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IM - COMMENTARY

Identifying patients with acute bacterial skin and skin structure infection who need blood cultures

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In this issue of *Internal and Emergency Medicine,* Chang and coworkers identify some factors associated with bacteremia in patients with acute bacterial skin and skin structure infections (ABSSSIs) [1]. The role of blood cultures in ABSSSIs remains controversial for several reasons. Patients with skin infections rarely have bacteremia: a systematic review of bacteremia episodes in patients with cellulitis and erysipelas shows that blood cultures are positive in only 7.9% and 4.6% of cases, respectively [2]. Other reports show that the incidence of bacteremia in patients with uncomplicated cellulitis is 4.8%, and are due to *Streptococcus* spp and *Staphylococcus aureus*, as expected considering the classical microbiology of non-purulent skin infection [3, 4]. Among patients needing hospitalization, methicillin-resistant *Staphylococcus aureus* (MRSA) appears as a leading pathogen, and an increasing prevalence of community-acquired MRSA has been reported in the last decade [5, 6]. Thus, guidelines from Infectious Diseases Society of America (IDSA) recommend the administration of antibiotics against this category of microrganisms, with particular attention when risk factors for MRSA are present [7]. However, in patients with ABSSSI and positive blood cultures, contamination rates are relatively high, and even when the etiological agent is isolated, blood cultures results are only rarely associated with a change in the empirical management [8]. For all these reasons, IDSA guidelines recommend blood cultures only for patients with deleterious conditions, such as malignancy, sepsis, neutropenia, and severe cell-mediated immunodeficiency [7].

An initial consideration is that the indiscriminate collection of blood cultures in all patients with ABSSSI would be expensive and counterproductive. As a matter of fact, identifying the right clinical indications for blood culture is necessary to avoid false-positive results from contamination that can lead to inappropriate antibiotic therapy, longer hospitalization stay and higher costs [9]. Nowadays, not only therapeutic but also diagnostic stewardship is needed to implement appropriate tests for the clinical setting, and to ensure prompt appropriate clinical action to translate diagnostic test results into improved patients' outcomes [10, 11]. Thus, the overuse of blood cultures might lead to negative clinical and economic outcomes. However, the presence of bacteremia in patients with ABSSSI notably increases the risk of mortality [1]. Thus, not only the overuse of blood cultures when not indicated, but also the omission of necessary blood cultures has important clinical consequences. Identifying patients with ABSSSI who should have blood cultures collection is important to reduce the risk of poor outcome minimizing the unnecessary use of a diagnostic tool and the risk of difficult-to-interpret results. But, the dilemmas that often clinicians faced are "Which patients with ABSSSI required blood cultures collection?", and "What blood cultures results can add to clinical management of these patients?".

To answer the first question, Chang and collaborators try to identify factors independently associated with positive blood cultures in patients with ABSSSI. They find that 9.2% of patients with ABSSSIs have positive blood cultures, and 2.1% of patients die. They identify diabetes mellitus, chronic kidney disease, hyperglycemia and hypoalbuminemia as factors associated with the highest risk of positive blood cultures in patients with ABSSSI, outlining a patient profile useful to select patients in whom blood cultures are necessary. Nevertheless, among patients with ABSSSI, blood cultures are more frequently performed in those with a severe acute clinical condition

Commentary to "Risk factors associated with bacteremia correlated with mortality in patients with acute bacterial skin and skin structure infection".

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or a severe comorbidity [12]. Consequently, it is difficult to discriminate if the factors proposed by Chang et al. are independently associated with higher risk of bacteremia in patients with ABSSSI, or if they are more frequently found in patients with positive blood cultures because this diagnostic test was performed more frequently in patients with multiple comorbidities. Further prospective studies including patients who systematically undergo blood cultures are necessary to compare patients with ABSSSIs with positive blood cultures and those with negative ones.

Replying to the second question is more difficult. No studies evaluate if among patients with ABSSSI at high risk of bacteremia, blood cultures results add something to the clinical management of patients. We think that the positivity of blood cultures could guide the selection of antibiotics with more adequate pharmacokinetics/pharmacodynamics target (for example, bactericidal instead of bacteriostatic drugs, antibiotics with higher maximum serum concentration) [13, 14], as well as the decision to hospitalize or not the patient and the duration of antibiotic therapy.

