaria fue del 14,9% y las variables asociadas a ella fueron la insuficiencia cardiaca (OR = 5,96; IC 95%: 1,93-18,47), la insuficiencia renal crónica (OR = 6,04; IC 95%: 1,80-20,22), la infección necrótica (OR = 4,33; IC 95%: 1,26-14,95) y el tratamiento antibiótico empírico inadecuado (OR = 44,74; IC 95%: 5,40-370,73). La mortalidad a 6 meses fue del 8%, y los principales factores asociados, la insuficiencia renal crónica (OR = 3,03; IC 95%: 1,06-8,66) y una puntuación en el índice de Barthel inferior a 20 puntos (OR = 3,62; IC 95%: 1,17-11,21). Reingresaron durante el seguimiento a 6 meses el 26,3% de los pacientes; las variables asociadas a este hecho fueron el sexo masculino (OR = 2,12; IC 95%: 1,14-3,94), la enfermedad vascular periférica (OR = 3,05; IC 95%: 1,25-7,41) y una puntuación en el índice de Charlson ajustado por edad superior a 3 puntos (OR = 3,27; IC 95%: 1,40-7,63).
Conclusiones: Variables clínicas como la insuficiencia cardiaca, la insuficiencia renal crónica, la enfermedad vascular periférica y la infección necrótica podrían ayudar a identificar pacientes con IPPB de alto riesgo. El principal factor asociado a una mayor mortalidad fue el tratamiento antibiótico empírico inadecuado. Debería considerarse la posibilidad de que bacterias gramnegativas, o incluso enterobacterias productoras de betalactamasas de espectro extendido, sean las responsables de IPPB, sobre todo en casos asociados a los cuidados sanitarios, a la hora de plantear el tratamiento antibiótico empírico en estos pacientes.
© 2016 Elsevier España, S.L.U. y Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Todos los derechos reservados.

Introduction

Skin and soft-tissue infections (SSTIs) include a wide variety of epidermis, dermis, subcutaneous tissue and muscle infections. They commonly present with a broad spectrum of clinical manifestations, ranging from mild to life-threatening forms.[1] Gram-positive microorganisms, and *Staphylococcus aureus* in particular, usually cause SSTIs, though gram-negative bacteria and anaerobes may also be implicated.[2,3] In most cases, the specific pathogen responsible cannot be identified, due to the low efficiency of microbiological cultures.[4] These diseases are commonly diagnosed in emergency wards[5] as well as among hospitalised[1,6] and critically ill patients,[7] with incidence being seen to rise in recent years.[6]

It is essential to consider the clinical characteristics of these patients (diabetes mellitus, obesity, vascular disease, traumatism, recent surgery) and/or the possible existence of immunocompromised status [human immunodeficiency virus infection, immunosuppressive therapy, advanced age], because of the potential role that these factors may play in predisposition to SSTI development and worse disease progression.[4] In this regard, there are few studies that describe clinical factors linked to SSTI development, and fewer still in the case of variables associated with higher mortality and readmission.[1,8] Moreover, most of previous series describe cases from both medical and surgical departments, whose characteristics could be quite different.[1,8]

The dual aim of this study was thus: to analyse the epidemiological, clinical, analytical and microbiological characteristics potentially linked to SSTIs in medical patients; and to identify the factors associated with higher mortality and readmission.

Patients and methods

We conducted a retrospective analysis which covered all patients diagnosed with SSTIs at the Internal Medicine Department of the Santiago de Compostela University Teaching Hospital (*Complejo Hospitalario Universitario de Santiago*) (NW Spain), from 1 October 2010 to 31 December 2013, as shown by the hospital discharge database. This search included all patients identified with the following ICD 10 (International Classification of Diseases, 10th edition) codes: 680.*; 681.*; 682.*; 683.*; 686.*; 035.* and 785.*. The diagnosis criteria followed to include patients and classify them into the different type of SSTIs were those published in current guidelines.[9]

Through patients' medical histories review, we first exclude all patients who did not met SSTIS criteria.[9] After that, we recorded their socio-demographic, clinical and analytical characteristics, and then followed them up for six months post-discharge. We evaluated and quantified case complexity using the age-adjusted Charlson Comorbidity Index (CCI),[10] and established patients' grade of physical dependence using the Barthel Index (BI).[11]

Cases were classified as follows: nosocomial, where diagnosis had been established later than the second day after hospital admission; and healthcare-associated, in those instances where they had come from nursing homes, been hospitalised, or been treated with intravenous antibiotics during the 90 previous days. All other cases were identified as community-acquired.

