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Pre-operative Colonization by *Staphylococcus aureus and* Cephalosporin Non-susceptible Bacteria in Patients with Proximal Femoral Fractures*

Colonização pré-operatória por Staphylococcus aureus e por bactérias não suscetíveis à cefalosporina, em pacientes com fratura proximal do fêmur

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Abstract

Objective To estimate the frequency of *Staphylococcus aureus* and cephalosporin nonsusceptible bacteria colonization in patients with proximal femoral fracture during preoperative hospitalization.

Methods Prevalence and incidence assessment in 63 hospitalized patients over 1 year. The median time of pretreatment hospitalization was 12 days. Samples were collected from the nostrils, groin skin and anal mucosa during the pretreatment hospitalization and were tested by the disc-diffusion technique.

Results The hospital colonization incidence and the prevalence of positive results were 14.3 and 44.4% for *S. aureus*; 3.2 and 6.4% for meticillin-resistant *S. aureus*; 28.6 and 85.7% for meticillin-resistant coagulase-negative *Staphylococcus*; 28.6 and 61.9% for cefazolin nonsusceptible *Enterobacteriaceae* (KFNSE); and 20.6 and 28.6% for cefuroxime nonsusceptible *Enterobacteriaceae* (CXNSE). In addition, factors such as

Keywords
- carrier state
- drug resistance
- Enterobacteriaceae
- femoral fractures
- risk factors
- Staphylococcus

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to the duration of the pretreatment hospitalization period, being non-walker before fracture, antimicrobial use, American Society of Anesthesiologists (ASA) 4 surgical risk, and previous hospitalization, were related to an increase in the incidence of hospital acquisition and prevalence of colonization by the evaluated strains. The prevalence of colonization by KFNSE was three times higher than by CXNSE on admission, and twice as high at the time of fracture treatment.

Conclusion There was a high incidence of hospital colonization and prevalence of colonization by all strains studied, which may guide the indication of prophylactic measures for infection.

Resumo

Objetivo Estimar a frequência da colonização por *Staphylococcus aureus* e por bactérias não suscetíveis à cefalosporina em pacientes com fratura proximal do fêmur durante a internação pré-operatória.

Métodos Avaliação da prevalência e incidência em 63 pacientes hospitalizados ao longo de 1 ano. O tempo médio de internação pré-tratamento foi de 12 dias. As amostras foram coletadas das narinas, da pele da virilha e da mucosa anal durante a internação prévia ao tratamento e testadas pela técnica de disco-difusão.

Resultados A incidência da colonização hospitalar e a prevalência de resultados positivos foram de 14,3 e 44,4% para *S. aureus*; 3,2 e 6,4% para *S. aureus* resistente à meticilina; 28,6 e 85,7% para *Staphylococcus* coagulase-negativo resistente à meticilina; 28,6 e 61,9% para *Enterobacteriaceae* não suscetível à cefazolina (KFNSE); e 20,6 e 28,6% para *Enterobacteriaceae* não suscetível à cefuroxima (CXNSE). Além disso, a duração do período de internação pré-tratamento cirúrgico, ser não-deambulador antes da fratura, uso de antimicrobianos, risco cirúrgico IV pela American Society of Anesthesiologists (ASA) e internação anterior, estiveram relacionados a um aumento na incidência de aquisição hospitalar e prevalência de colonização pelas cepas avaliadas. A prevalência de colonização pela KFNSE foi três vezes maior do que pela CXNSE na admissão e duas vezes maior no momento do tratamento da fratura.

Conclusão Observou-se uma alta incidência da colonização hospitalar e prevalência da colonização por todas as cepas estudadas, o que pode orientar a indicação de medidas profiláticas contra a infecção.