To better describe the clinical characteristic and outcome of patients with ABSSSI and positive blood cultures, we perform an analysis of cases with bacteremia secondary to ABSSSI included in the prospective multicenter observational study SNOOPII [15, 16]. Among 533 episodes of bacteremia, 49 (9.2%) had a bacteremia arising from a skin and soft tissue infection. This is a considerable proportion of patients, suggesting that ABSSSIs can be a cause of BSI more frequent than that expected. Table 1 shows clinical features of the 49 patients with ABSSSI and bacteremia. Median age was 74 (interquartile ranges 62.5–83) years, with the majority of patients older than 65 years. Seventeen (34.7%) cases were community-acquired, 21 (42.9%) healthcare-associated and 11 (22.4%) nosocomial. The majority (85.7%), but not all patients, present with fever (> 38 °C). However, this proportion is reduced to 78.3% when patients ≥ 75 years are considered (data not shown). In about one-third of patients, hyperglycemia, tachypnea or altered mental status are present (38.8%, 36.7%, 28.6%, respectively). In-hospital mortality rate is 14.3%.

Figure 1 shows the etiology of the 49 cases. Staphylococci and streptococci are the most frequent isolated pathogens. Among 21 *S. aureus*, 6 (28.6%) are MRSA. Our findings confirm that mortality rates of patients with ABSSSI with positive blood cultures are higher than that reported when all patients with ABSSSI (including those without bacteremia) are considered. Thus, the identification of patients with ABSSSI with positive blood cultures is crucial because they have a worse outcome than patients with negative blood cultures. In our study population, fever is the most frequent clinical feature followed by hyperglycemia, tachypnea and altered mental status.

Table 1 Clinical characteristics and outcome of patients with ABSSSIs with positive blood cultures

	N = 49
Demographic characteristics	
Age, years, median (IQR)	74 (62.5–83)
Age ≥ 65 years	35 (71.4%)
Age ≥ 75 years	23 (46.9%)
Gender, male	28 (57.1%)
Hospital admission in the last 3 month	20 (40.8%)
Antibiotic treatment in the last 3 months*	23 (46.9%)
Way of acquisition	
Community-acquired	17 (34.7%)
Healthcare associated	21 (42.9%)
Nosocomial	11 (22.4%)
Transfer from LTCF	6 (12.2%)
Comorbid conditions	
Solid malignancy	9 (18.4%)
Cardiovascular disease	9 (18.4%)
COPD	16 (32.7%)
Liver disease	5 (10.2%)
Chronic kidney disease	12 (24.5%)
Diabetes	18 (36.7%)
Neurological disorder	13 (26.5%)
Charlson comorbidity index, median (IQR)	3 (2–4.5)
Clinical manifestations	
Fever (> 38 °C)	42 (85.7%)
Hypotension[a]	7 (14.3%)
Tachycardia	33 (6.3%)
Tachypnea	18 (36.7%)
$PaO_2/FiO_2 < 300$	13 (26.5%)
Altered mental status	14 (28.6%)
Hepatic dysfunction[b]	4 (8.2%)
Renal dysfunction[c]	11 (22.4%)
Altered coagulation[d]	7 (14.3%)
Lactates > 2 mmol/L	9 (18.4%)
Hyperglycemia	19 (38.8%)
Septic shock	8 (16.3%)
Length of hospital stay, days, median (IQR)	18 (11–29)
In-hospital mortality	7 (14.3%)

[a]Hypotension is defined as systolic blood pressure (SBP) < 90 mm Hg, mean arterial pressure < 70 mm Hg, or an SBP decrease > 40 mm Hg

[b]Hepatic dysfunction is defined as bilirubin > 2 mg/dl or transaminases > 2 times the upper limit

[c]Renal dysfunction is defined as urine output < 0.5 mL/kg/h for at least 2 h despite adequate fluid resuscitation or creatinine increase > 0.5 mg/dL or 44.2 µmol/L

[d]Altered coagulation is defined as INR > 1.5 or aPTT > 60 s or platelets count $< 100 \times 10^3$/µL

ABSSSI acute bacterial skin and skin structure infections, *IQR* interquartile ranges, *LTCF* long-term care facilities