We considered as fever a corporal temperature higher than 37.8 °C and sepsis was defined according to the Surviving Sepsis Campaign criteria, current during the study period.[12] Empirical antibiotic treatment was deemed inadequate in the following cases: if the first administered antibiotic proved ineffective for the isolated bacteria after culture (microbiological criteria); or if it was changed due to therapeutic failure during the first 72 h, based on clinical criteria.

All patients deceased during their hospitalisation were included as in-hospital mortality. A 6-month follow up was made in all survivors; in those cases mortality and readmission by any cause were recorded and also specific SSTIs-related mortality and readmission.

A descriptive analysis was performed, by calculating qualitative-variable rates plus mean and standard deviation. We used the Chi-square test or Fisher's exact test, as appropriate (expected frequency value <5), to compare qualitative variables, and the Student's t test for quantitative variables. A multivariate logistic regression analysis was conducted to identify factors associated with mortality and readmission. Akaike's information criterion (AIC), which combines the goodness of fit with the number of parameters, was used to select the best model.[13] The model with the lowest AIC value was considered to have the best fit. A *P*-value <0.05 was regarded as significant. All analyses were performed using the SPSS v. 22.0 software package (SPSS Inc., Chicago, IL, USA).

Results

During the study period, there was a total of 308 patients with SSTIs, 50.6% men, mean age 71.3 years (standard deviation [SD] = 16.2). In 11.2% of cases, BI scores were less than 20, indicating a severe degree of physical dependence. All patients' histories

Table 1
Clinical and epidemiological characteristics of the 308 included patients.

Characteristic (n = 308)	No. (%)
Age (year, mean ± SD)	71.0 ± 16.2
Gender	
Male	156 (50.6)
Female	152 (49.4)
Comorbid conditions	
Diabetes mellitus	95 (30.8)
Heart failure	113 (36.7)
Hepatic disease	37 (12.0)
Cancer	47 (15.4)
Peripheral vascular disease	36 (11.7)
Chronic venous disease	65 (21.1)
Chronic renal disease	56 (18.2)
Chronic lung disease	51 (16.6)
Immunosuppression	72 (23.6)
Autoimmune disease	17 (5.5)
Glucocorticoids treatment	20 (6.5)
IDU	7 (3.3)
Dementia	36 (11.7)
Reason for hospitalisation	
SSTI	209 (67.8)
Other infection	23 (7.4)
Other cause	76 (24.7)
Origin	
Community-acquired infection	144 (46.7)
Healthcare-associated infection	136 (44.3)
Nosocomial	28 (9.1)
Form of presentation	
Fever	170 (55.2)
Sepsis	44 (14.3)
Bacteremia	44 (14.3)
Necrotising infection	34 (11.0)
Other	16 (5.2)
Treatment in an intensive care unit	30 (9.9)
Surgical treatment	29 (9.6)

SD: standard deviation. IDU: intravenous drug user. SSTI: skin and soft tissue infection.

Table 2
Microbiological profile and empirical antibiotic treatment.

Microorganism (n = 95)	No. of isolates (%)
Gram-positive	**66 (69.5)**
Staphylococcus aureus MS	22 (23.2)
Streptococcus	13 (13.7)
Other *Staphylococcus*	11 (11.6)
MRSA	11 (11.6)
Other gram-positive	9 (9.5)
MR gram positive	20 (21)
Gram-negative	**53 (55.8)**
Proteus mirabilis	16 (16.8)
Escherichia coli	11 (11.6)
Pseudomonas aeruginosa	8 (8.4)
Klebsiella sp	6 (6.3)
ESBL *Klebsiella sp*	5 (5.3)
MR *Pseudomonas aeruginosa*	4 (4.2)
ESBL *Escherichia coli*	3 (3.2)
MR gram negative	17 (17.9)
Anaerobes	**11 (11.6)**
Antibiotic (n = 308)	**No. (%)**
Amoxicillin plus clavulanate	102 (33.1)
Cloxacillin	80 (26.0)
Cephalosporins (2ª, 3ª or 4ª generation)	45 (14.6)
Piperacillin plus tazobactam	27 (8.8)
Ciprofloxacin	22 (7.1)
Linezolid	21 (6.8)
Clindamycin	18 (5.8)
Levofloxacin	12 (3.9)
Vancomycin	9 (2.9)
Meropenem	7 (2.3)
Metronidazol	7 (2.3)
Teicoplanin	6 (1.9)
Rifampicin	5 (1.6)
Gentamicin	3 (1.0)
Aztreonam	3 (1.0)
Penicillin (V and G)	2 (0.6)
Trimethoprim-sulfamethoxazole	2 (0.6)
Amikacin	2 (0.6)
Norfloxacin	1 (0.3)