Palavras-chave
- portador sadio
- resistência a medicamentos
- fraturas do fêmur
- Enterobacteriaceae
- fatores de risco
- Staphylococcus

Introduction

In low-income countries, the most common cause of healthcare-associated infections are surgical site infections (SSI), including orthopaedic procedures.[1] *Staphylococcus aureus* is the main etiological agent after proximal femoral fractures (PFF), followed by coagulase-negative *Staphylococcus* (CoNS) and *Enterobacteriaceae*.[2]

S. aureus stands out as the main risk factor for SSI. Therefore, decolonization of patients is one of the measures proposed to prevent this infection.[1,3]

Preoperative antibiotic prophylaxis is a proven measure to SSI prevention in patients with PFF.[4] Long-acting cephalosporins are the most indicated, with no consensus regarding the use of cefazolin or cefuroxime.[5] However, the effectiveness is related to susceptibility, and therapy adjustment may be necessary.[6]

Infections caused by meticillin-resistant *S. aureus* (MRSA) renders ineffective the treatment with β-lactams, and their spread in non-hospital environments, colonizing healthy individuals, have been described.[7] Also, the high of methicillin-resistant CoNS (MRCoNS)[8] may compromise the efficacy of cephalosporins as prophylactic antibiotics. Similarly, cephalosporins are unable to prevent the spread of *Enterobacteriaceae* that infect the surgical site and produce β-lactamases.[9,10]

The objective of the present study was to estimate the frequency of colonization by *Staphylococcus* and *Enterobacteriaceae* involved in the SSI and who are not susceptible to the antibiotics commonly used in intraoperative prophylaxis in patients with PFF, as well as to estimate the impact of prolonged preoperative hospitalization and other risk factors.

Methods

All patients hospitalized consecutively between April 2015 and March 2016 at a military hospital in Rio de Janeiro for treatment of PFF were evaluated. The inclusion criteria were that the fractures had to have been caused by low energy

trauma. The exclusion criteria were patients hospitalized for treatment of complications of a previously treated femur fracture. Of the 66 hospitalized patients who met the inclusion criteria, 3 were excluded because they did not agree to participate.

Screening samples were collected using a swab in the anterior region of the nostrils, in the skin of the groin on the fracture side, and in the anal mucosa and were seeded in Mannitol Salt and MacConkey Agar, respectively. The samples were collected at the time of admission (within 72 hours; sample 1), between 72 hours and 7 days of hospitalization (sample 2), and once a week after the 1st week (samples 3 to 9), until the date of femoral osteosynthesis, definition by nonsurgical treatment, or occurrence of death before treatment.

Bacterial identification was performed by Microflex/Bruker – Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry.

The antibiotic susceptibility was obtained by disk-diffusion, following the Clinical & Laboratory Standards Institute (CLSI).[11] Cefoxitin was administered for CoNS and for MRSA, and ciprofloxacin, erythromycin, clindamycin, sulfamethoxazole/trimethoprim, linezolid, and rifampicin were evaluated. For *Enterobacteriaceae*, cefazolin and cefuroxime were administered. Intermediate and resistant results were classified as "nonsusceptible ".

All MRSA isolates were subjected to polymerase chain reaction (PCR) analysis for SCC*mec* typing,[12] *lukS-PV* gene related to the production of Panton-Valentine leucocidin (PVL)[13] and *qacA/B* genes,[14] related to chlorhexidine resistance.

After the first positive result for nonsusceptible bacteria, the patients were considered colonized. Colonization in patients whose admission screening was negative for antibiotic resistant bacteria was classified as hospital colonization. The analysis of hospital colonization incidence was performed from the second sample, considering the patients with negative results in all the previous samples.

The risk factors for colonization by antibiotic resistant bacteria were adapted from the risk factors for MRSA colonization[15] (►**Table 1**). The statistical analysis of the relationship between the incidence of hospital colonization and the median length of hospital stay before fracture treatment or death before treatment was performed using the Mann-Whitney test for two samples. The statistical analysis of the relationship between the risk of antibiotic nonsusceptible bacteria colonization and the incidence of hospital colonization, the prevalence of colonization in the admission screening or in any sample prior to femoral fracture treatment and the incidence of cefazolin or cefuroxime nonsusceptible *Enterobacteriaceae* were performed using the Fisher exact test. In both cases, the null hypothesis was rejected for p-values > 0.05. All statistical analyses were performed using the Epi Info 7.1.5.2 software (Atlanta, Georgia, United States).

