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ORIGINAL PAPER

Microbiological profile and susceptibility pattern of surgical site infections related to orthopaedic trauma

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Abstract

Background Understanding the epidemiology of microorganisms associated with surgical site infections related to orthopaedic trauma (SSI-ROT) is important in establishing treatment protocols. The aim of this study was to evaluate the etiology and susceptibility pattern of SSIs related to orthopaedic trauma in a Brazilian reference hospital for trauma.

Methods Patients with SSI-ROT in a Brazilian reference hospital for trauma were retrospectively analyzed. All patients with orthopaedic trauma who underwent a surgical procedure and developed SSI within one year were included. All patients had culture samples from the surgical site obtained from biopsy of bone or soft tissue. Clinical and epidemiological data of the patients were collected.

Results A total of 147 patients with trauma-related infection were included in the analysis. The mean time to infection was 55.5 days, and the mean duration of hospitalization was 20.0 days. The in-hospital mortality rate after infection was 5.4%. Cultures were obtained from all patients, with 104 samples obtained from soft tissues and 43 samples from bone. The positivity rate was 93.2%. Among the isolates, 56.5% (77 patients) were gram-negative bacteria and 43.8% (60 patients) were gram-positive bacteria. *Staphylococcus aureus* was identified in 34%, *Enterobacter* spp. in 14.9%, and *Pseudomonas aeruginosa* in 11.6%. *Staphylococcus aureus* presented a higher positivity in bone samples (odds ratio, 1.29; 95% CI, 1.01–1.70; $p = 0.04$). Few microorganisms were multi-resistant.

Conclusion SSI in orthopaedic trauma can be associated with gram-negative bacilli, the susceptibility profile of which suggested that most infections occur after discharge. *Staphylococcus aureus* infections were commonly caused by methicillin-susceptible isolates, and this susceptibility to oral antibiotic options helps in the dehospitalization of patients.

Keywords Trauma · Infection · Orthopaedic · *Staphylococcus aureus* · Culture

Introduction

In Brazil, trauma is the third major cause of death. In 2014, trauma caused a million hospital admissions, and trauma cases confer an economic burden of more than US$300 million to the public health system each year [1]. The main complication of orthopaedic trauma is surgical site infection (SSI) due to tissue damage and circulation impairment [2]. Treatment of infection associated with trauma is twice as expensive as treatment without infection [3]. The incidence of infection is influenced by factors such as the requirement for damage control and soft tissue contamination.

The useful parameters in diagnosing fracture-related infections have been recently defined, including a positive culture, elevated C-reactive protein level, purulent drainage, and clinical signs of local infection [2]. The gold standard in the diagnosis and handling of osteomyelitis is culture of bone, spinal canal fluid, and deep soft tissue samples collected in operation rooms in an aseptic manner and after removal of devitalized tissues, as cultures of soft tissues are more prone to contamination [4]. Accurate identification of the aetiological agent is one of the major challenges in the treatment of post-traumatic infections in orthopaedic surgery [5].

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In a percentage of cases, cultures can be negative despite intensive investigation, which then indicates the need for empirical therapy. Empirical therapy is also indicated in critically ill patients while waiting for the final results of culture tests. Considering these facts, it is important to elucidate the epidemiology of microorganisms associated with SSIs related to orthopedic trauma (SSI-ROT). We hypothesized that SSI-ROT would show high culture positivity for multi-resistant bacteria. The aim of this study was to evaluate the aetiology and susceptibility pattern of SSI-ROT in a Brazilian reference hospital for trauma.

Methods

This is a cross-sectional study of patients with SSI from January 2014 to December 2017 at Hospital Universitario Cajuru, Curitiba, Brazil. The hospital has 210 beds and is a reference center for trauma in the city with 1,752,000 habitants. This study was approved by the local ethics committee. The STROBE statement checklist was used in reporting this study.

We included patients older than 18 years who had orthopedic trauma requiring a surgical procedure and developed SSI-ROT within one year according to the Centers for Disease Control (CDC) criteria for SSI [6]. All patients had culture samples from the surgical site obtained from biopsy of bone or soft tissue. Swab cultures were excluded from this study. The biopsy samples from soft tissue or bone were immediately sent to the laboratory for inoculation in thioglycolate broth. Identification of microorganisms and susceptibility tests were performed using an automated method (VITEK 2®; Biomerieux, Durham, NC, USA). Carbapenem-resistant bacteria were tested for resistance genes by molecular methods, including bla_{NDM}, bla_{KPC}.