MS: methicillin-sensible. MRSA: methicillin-resistant *Staphylococcus aureus.* MR: multi-drug resistant. ESBL: extended-spectrum beta-lactamases.

could be reviewed and 6-month follow up was fulfilled in all cases. The median of age-adjusted CCI score was 5.5 (IQR = 3) and 172 (56%) patients had 2 or more chronic diseases. The majority of patients (68.2%) lived at home, with the result that most of the cases (47%) were classified as community-acquired, followed by healthcare-associated (44%) and nosocomial (9%). The main comorbid conditions were heart failure (36.7%), diabetes mellitus (30.8%) and immunosuppression (23.6%). Other socio-demographic and overall clinical characteristics are shown in Table 1.

Insofar as the localisation of infection was concerned, the point of entry was identified in 44.8% of cases. The lower extremities were the principal infection site (70.9%) followed by the upper extremities (7.8%). Cellulitis was the most frequent type of infection (70.8%), followed by abscesses (12.3%) and pressure ulcers (6.8%). Abscesses were in all cases complications from cellulitis or pyomyositis and pressure ulcers were located in sacral region and hips.

Sepsis criteria were identified in 39.9% (123 patients) and bacteraemia in 14.3% (44 patients) of cases, though blood cultures were drawn in 218 patients (70.8%). Of the 144 patients (46.8%) on whom local cultures were performed, 95 (30.8%) tested positive and were defined as patients with known responsible bacteria. Gram-positive bacteria were isolated in 64 (67.4%) and gram-negative in 53 cases (55.8%). Of these, 41 patients (43.2%) were infected exclusively by gram-positive bacteria and 24 (25.3%) exclusively by gram-negative bacteria; anaerobes were isolated in 11 cases (11.6%), all in combination with other types of bacteria. Two or more responsible bacteria (multi-bacterial origin) were identified in 46 (48.4%) cases. Multi-drug resistant (MR) gram-positive bacteria were isolated in 21% and MR gram-negative bacteria in 17.9% of patients with known responsible bacteria [8.4% extended-spectrum betalactamase (ESBL) producing bacteria]. The most common responsible organism was methicillin-sensible (MS) *Staphylococcus aureus* (23.2%), followed by *Proteus mirabilis* (16.8%). In healthcare-associated cases, the presence of gram-negative bacteria and multi-bacterial origin was much higher (69.4% and 51% respectively). A complete outline of the microbiological data is shown in Table 2. The etiological agent prevalence was similar in all types of SSTIs, without significant differences between them.

The most commonly used empirical antibiotic treatments were amoxicillin and clavulanate in 102 patients (33.1%) and cloxacillin in 80 patients (26.0%). In 91 (29.5%) cases a combination of antibiotics was used. The initial empirical treatment was inadequate in 78 cases (25.3%), 51 according to microbiological criteria and 27 according to clinical criteria. The factors associated with inadequate empirical treatment were peripheral vascular disease, surgery in the 90 days before current admission, nosocomial origin, and multi-bacterial infection ($P < 0.05$).

In-hospital mortality was 14.9% (46 patients) and mortality across six-month follow-up was 8% (21 patients). Readmission was necessary in 69 (26.3%) cases (34 of them, 49%, caused by a SSTIs).

While the main factors shown by the univariate analysis ($P < 0.05$) to be associated with in-hospital mortality, six-month mortality and six-month readmission are listed in Table 3. If we focus in readmission caused by SSTIs, the only variables associated with this fact ($P < 0.005$) were the presence of cancer and

Table 3
Univariate analysis. Factors associated with mortality and readmission.