All patients were followed-up for a minimum of 1 year (except in cases of death), in outpatient consultations and by telephone contacts.

Table 1 Prevalence of risk factors for colonization by bacteria nonsusceptible to antibiotics in the studied population at the time of hospitalization (hospital admission) and at the femoral fracture treatment or death prior to treatment (treatment date)

	Hospital admission	Treatment date
Risk factor		
Nonwalkers[a]	11 (17.5%)	11 (17.5%)
Diabetes mellitus	19 (30.2%)	19 (30.2%)
Hospitalization prior to fracture (12 months)	13 (20.6%)	13 (20.6%)
Use of antibiotics[b]	20 (31.7%)	37 (58.73%)
Institutionalized[c]	13 (20.6%)	13 (20.6%)
Bedsores[d]	7 (11.1%)	13 (20.6%)
ASA 4[e]	20 (31.75%)	20 (31.75%)
Bladder catheterization[f]	0	13 (20.63%)
ICU stay[f]	0	8 (12.7%)

Abbreviations: ASA, American Society of Anesthesiologists; ICU, intensive care unit.
[a]Patients who moved only with the aid of a wheelchair or those who were bedridden prior to the occurrence of the fracture.
[b]Use of antibiotic before hospitalization (6 months), or during hospitalization and before fracture treatment.
[c]Patients hospitalized or residing in nursing homes, home hospitalization, or in hemodialysis treatment.
[d]Presence of bedsores at hospital admission or acquired during hospitalization and before fracture treatment.
[e]ASA, American Society of Anesthesiologists Physical Status score.
[f]Bladder catheterization or ICU stay occurring during hospitalization and before fracture.

Ethical Aspects

The research protocol was approved by a local ethics committee and all the included patients or their legal guardians signed a free and informed consent form (CAAE: 39070314.0.0000.5256). The clinical data were obtained by interview and by medical-hospital records.

Results

The mean age of the patients was 79 ± 10 years old, and 79.4% were female. Trochanteric fractures occurred in 28 (44.4%) patients, 26 (41.3%) patients had fractures in the femoral neck, 7 (11.1%) had subtrochanteric fractures, and 2 patients (3.2%) had an isolated fracture of the greater trochanter. The prevalence of risk factors for colonization by bacteria nonsusceptible to antibiotics in the studied population, at the time of hospital admission and at the date of treatment of the fracture, is shown in ►**Table 1**.

Fracture treatment was performed with nailing in 22 (34.9%) patients, with dynamic hip screw and plate in 10 (15.9%), with partial hip arthroplasty in 10 (15.9%), with total hip arthroplasty in 7 (11.1%), with dynamic condylar screw

and plate in 2 (3.2%), and with resection arthroplasty in 1 (1.6%). Cefazolin was applied during anesthetic induction in all operated cases. The mean surgery duration was 103.4 ± 39.5 minutes. Five patients (7.9%) were not submitted to surgical treatment because of the high surgical risk due to their clinical conditions, 2 (3.2%) due to the fracture pattern, and 4 patients (6.3%) died before the possibility of surgical treatment.

The median length of hospital stay before fracture treatment or death before treatment was 12 days (interquartile range [IQR] = 8–19). Of the 63 patients evaluated, only 1 received treatment for the fracture in < 3 days, 15 received treatment in between 3 and 7 days, 24 in between 8 and 14 days, and 23 after 14 days of hospitalization.

The sample 1 was collected in all patients. The sample 2 was collected in 62 patients, sample 3 in 50, sample 4 in 22, sample 5 in 8, sample 6 in 5, sample 7 in 2, and samples 8 and 9 in 1 patient.