The clinical and epidemiological data of patients were collected, including age, sex, duration of admission and time to infection, type of trauma, site of biopsy (bone or soft tissue), and outcome. All data were obtained from electronic medical records.

Qualitative data were described as percentages and quantitative data as average or median values according to the distribution pattern. Risk factors associated with outcomes and microorganism classification (gram-positive or gram-negative) were calculated according to the variable and its distribution, such as *t*-Student, Mann-Whitney, chi-square, or Fisher's exact test. Values were considered statistically significant when the difference was $< 5\%$ ($p < 0.05$). Missing data were excluded from the study.

Results

Of 151 patients with SSI-ROT, 147 were included in the analysis. Four patients were excluded owing to missing clinical data for analysis. Of 147 patients, 110 were men (74.8%) and the mean age was 44.7 years (median 44 years, interquartile [IQ] 25–75% = 31–58 years). Trauma occurred in the lower limbs in 117 patients (79.6%). Most traumas were due to automotive accidents (44, 29.9%), followed by fall from a height (41, 27.9%), direct trauma (39, 26.5%), trampling (15, 10.2%), and gunshot wound (7, 4.8%). Of 147 patients who underwent surgery for trauma, 72 (49%) were classified as having a clean operative wound.

The mean time to SSI-ROT was 55.5 days after surgery (median 25 days, IQ 25–75% = 13–67 days), and the mean duration of hospitalization for SSI-ROT was 20.0 days (median 13 days, IQ 25–75% = 6–23 days). The in-hospital mortality rate after SSI-ROT was 5.4% (8 patients). Cultures were obtained from all patients, with 104 samples obtained from soft tissues and 43 samples from bone. The positivity was 93.2%. Among the isolates, 56.5% (77 patients) were gram-negative bacteria and 43.8% (60 patients) were gram-positive bacteria. Only ten patients had negative cultures (6.8%).

The most common isolate was *Staphylococcus aureus* (n = 50, 34%), followed by *Enterobacter* spp. (n = 22, 14.9%), *Pseudomonas aeruginosa* (n = 17, 11.6%), and *Serratia* spp. (n = 12, 8.2%) (Table 1). The susceptibility profile of the microorganisms is detailed in the Table 2. All gram-positive bacteria were susceptible to vancomycin, and 96% of *S. aureus* were susceptible to sulfamethoxazole-trimethoprim. Only 12% of *S. aureus* were methicillin-resistant (MRSA). Meropenem, polymyxin, and amikacin were the drugs with higher activity against gram-negative bacilli. *Acinetobacter baumannii* is resistant to carbapenem in 71%. Two isolates of *Klebsiella* were resistant to cefepime, one due to extended spectrum beta-lactamases (ESBL) and other by carbapenemase-producing mechanism. The molecular test identified bla_{KPC} as the gene associated with carbapenem resistance.

The time from trauma to infection was longer in patients with gram-positive bacteria (71.8 ± 15.9 days) than in those with gram-negative infections (42.5 ± 23.4 days, $p = 0.02$). The probability to recover from gram-positive infection was higher in patients with bone than soft tissue cultures (odds ratio [OR], 1.57; 95% confidence interval [CI], 1.04–2.36; $p = 0.012$). Other data were similar between gram-negative and gram-positive infections. Clinical variables were similar between fermenter and non-fermenter gram-negative bacilli. Among gram-positive bacteria, *S. aureus* presented a higher positivity in bone (OR, 1.29; 95% CI, 1.01–1.70; $p = 0.04$) and was more common after clean wound surgery (OR, 1.34; 95% CI, 1.06–1.68; $p = 0.011$).