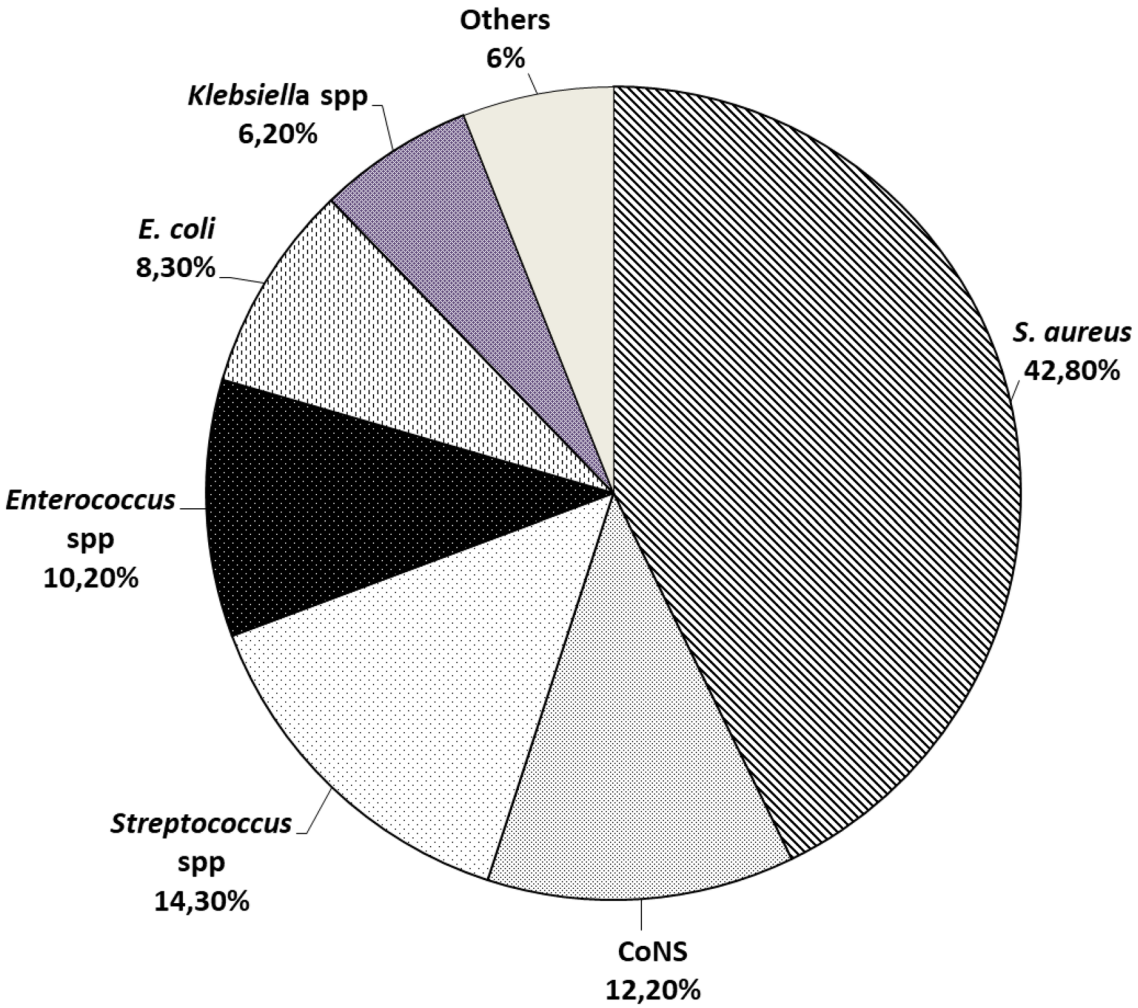

Fig. 1 Etiology of 49 cases of ABSSSI with bacteremia. *CoNS* coagulase-negative staphylococci. Others include: 1 *Pseudomonas* spp, 1 *Enterobacter* spp, 1 *Fusobacterium* spp

In conclusion, clinicians should select patients with ABSSSIs who should undergo blood culture collection, but available data are already limited to produce strength recommendations about the category of subjects who need this diagnostic assessment. Signs of systemic infection (fever, tachypnea, and altered mental status) are predictive of bloodstream infection, and should alert physicians to the need for blood cultures collection.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights The data provided are part of an observational study. All procedures performed in the study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Informed consent The data provided are part of an observational study. Approval of the study protocol was obtained from the institutional review boards at each hospital, which waived the requirement for obtaining informed consent.

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