From the nasal and groin samples, 637 *Staphylococcus* isolates were identified, as well as 377 isolates of *Enterobacteriaceae* obtained from the anal samples. The prevalence of positive results in the admission screening sample was 30.2% for *S. aureus*, 3.2% for MRSA, 57.1% for MRCoNS, 33.3% for cefazolin non-susceptible *Enterobacteriaceae* (KFNSE), and 7.9% for cefuroxime non-susceptible *Enterobacteriaceae* (CXNSE).

The incidence of hospital colonization and the prevalence of positive results in any sample before the treatment or death before treatment were 14.3 and 44.4% for *S. aureus*; 3.2 and 6.4% for MRSA; 28.6 and 85.7% for MRCoNS; 28.6 and 61.9% for KFNSE; and 20.6 and 28.6% for CXNSE, respectively.

During the follow-up period, three surgical site infections were diagnosed, one caused by MRSA, one by enterobacteria, and one by MRCoNS (*S. epidermidis* and *S. haemolythicus*).

Staphylococcus Aureus

A total of 89 *S. aureus* isolates were identified, and the most frequent identification site was the nostril (77.5%). There was a progressive increase in the incidence of hospital colonization by *S. aureus* (►**Fig. 1**). In the period between 14 and 21 days of hospitalization, 18% of the patients who were still hospitalized were colonized. In this same period, 50% of the patients who remained hospitalized presented some positive sample for *S. aureus* (►**Fig. 1**).

Analyzing the group of patients with negative results for *S. aureus* in the admission screening (44 patients), we observed that the median length of hospital stay before fracture treatment or death before treatment in patients who acquired hospital colonization was 17 days (IQR = 15–31) days, versus 11 days (IQR= 9–18) in those who did not acquire it ($p = 0.06$).

Two patients presented positive results in the admission screening (3.2%), both only in the groin swab. One of them had superficial postoperative infection caused also by MRSA, diagnosed by culture of secretion obtained by surgical site puncture, which was treated with antibiotics.

Two other patients had positive samples for MRSA, with a negative admission screening. All MRSAs tested were