Table 1 Clinical characteristics of orthopedic trauma-related surgical site infection according to bacterial aetiology. *SD* standard deviation

Microorganisms		*N*	%	Age (years ± SD)	Sex (male%)	Mortality (%)	Time trauma to infection (days ± SD)	Hospitalization (days ± SD)
Gram positive		60	43.8	44.0 ± 16.6	75	3	71.8 ± 76.1	15.9 ± 21.6
	Staphylococcus aureus	50	34.0	43.8 ± 15.7	78	4	66.4 ± 63.9	13.8 ± 21.0
	Enterococcus faecalis	4	2.7	42.7 ± 19.6	75	0	161.7 ± 165.7	27.0 ± 15.5
	Staphylococcus spp.	3	2.0	61.3 ± 15.9	33	0	49.6 ± 46.3	22.3 ± 31.0
	Streptococcus pyogenes	2	1.4	28.5 ± 33.2	50	0	95.0 ± 118.8	12.5 ± 06.3
	Bacillus cereus	1	0.7	36.0 ± 00.0	100	0	5.0 ± 00.0	63.0 ± 00.0
Gram negative		77	56.5	45.5 ± 17.5	72	6	42.5 ± 69.2	23.4 ± 31.8
	Enterobacter spp.	22	14.9	41.1 ± 16.2	91	0	58.3 ± 97.6	28.6 ± 54.0
	Pseudomonas aeruginosa	17	11.6	40.4 ± 12.9	88	17	39.1 ± 48.7	20.1 ± 14.3
	Serratia spp.	12	8.2	49.9 ± 16.4	50	0	44.8 ± 64.2	21.5 ± 14.9
	Escherichia coli	8	5.4	43.2 ± 21.2	50	25	25.6 ± 23.9	13.8 ± 3.8
	Acinetobacter baumannii	7	4.8	54.0 ± 21.0	71	14	15.0 ± 8.7	25.5 ± 17.4
	Proteus mirabilis	6	4.1	67.1 ± 15.5	67	33	29.3 ± 15.0	15.8 ± 17.1
	Klebsiella pneumoniae	2	1.4	32.0 ± 00.0	0	0	7.5 ± 3.5	60.0 ± 39.5
	Morganella morganii	2	1.4	47.0 ± 02.8	50	0	142.0 ± 192.3	17.5 ± 13.4
	Citrobacter freundii	1	0.7	28.0 ± 00.0	100	0	3.0 ± 00.0	37.0 ± 00.0
Negative culture		10	6.8	43.3 ± 20.9	90	10	57.5 ± 102.5	18.4 ± 10.8

Discussion

Patients with infection related to trauma require a higher number of surgical procedures, longer periods of internment, more subsequent hospitalizations, and longer periods of antibiotic therapy owing to their higher rate of complications. These characteristics justify the importance of isolating the aetiological agent of osteomyelitis through microbiological cultures in order to determine the ideal antibiotic therapy [7]. Furthermore, the susceptibility profile of bacteria facilitates the use of oral antibiotics for outpatient therapy, decreasing hospitalization costs and the complications associated with parenteral drugs [8]. In our study, >90% of cases classified as infection by the CDC criteria presented a positive culture. At our hospital, tests for culture positivity were made possible by our protocol of collecting several samples from SSI (at least three fragments of tissue). Swabs are not allowed because their disposal is not available in the surgery room. Every year, each surgical staff is trained by infectious disease specialists for the proper collection of cultures.

We identified a high incidence of gram-negative bacilli; however, *S. aureus* was the most common isolate. The high incidence of gram-negative bacilli is common in developing countries such as Brazil, mainly *Enterobacteriaceae*, followed by *P. aeruginosa* and *Acinetobacter baumannii* [9]. Anaerobes are not found in these materials because our laboratory does not use anaerobic procedures and these bacteria are uncommon aetiological agents. Anaerobes associated with SSI-ROT are commonly toxigenic and fast-growing bacteria causing severe infections with high mortality [10].