Variable	In-hospital mortality			Six-month mortality			Six-month readmission		
	No. (%) Died (46)	No. (%) Survivors (262)	*P*	No. (%) Died (21/262)	No. (%) Survivors (241/262)	*P*	No (%) Readmitted (69/241)	No. (%) Not readmitted (172/241)	*P*
Male sex	22 (47.8)	134 (51.1)	NS	11 (52.4)	112 (46.5)	NS	44 (63.8)	88 (51.2)	0.016
Comorbid condition									
Vascular disease	11 (23.9)	25 (9.5)	0.005	1 (4.8)	22 (9.1)	NS	14 (20.3)	11 (6.4)	0.001
Heart failure	26 (56.5)	87 (33.2)	0.003	9 (42.9)	71 (29.5)	NS	27 (39.1)	57 (33.1)	NS
Chronic renal disease	18 (39.1)	28 (10.7)	<0.001	6 (28.6)	29 (12)	0.050	13 (18.8)	25 (14.5)	NS
Cancer	14 (30.4)	33 (12.6)	0.002	5 (23.8)	27 (11.2)	NS	14 (20.3)	19 (11)	0.020
Dementia	10 (21.7)	26 (9.9)	0.022	6 (28.6)	19 (7.9)	0.004	6 (8.7)	19 (11)	NS
Diabetes mellitus	18 (39.1)	76 (29)	NS	9 (42.9)	59 (24.5)	NS	22 (31.9)	52 (30.2)	NS
Glucocorticoids	5 (10.9)	15 (5.7)	NS	2 (9.5)	10 (4.1)	NS	4 (5.8)	11 (6.4)	NS
Immunosuppression	18 (39.1)	54 (20.6)	0.007	6 (28.6)	44 (18.3)	NS	18 (26.1)	36 (20.9)	NS
Liver disease	5 (10.9)	32 (12.2)	NS	2 (9.5)	29 (12)	NS	10 (14.5)	22 (12.8)	NS
Barthel's Index < 20	9 (19.6)	27 (10.3)	NS	5 (23.8)	20 (8.3)	0.032	7 (10.1)	19 (11)	NS
Charlson's Index > 3	44 (95.7)	193 (73.9)	0.001	21 (100)	159 (66)	0.004	61 (88.4)	130 (75.6)	0.002
Origin									
HA infection	23 (50)	113 (43.1)	NS	10 (47.6)	96 (39.8)	NS	38 (55)	75 (43.6)	0.030
Nosocomial	6 (13)	22 (8.4)	NS	1 (4.8)	17 (7)	NS	6 (8.7)	16 (9.3)	NS
Form of presentation									
Fever	25 (54.3)	145 (55.3)	NS	8 (38)	129 (53.5)	NS	30 (43.4)	111 (64.5)	0.034
Sepsis	22 (47.8)	101 (38.5)	NS	8 (38)	90 (37.3)	NS	25 (36.2)	75 (43.6)	NS
Necrotic infection	15 (32.6)	19 (7.3)	<0.001	1 (4.8)	15 (6.2)	NS	9 (13)	9 (5.2)	0.022
Microorganism									
GP infection	12 (26.1)	52 (19.8)	NS	9 (42.9)	39 (16.2)	NS	16 (23.2)	34 (19.8)	NS
GN infection	10 (21.7)	43 (16.4)	NS	9 (42.9)	30 (12.4)	NS	21 (30.4)	21 (12.2)	0.037
Anaerobic infection	2 (4.3)	9 (3.4)	NS	0 (0)	6 (2.5)	NS	3 (4.3)	6 (3.5)	NS
MB infection	13 (28.3)	33 (12.6)	NS	7 (33.3)	22 (9.1)	NS	15 (21.7)	17 (9.9)	NS
Treatment									
Surgical treatment	4 (8.7)	25 (9.5)	NS	0 (0)	23 (9.5)	NS	12 (17.4)	12 (7)	0.007
Inadequate treatment	21 (45.7)	30 (11.4)	<0.001	2 (9.5)	26 (10.8)	NS	11 (15.9)	19 (11)	NS
Treatment in ICU	10 (21.7)	20 (7.6)	0.004	3 (14.3)	15 (6.2)	NS	6 (8.7)	13 (7.6)	NS

HA: healthcare-associated. GP: gram-positive. GN: gram-negative. MB: multi-bacterial. ICU: Intensive-care Unit. NS: no significance.