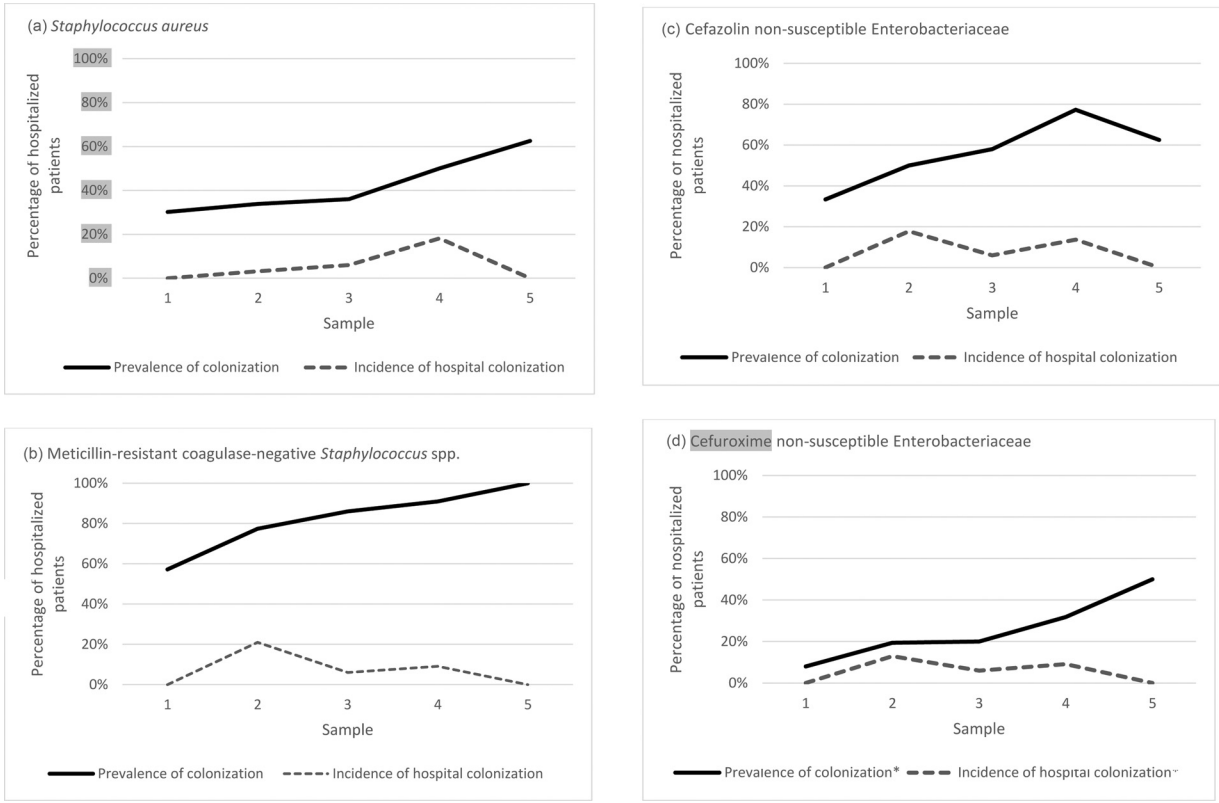

Fig. 1 Prevalence of colonized patients and incidence of hospital colonization for each group of bacteria studied, from the admission screening sample (1st) to the 5th screening sample.

positive for SCC*mec*-IV, negative for *lukS-PV* and *qacA/B* genes and were susceptible to sulfamethoxazole/trimethoprim.

Coagulase-Negative Staphylococci

About 43% of CoNS were only identified up to the genus level. *S. haemolyticus* (29.6%) and *S. epidermidis* (20.6%) were the most observed. In the MRCoNS, the most isolated was *S. haemolyticus* (43.2%).

The peak hospital colonization incidence by MRCoNS occurred between the 4th and 7th days of hospitalization, reaching 21% of hospitalized patients at that time, with a prevalence of 77.4% of patients already colonized by MRCoNS (►**Fig. 1**).

Analyzing the patients with negative results for MRCoNS in the admission screening (27 patients), we observed that the median length of hospital stay before fracture treatment or death before treatment in patients who acquired hospital colonization was 17 days (IQR= 12–22) versus 9 days (IQR = 8–12) in those who did not acquire it ($p < 0.01$).

One patient with 2 positive screening samples (1st and 2nd) for MRCoNS had postoperative osteomyelitis caused by *S. haemolythicus* and *S. epidermidis*, diagnosed by culture of bone obtained during the removal of the total hip prosthesis.

Enterobacteriaceae

Of the 377 *Enterobacteriaceae*, 100 (26.5%) presented a non-susceptible result to cefazolin (KFNSE) and 30 (8%) to cefuroxime (CXNSE) ($p < 0.01$). *Escherichia coli* (62.1%) was the most isolated, followed by *Proteus mirabilis* (17.2%) and *Klebsiella pneumoniae* (5.8%).

The peak hospital colonization incidence by KFNSE and CXNSE occurred between the 4th and 7th day of hospitalization, after which 50% of patients were already colonized by KFNSE and 18% by CXNSE (►**Fig. 1**).

The median length of hospital stay before fracture treatment or death before treatment in patients who acquired hospital colonization by KFNSE was 17 days (IQR= 14–25) versus 9 days (IQR= 7–12) in those who did not acquire it ($p < 0.01$). In patients who acquired hospital colonization by CXNSE, the median length of hospital stay before fracture treatment or death before treatment was 17 days (IQR = 10–22), versus 12 days (IQR= 9–17) in those who did not acquire it ($p = 0.34$).

One patient had a postoperative infection caused by *Enterobacteriaceae* intrinsically resistant to cephalosporins diagnosed by culture of bone obtained during surgical debridement and confirmed by another culture of bone obtained during the removal of hemiarthroplasty. The three preoperative screening samples from this patient were negative for KFNSE and CXNSE.