Determining the susceptibility profile of the microorganism is fundamental. The epidemiology of gram-negative bacilli in Brazil is associated with multi-resistant microorganisms, as previously described by our group. *Acinetobacter baumannii* is a common carbapenem-resistant bacterium associated with OXA-23-producing carbapenemase, a clonal profile common in the State of Parana [11]. This was the profile found in 70% of the *A. baumannii* isolates, but not for *P. aeruginosa* isolates, which were 100% susceptible to carbapenem, a different profile from *P. aeruginosa* associated with nosocomial infections [12]. This suggests that most infections occur after hospital discharge and can be related to poor wound care by the patient. The profile of *Klebsiella pneumoniae* was associated with carbapenemase-producing isolates, previously described in relation to an outbreak [13, 14]. However, methicillin-resistant *S. aureus* (MRSA) was the most common *S. aureus*, a profile not found in our study in which only 12% of isolates were MRSA. Most of the methicillin-susceptible *S. aureus* were susceptible to quinolones and sulfamethoxazole, which are antibiotic options for soft tissue infections. Furthermore, most *Staphylococcus* spp. were found exclusively on bone biopsy cultures, suggesting that most of these infections could be osteomyelitis, different from gram-negative bacilli infection. These oral options are important for the dehospitalization of patients with oral switch therapy, and are drugs available through the public health system in Brazil, increasing the compliance to antibiotic therapy of most patients [15].

Open fractures have a higher risk of leading to bone infection: 0–9%, 1–12%, and 9–20% for Gustilo grades I, II, and III

Table 2 Susceptibility profile of microorganisms identified in orthopedic trauma-related surgical site infection. *SMX/TMP* sulfamethoxazole/trimethoprim

	N	Amikacin	Ampicillin/ Sulbactam	Cefazolin	Ceftriaxona	Cefepime	Ceftazidime	Ciprofloxacin	Meropenem	Oxacillin	SMX/TMP	Vancomycin	Polimixina B
Gram negative													
Acinetobacter baumannii	7	71%	14%			57%	14%	43%	29%		29%		29%
Citrobacter freundii	1	100%	0%	0%	0%	100%	0%	100%	100%				100%
Enterobacter spp.	22	100%	5%	5%	9%	77%	9%	91%	100%		72%		100%
Escherichia coli	8	100%	14%	38%	71%	75%	75%	50%	100%		25%		100%
Klebsiella pneumoniae	2	50%	0%	50%	50%	0%	50%	50%	50%		0%		50%
Morganella morgannii	2	100%	0%	0%	0%	100%	0%	100%	100%		100%		100%
Proteus mirabilis	6	100%	67%	67%	83%	100%	83%	100%	100%		80%		100%
Pseudomonas aeruginosa	17	100%				81%	93%	100%	100%				100%
Serratia spp.	12	92%	0%	0%	40%	83%	55%	83%	100%		92%		
Gram positive													
Staphylococcus aureus	50		88%	88%		88%		88%	88%	86%	96%	100%	
Streptococcus spp.	2		100%	100%	100%	100%						100%	
Staphylococcus spp.	3		100%	100%				100%	100%	67%	100%	100%	
Enterococcus faecalis	4		100%									100%	

fractures, respectively. Patients > 60 years of age undergoing open reduction and internal fixation of their tibial plateau fractures present 15.7% of wound infection [16]. However, these rates can be lower (< 6%) in younger patients [17]. Age, male gender, diabetes mellitus, smoking, a lower extremity fracture and Gustilo grade III open fracture are risk factors for the development of infectious complications [18].

Current guidelines recommend gram-positive prophylaxis (first-generation cephalosporin) for grades I and II fractures, in order to cover the predominance of *S. aureus* in these infections. One limitation of our study was that it did not classify the severity of trauma. Moreover, we did not evaluate whether the appropriate prophylaxis was performed and did not analyze the detailed surgical procedures after infection. Nevertheless, it is important to exclude non-surgical treatable diseases mimicking SSI (i.e., pyoderma gangrenosum), whose treatment is essentially clinical in the first moment [19]. Although it seems highly important to focus on diagnosis of SSI-ROT, we need to improve the preventive measures to avoid this complication. Preventive measures are divided into preoperative, peri-operative, and post-operative phases, which are detailed in some guidelines [20].

In conclusion, this study shows that SSI-ROT can be associated with gram-negative bacilli in some hospitals. The susceptibility profile of microorganisms suggests that most infections occur after discharge, although *A. baumannii* and *Klebsiella* are commonly multi-resistant. Infections by *S. aureus* are commonly caused by methicillin-susceptible isolates, and this susceptibility to oral antibiotic options help in the dehospitalization of patients.

Compliance with ethical standards

This study was approved by the local ethics committee.

Conflict of interest Felipe Tuon is a CNPq (National Council for Scientific and Technological Development) researcher.

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