immunosuppression, which differences this subgroup from overall results. The results of the multivariate logistic regression analysis were as follows. The variables associated with in-hospital mortality were heart failure (odds ratio [OR] = 5.96; 95% confidence interval [CI]: 1.93–18.47), chronic renal disease (OR = 6.04; 95%CI: 1.80–20.22), necrotic infection (OR = 4.33; 95%CI: 1.26–14.95), and inadequate empirical treatment (OR = 44.74; 95%CI: 5.40–370.73). The variables associated with six-month mortality were chronic renal disease (OR: 3.03; 95%CI: 1.06–8.66) and a BI score of less than 20 (OR: 3.62; 95%CI: 1.17–11.21). Lastly, the variables associated with six-month readmission were male gender (OR: 2.12; 95%CI: 1.14–3.94), peripheral vascular disease (OR: 3.05; 95%CI: 1.25–7.41), and an age-adjusted CCI score of more than 3 (OR: 3.27; 95%CI: 1.40–7.63). There were no significant differences in subgroup analysis between patients with different ages, sex and type of infection when comparing in-hospital mortality, readmission or six-month mortality.

Discussion

Our study describes de main characteristics of a cohort of medical patients diagnosed with SSTIs. We found a higher prevalence of MR gram-negative bacteria and ESBL-producing bacterial as etiologic agent of these infections. We also found variables lined to a poorer prognosis in our patients, which could be useful to identify high risk patients and treat them more aggressively since the diagnosis.

The incidence of SSTIs (100 admissions per 500 000 persons/year) in our environment is similar to that reported by other authors in Spain[1] but lower than in the United States (USA).[14] As reported elsewhere, the most frequent comorbidities were heart failure and diabetes mellitus.[5,9]

The study population's degree of dependence was low, with only 11.7% registering a BI score of less than 20. Although there were no previous data against which to compare this finding, this might well explain the low percentage of pressure ulcers observed in our series.

Local cultures were performed in 46.8% and tested positive in 66% of cases (95/144); blood cultures were performed in 70.8% and proved positive in 20.2% of cases (44/218). Other studies have described local culture performance in 33%–41% of patients (47%-85.8% positive)[1,5,8] and blood culture extraction in 6.6%–47.8% of patients (18.8%–22.3% positive).[1,5,8] In light of these data, we suggest that a correct collection of local cultures could increase the percentage of adequate empirical treatment and maybe the routine extraction of blood cultures could be not always necessary (e.g. patients with difficult venous access), due to the low yield of blood cultures in SSTIs.

In terms of the microbiological profile, responsible bacteria were only obtained in 95 cases. The percentage of methicillin-resistant *Staphylococcus aureus* (MRSA) corresponds to the prevalence of positive cultures for MRSA at our hospital (approximately 18%) but is lower than the percentage found at other health facilities around Spain (approximately 30%)[3,4] and the USA (as high as 46% in some cohorts), where this microorganism is the leading cause of SSTIs.[6] In contrast to reports from other countries, we observed a higher proportion of ESBL-producing *Enterobacteriaceae* (8.4%), mainly in healthcare-associated infections (12.2%). In our series, the presence of these bacteria was not associated with prior surgery or the presence of cirrhosis, as reported by other authors,[15,16] which

probably indicates the existence of a high prevalence of ESBL-producing *Enterobacteriaceae* skin colonisation and transmission in nursing homes in our area, rather than MRSA or other MR gram-positive bacteria.

If we focus in the empirical antibiotic treatment, attention should be drawn to the low use of active antibiotics for MRSA, such as vancomycin (2.9%) and linezolid (6.8%), and the absence of use of daptomycin and tigecycline. This finding is attributable to the low prevalence of MRSA at our hospital and to the fact that these antibiotics are recommended as empirical treatment in nosocomial infections, which were uncommon in our study.

The frequent absence of response to the initial empirical treatment in our study may be explained by the high incidence of gram-negative bacteria (55.8%), which are usually less common in SSTIs than are gram-positive bacteria.[1,4,5] Other authors have likewise reported both gram-negative and multi-bacterial aetiology as factors linked to inappropriate initial antibiotic treatment.[17] Hence, while empirical treatment of SSTIs is traditionally focused on gram-positive bacteria, in view of our results the need for empirical antibiotic coverage against gram-negative bacteria should perhaps be reassessed. Some factors linked to an absence of response to the initial antibiotic treatment, like previous surgery, nosocomial origin or multi-bacterial aetiology, could reflect a different microbiological profile of SSTISs in these patients. Furthermore, in the light, not only of our findings, but also of the relevance of these infections and their impact on mortality and poor prognosis,[18,19] we suggest that the possibility of ESBL-producing bacteria be borne in mind when it comes to establishing an empirical treatment in health-care associated SSTIs.