Risk Factors

The prevalence ratio of colonization in the admission or in any screening before the fracture treatment or death before treatment and the risk ratio of hospital colonization, according to the presence of one of the risk factors for colonization by antibiotic non-susceptible bacteria, is shown in ►**Tables 2** and **3**.

Discussion

The hospital in which the present study was conducted faced several difficulties regarding the large number of hospitalized patients and the availability of operating rooms and of medical staff, increasing the hospitalization period before the femoral fracture treatment. Although these are not the ideal conditions for the treatment of patients with PFF, they are not uncommon in Brazilian public hospitals. Thus, the analysis of the present data can allow the assembly of strategies to minimize postoperative infections in similar situations.

In the present study, ~ 30% of the patients presented *S. aureus* in the admission screening, which is in line with the literature data.[16] In the hospitalization period before fracture treatment, another 14% of the patients were colonized by *S. aureus*. Considering the importance of preoperative colonization in the SSI,[1] the high rate of hospital colonization observed suggests the need to implement control protocols, especially in patients with related risk factors, which in our series were non-walkers, those who used antimicrobial medication, who were institutionalized, and who were hospitalized in the intensive care unit (ICU).

The small number of patients who had MRSA colonization does not allow us to analyze risk factors or dissemination patterns. However, we highlight that all MRSA were SCC*mec*-IV and susceptible to sulfamethoxazole/trimethoprim, suggesting CA-MRSA strains.[17] Besides, the predominance of positive cultures from the groin samples show the importance of multiple site search in MRSA screening.[18] Still, the relationship between non-nasal and nonmucous colonization and the increase in the SSI rate is still under discussion.[19,20]

More than half of the patients presented positive for MRCoNS at admission, while at the time of femoral fracture treatment, ~ 86% were colonized, with a peak incidence of hospital colonization occurring in the 1st week. The use of antibiotics during hospitalization or in the previous 6 months and surgical risk classified as ASA 4 were related to a higher chance of colonization by MRCoNS. We theorize that these relationships are probably due to the increased need for care and manipulation of these patients.

Hospital colonization by MRCoNS is important in the dissemination of resistance genes.[3,21] In addition, these strains show special importance in SSI after PFF treatment.[2,22,23] Considering the high incidence of colonization at admission and the rapid acquisition in patients not previously colonized (►**Fig. 1B**), when a high MRCoNS SSI rate is observed, the addition of glycopeptides in the preoperative prophylaxis can be useful.[6] Although this association may increase the incidence of renal complications[24] and cause dissemination of resistance, it is effective in reducing SSI.[6]

The prevalence of patients colonized at admission by KFNSE was three times higher than those colonized by CXNSE, and twice as high at the time of fracture treatment. None of the risk factors surveyed showed statistical

Table 2 Prevalence ratio of colonization in the admission screening sample (PR adm) and prevalence ratio of colonization in any screening sample before the fracture treatment or death before treatment (PR ttmt) according to the presence of one of the risk factors for colonization by bacteria nonsusceptible to antibiotics [95% CI] (*p*-value)