In-hospital mortality was higher than that reported elsewhere (0.2%–10.9%).[1,5,7,8] This finding might be related to a higher prevalence of multiple comorbidities and to the above-mentioned differences in the microbiological profile of SSTIs. Thus, our study included a 56% of patients with at least 2 chronic diseases, much higher than previous studies, with a prevalence of patients with any chronic disease near to 50%.[1,5] Regarding the variables linked to in-hospital mortality, some of these factors have previously been described in surgical patients,[1,8,20] to our knowledge there are no previous reports, such as ours, which describe in-hospital mortality associated with SSTIs in medical patients alone. The association between heart failure and in-hospital mortality could be due to the capital role of SSTIs as a precipitating factor of congestive heart failure episodes. As regards chronic renal disease, a lower antibiotic dosage is common in these patients, which could lead to a reduced treatment efficacy.[21] In contrast, we found that in-hospital mortality was not associated with the existence of sepsis or septic shock, as in other series[8] and neither with other conditions like diabetes mellitus or liver disease.[1] These differences might reflect the higher complexity of our patients and the higher prevalence of cardiovascular and concomitant renal disease. The relevance of our findings therefore highlights the importance of correct identification of high-risk patients and provides tools for drawing up a more intensive treatment strategy for such patients.

Mortality across the six-month follow-up has, to our knowledge, not previously been analysed. The high mortality found in our study probably reflects the severity and repercussion of SSTIs in patients with multiple comorbidities. In this regard, the main factors associated with six-month mortality were chronic renal disease and a BI score of less than 20, which reflect greater frailty and poor prognosis. While the usefulness of BI and other indices to predict a higher mortality risk in aged and polypathological patients is well known,[22,23] this study points, for the first time, to a potential role in SSTIs, by identifying high-risk patients. There are no previous data relating to the readmission risk in such infections. Our results suggest that vascular compromise and mobility limitations could lead to greater difficulty in healing and tissue regeneration, rendering it necessary to readmit these patients in order to optimise their care.

In summary, we propose that the variables associated with mortality and readmission (male gender, a BI score of less than 20, an age-adjusted CCI score of more than 3, heart failure, chronic renal disease, peripheral vascular disease and necrotic infection) could be useful for stratifying SSTI patients according to their respective risks of a poor outcome.

The main limitation of this study lies in the retrospective nature of the analysis, which could compromise the accuracy of some of the clinical data included. In addition, the absence of an established protocol for SSTI management at our hospital might be an important bias, due to the lack of uniformity in the diagnosis and treatment of such patients. Finally, the inclusion of the absence of response to the initial antibiotic treatment due both to clinical and microbiological criteria could also be a significant bias.

Conclusions

The relevance of SSTIs as a health problem in our area is high, as is the impact of these diseases on mortality, principally among patients with multiple comorbidities. There are clinical variables, such as heart failure, chronic renal disease, peripheral vascular disease and necrotic infection, which could help identify high-risk patients. The main factor associated with higher mortality is inadequate initial empirical treatment, something that is very common; in the light of our findings, physicians should consider gram-negative bacteria and even ESBL-producing bacteria when designing the initial empirical treatment for SSTIs, particularly in health-care associated cases. In this regard, correct extraction of local cultures could both help and guide antibiotic treatment strategy.

Funding

No funding was required to develop this work.

Conflict of interest

All authors declare that they have no conflict of interest.

References

1. Raya-Cruz M, Ferullo I, Arrizabalaga-Asenjo M, Nadal-Nadal A, Díaz-Antolín MP, Garau-Colom M, et al. Infecciones de piel y partes blandas en pacientes hospitalizados: factores epidemiológicos, microbiológicos, clínicos y pronósticos. Enfermedades Infecc Microbiol Clín. 2014;32:152–9.
2. Moran GJ, Abrahamian FM, Lovecchio F, Talan DA. Acute bacterial skin infections: developments since the 2005 Infectious Diseases Society of America (IDSA) guidelines. J Emerg Med. 2013;44:e397–412.
3. Sociedad Española de Quimioterapia, Sociedad Española de Medicina Interna, Asociación Española de Cirujanos. Guía de tratamiento de las infecciones de piel y partes blandas. Rev Esp Quimioter Publ Of Soc Esp Quimioter. 2006;19:378–94.
4. Ibáñez Barceló M, Pomar Solchaga V, Castañeda S. Infecciones de partes blandas. Med Clín. 2009;133:139–46.
5. Llopis F, González-Castillo J, Julián-Jiménez A, Ferré C, Gamazo-Río JJ, Martínez M. Análisis de 1.250 episodios de infección de piel y partes blandas registrados en 49 servicios de Urgencias hospitalarios. Rev Española Quimioter. 2014;27:115–21.
6. Edelsberg J, Taneja C, Zervos M, Haque N, Moore C, Reyes K, et al. Trends in US hospital admissions for skin and soft tissue infections. Emerg Infect Dis. 2009;15:1516–8.
7. Shen H-N, Lu C-L. Skin and soft tissue infections in hospitalized and critically ill patients: a nationwide population-based study. BMC Infect Dis. 2010;10:151.
8. Carratalá J, Rosón B, Fernández-Sabé N, Shaw E, del Rio O, Rivera A, et al. Factors associated with complications and mortality in adult patients hospitalized for infectious cellulitis. Eur J Clin Microbiol Infect Dis. 2003;22:151–7.
9. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJC, 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.

10. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–83.
11. Mahoney FI, Barthel DW. Functional evaluation. The Barthel Index. Md State Med J. 1965;14:61–5.
12. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41:580–637.
13. Akaike H. A new look at the statistical model identification. IEEE Trans Autom Control. 1974;19:716–23.
14. Ray GT, Suaya JA, Baxter R. Incidence, microbiology, and patient characteristics of skin and soft-tissue infections in a U.S. population: a retrospective population-based study. BMC Infect Dis. 2013;13:252.
15. Fernandes R, Prudêncio C. Post-surgical wound infections involving Enterobacteriaceae with reduced susceptibility to β-lactams in two Portuguese hospitals. Int Wound J. 2010;7:508–14.
16. Chang C-M, Lee H-C, Lee N-Y, Lee I-W, Wu C-J, Chen P-L, et al. Community-acquired Klebsiella pneumoniae complicated skin and soft-tissue infections of extremities: emphasis on cirrhotic patients and gas formation. Infection. 2008;36:328–34.
17. Lipsky BA, Napolitano LM, Moran GJ, Vo L, Nicholson S, Kim M. Inappropriate initial antibiotic treatment for complicated skin and soft tissue infections in hospitalized patients: incidence and associated factors. Diagn Microbiol Infect Dis. 2014;79:273–9.
18. Perianes-Díaz ME, Novo-Veleiro I, Solís-Díaz K, Prolo-Acosta A, García-García I, Alonso-Claudio G. Bacteriemia por Escherichia coli y Klebsiella pneumoniae productoras de betalactamasas de espectro extendido: factores asociados a mortalidad y reingreso hospitalario. Med Clín. 2014;142:381–6.
19. Angel Díaz M, Ramón Hernández J, Martínez-Martínez L, Rodríguez-Baño J, Pascual A, Grupo de Estudio de Infección Hospitalaria (GEIH). Escherichia coli y Klebsiella pneumoniae productoras de betalactamasas de espectro extendido en hospitales españoles: segundo estudio multicéntrico (proyecto GEIH-BLEE 2006). Enfermedades Infecc Microbiol Clín. 2009;27:503–10.
20. Krieg A, Dizdar L, Verde PE, Knoefel WT. Predictors of mortality for necrotizing soft-tissue infections: a retrospective analysis of 64 cases. Langenbecks Arch Surg Dtsch Ges Für Chir. 2014;399:333–41.
21. Lewis SJ, Mueller BA. Antibiotic dosing in patients with acute kidney injury: enough but not too much. J Intensive Care Med. 2014.
22. Corrao S, Santalucia P, Argano C, Djade CD, Barone E, Tettamanti M, et al. Gender-differences in disease distribution and outcome in hospitalized elderly: data from the REPOSI study. Eur J Intern Med. 2014;25:617–23.
23. Bernabeu-Wittel M, Formiga F, Ollero-Baturone M, PROFUND Researchers. A new prognostic index centered on polypathological patients. The Profund Index. J Gerontol A Biol Sci Med Sci. 2011;66:1393–4, author reply 1395–6.