Risk factor	*S. aureus*		MRCoNS		KFNSE		CXNSE	
	PR adm	PR ttmt	PR adm	PR ttmt	PR adm	PR ttmt	PR adm	PR ttmt
Nonwalkers[a]	1.68 [0.77–3.7] (0.19)	1.89 [1.15–3.11] (0.04)	1.14 [0.69–1.9] (0.45)	0.82 [0.57–1.2] (0.18)	0.79 [0.28–2.21] (0.46)	0.86 [0.48–1.53] (0.41)	0 (0.37)	0.95 [0.33–2.72] (0.62)
Diabetes mellitus	1.07 [0.48–2.4] (0.55)	1.09 [0.61–1.97] (0.49)	1.16 [0.74–1.8] (0.36)	0.98 [0.78–1.22] (0.65)	0.93 [0.43–2.02] (0.54)	0.91 [0.59–1.42] (0.44)	0.58 [0.07–4.84] (0.52)	1.47 [0.68–3.21] (0.25)
Hospitalization prior to fracture (12 months)	0.72 [0.25–2.11] (0.40)	0.84 [0.39–1.77] (0.43)	1.28 [0.82–2] (0.25)	0.98 [0.76–1.27] (0.60)	0.64 [0.22–1.85] (0.30)	0.99 [0.61–1.61] (0.61)	0 (0.30)	1.92 [0.89–4.14] (0.11)
Use of antibiotics[b]	1.25 [0.58–2.7] (0.40)	1.48 [0.8–2.74] (0.14)	1.54 [1.03–2.28] (0.04)	1.29 [1.01–1.66] (0.02)	0.51 [0.2–1.31] (0.10)	0.67 [0.46–0.97] (0.03)	0.54 [0.06–4.51] (0.49)	0.56 [0.26–1.23] (0.12)
Institutionalized[c]	2.53 [1.24–5.17] (0.06)	2.06 [1.28–3.33] (0.06)	0.56 [0.18–1.77] (0.21)	0.76 [0.43–1.35] (0.20)	0.47 [0.08–2.94] (0.34)	0.79 [0.35–1.81] (0.42)	0 (0.60)	1.90 [0.76–4.72] (0.22)
Bedsores[d]	0.94 [0.27–3.24] (0.65)	1.05 [0.54–2.04] (0.57)	1.60 [1.08–2.36] (0.11)	1.22 [1.07–1.39] (0.11)	0.84 [0.25–2.87] (0.57)	0.57 [0.28–1.15] (0.05)	0 (0.54)	0.48 [0.13–1.83] (0.20)
ASA 4[e]	1.25 [0.58–2.7] (0.39)	1.39 [0.81–2.39] (0.19)	1.22 [0.79–1.86] (0.28)	1.26 [1.08–1.47] (0.02)	0.67 [0.29–1.58] (0.25)	0.96 [0.62–1.46] (0.52)	1.43 [0.26–7.91] (0.51)	2.15 [1.01–4.58] (0.05)
Bladder catheterization[f]	–	0.84 [0.39–1.77] (0.43)	–	1.22 [1.07–1.39] (0.11)	–	0.84 [0.49–1.45] (0.36)	–	1.1 [0.43–2.78] (0.55)
ICU stay[f]	–	1.15 [0.54–2.44] (0.51)	–	1.20 [1.06–1.34] (0.27)	–	1.01 [0.57–1.8] (0.64)	–	1.96 [0.86–4.49] (0.15)

Abbreviations: ASA, American Society of Anesthesiologists; ICU, intensive care unit.
[a]Patients who moved only with the aid of a wheelchair or those who were bedridden prior to the occurrence of the fracture.
[b]Use of antibiotic before hospitalization (6 months), or during hospitalization and before fracture treatment.
[c]Patients hospitalized or residing in nursing homes, home hospitalization, or in hemodialysis treatment.
[d]Presence of bedsores at hospital admission or acquired during hospitalization and before fracture treatment.
[e]ASA, American Society of Anesthesiologists Physical Status score.
[f]Bladder catheterization or ICU stay occurring during hospitalization and before fracture.

Table 3 Risk ratio of hospital colonization (RR hc), according to the presence of one of the risk factors for colonization by bacteria nonsusceptible to antibiotics [95% CI] (*p*-value)

Risk factor	*S. aureus*	MRCoNS	KFNSE	CXNSE
Nonwalkers[a]	3.17 [1.07–9.38] (0.09)	0.34 [0.06–1.88] (0.09)	0.85 [0.32–2.25] (0.53)	1.28 [0.42–3.89] (0.47)
Diabetes mellitus	1.19 [0.35–4.06] (0.54)	0.82 [0.40–1.65] (0.43)	0.86 [0.39–1.90] (0.48)	1.91 [0.75–4.87] (0.15)
Hospitalization prior to fracture (12 months)	0.97 [0.24–3.96] (0.67)	0.72 [0.26–1.99] (0.41)	1.23 [0.58–2.6] (0.43)	2.97 [1.21–7.29] (0.03)
Use of antibiotics[b]	5.54 [0.76–40.52] (0.04)	1.56 [0.91–2.67] (0.11)	0.62 [0.32–1.22] (0.16)	0.56 [0.22–1.46] (0.19)
Institutionalized[c]	2.62 [0.57–12] (0.37)	0.72 [0.26–1.99] (0.41)	0.92 [0.3–2.88] (0.64)	2.60 [0.98–6.89] (0.12)
Bedsores[d]	1.70 [0.52–5.61] (0.33)	1.56 [1.16–2.1] (0.44)	0.40 [0.11–1.45] (0.09)	0.32 [0.05–2.22] (0.18)
ASA 4[e]	1.91 [0.61–5.99] (0.24)	1.82 [1.22–2.7] (0.03)	1.15 [0.57–2.32] (0.48)	2.59 [1.01–6.62] (0.05)
Bladder catheterization[f]	1.50 [0.45–5.01] (0.39)	1.69 [1.2–2.4] (0.11)	0.53 [0.15–1.86] (0.23)	1.54 [0.56–4.2] (0.32)
ICU stay[f]	2.64 [0.86–8.15] (0.14)	1.60 [1.17–2.18] (0.28)	0.92 [0.3–2.88] (0.64)	2.19 [0.79–6.06] (0.18)

Abbreviations: ASA, American Society of Anesthesiologists; ICU, intensive care unit.
[a]Patients who moved only with the aid of a wheelchair or those who were bedridden prior to the occurrence of the fracture.
[b]Use of antibiotic before hospitalization (6 months), or during hospitalization and before fracture treatment.
[c]Patients hospitalized or residing in nursing homes, home hospitalization, or in hemodialysis treatment.
[d]Presence of bedsores at hospital admission or acquired during hospitalization and before fracture treatment.
[e]ASA, American Society of Anesthesiologists Physical Status score.
[f]Bladder catheterization or ICU stay occurring during hospitalization and before fracture.

correlation with the prevalence of colonization at admission, while having the surgical risk classified as ASA 4 was related to a higher risk of CXNSE colonization at the time of the fracture treatment, as well as to the incidence of hospital colonization. Like the MRCoNS colonization, the peak of colonization by KFNSE and CXNSE was in the 1st week.

Hand washing and other precautions have less impact on preventing the spread of resistant Enterobacteriaceae, increasing the importance of programs to rationalize the use of antibiotics when compared to Gram-positive..[25] The use of cotrimoxazole in perioperative prophylaxis to prevent SSI by MRSA in femoral fracture surgery has led to an increase in infections caused by Gram-negative.[26]

According to the observed data, the choice of cefuroxime for preoperative prophylaxis may increase the coverage against *Enterobacteriaceae*. Although colonization by CXNSE suggests the use of other antibiotics as prophylaxis,[26] the risk of dissemination of other resistance mechanisms makes additional studies indispensable.[27,28]

Some risk factors for colonization by resistant bacteria showed a relationship with the reduction in colonization by cephalosporin-resistant *Enterobacteriaceae*, notably antibiotic use prior to fracture treatment and the presence of bedsores. Although we did not perform this evaluation, we theorize that this is due to intestinal dysbiosis and to the proliferation of noncommensal microorganisms.[29]

Conclusion

In the present study, we highlight the incidence of hospital colonization and the prevalence of colonization by *S. aureus*, MRCoNS and *Enterobacteriaceae* not susceptible to cefazolin, directly related to the duration of the preoperative hospitalization. These data emphasize the importance of reducing the preoperative hospitalization in patients with PFF, and when this is not possible, of implementing prophylactic measures such as decolonization, isolation, and adjustments in antibiotic prophylaxis.

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Conflict of Interests
The authors have no conflict of interests to declare.

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