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Outcome of orthopedic implant infections due to different staphylococci☆

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ABSTRACT

Background: Comparisons of different staphylococci in orthopedic implant infections have rarely been reported. In this study we assessed total joint arthroplasty infections and other orthopedic implant infections due to methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), and coagulase-negative staphylococci (CoNS).
Methods: This was a retrospective study performed at the Geneva University Hospitals for the period January 1996 to June 2008.
Results: There were 44 infections due to MRSA, 58 due to MSSA, and 61 due to CoNS. Overall cure was achieved in 57% (25/44) of MRSA infections, 72% (42/58) of MSSA infections, and 82% (50/61) of CoNS infections, after a minimum follow-up of 1 year. In the subgroup of arthroplasty infections only, cure was achieved in 39% (7/18) of MRSA, 60% (15/25) of MSSA, and 77% (30/39) of CoNS episodes. In multivariate analysis, arthroplasty (odds ratio (OR) 0.2, 95% confidence interval (95% CI) 0.1–0.6) and MRSA infections (OR 0.3, 95% CI 0.1–0.9) were inversely associated with overall cure for all implants. CoNS infection (OR 3.0, 95% CI 1.2–8.0) and the insertion of a new implant (OR 4.5, 95% CI 1.6–13.1) were associated with higher cure results. Methicillin resistance, immunosuppression, sex, age, duration of antibiotic therapy, one-stage revision, rifampin use, and total number of surgical interventions did not influence cure. MRSA-infected patients had more post-infection sequelae than patients with MSSA or CoNS (Chi-square test 13/44 vs. 93/119, OR 3.4, 95% CI 1.3–8.9, $p = 0.004$).
Conclusions: In orthopedic implant infections, *S. aureus* is more virulent than CoNS. MRSA has the worst outcome and CoNS the best.

1. Introduction

Staphylococci comprise up to two-thirds of all pathogens in orthopedic implant infections;[1,2] these infections are difficult to treat because of the ability of the organisms to form small-colony variants[3] and to grow into biofilms.[4] Additionally, foreign material itself inhibits neutrophil antibacterial activity.[5,6]

Methicillin-resistant staphylococcal species may adversely influence treatment outcome, as has previously been shown for staphylococcal bacteraemia[7,8] and for implant infections.[9,10] Comparative studies regarding the epidemiology and outcomes of localized orthopedic implant-related infections stratified by staphylococci or type of orthopedic implant are rare. Clinical experience suggests that methicillin-resistant infections might have more recurrences and more sequelae than methicillin-sensitive infections.

The objective of this study was to assess the clinical features and outcome in patients with orthopedic implant infections (total joint arthroplasties and fracture fixation devices) due to the three main groups of staphylococci: methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-sensitive *Staphylococcus aureus* (MSSA), and coagulase-negative staphylococci (CoNS). In a second step, we assessed risk factors for recurrent disease for implant infections overall, and stratified by total joint arthroplasties and fracture fixation devices separately.

2. Methods

2.1. Setting

The Geneva University Hospitals form a 2200-bed tertiary hospital with a high MRSA endemicity (30% of all clinical *S. aureus* isolates);[11] sequence type 228 is the predominant MRSA strain.

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The Orthopedic Surgical Service has 119 acute care beds and a dedicated infectious diseases specialist; 5374 surgical procedures were performed here in 2007. This service has run a cohort for total joint arthroplasties since 1996.[12]

2.2. Data collection

Databases from the Laboratory of Bacteriology, the Geneva Arthroplasty Registry,[12] the Septic Orthopedic Cohort, and the hospital's administrative coding were retrospectively searched for staphylococcal infections related to orthopedic implants for the period January 1996 to June 2008. Sixty variables for each episode were assessed with information pertaining to demographic characteristics, microbiology, treatment modalities, and outcomes. A surgeon and a physician independently recorded each variable on a spreadsheet for analysis. In the case of discordance, a consensus was obtained by involving a third co-author. Patients were followed-up to 30 September 2009. A minimum follow-up time of 1 year after the end of treatment was required for study inclusion.

2.3. Microbiological procedures

The microbiological procedures were unchanged during the study period and based on the Clinical and Laboratory Standards Institute (CLSI) guidelines.[13] In order to enhance specificity, only cultures that were grown on plates were considered. Staphylococci were characterized to the species level by slidex agglutination (Pastorex®, Bio-Rad), DNAse tests (homemade), the ID32 Staphylococcus Gallery (bioMérieux, Marcy l'Etoile, France), and/or the Vitek ID system. The staphylococci were interpreted as the same if surrogate markers such as species, staphylococcal chromosomal cassettes (SCC), presence of exfoliatins A and B, Panton–Valentine leukocidin, toxic shock syndrome toxins and *agr* gene regulator genes, and antibiotic susceptibility patterns were identical. No typing was performed. Since clinical specimens had not been stored, no retrospective analyses of minimal inhibitory concentrations, e.g., for vancomycin against MRSA, could be performed.

2.4. Definitions

Inclusion criteria were: the presence of an implant; local signs of infection such as heat, erythema, pus, or functional impairment; a medical report; a targeted antibiotic treatment; and the presence of the same *Staphylococcus sp* in more than one intraoperative sample.

Exclusion criteria were: antibiotic medication in the preceding four weeks (to avoid a potential bias by 'selection' of methicillin-resistant strains in microbiological samplings that might have been pre-treated with beta-lactam antibiotics, thus hiding other susceptible pathogens); an active follow-up shorter than 3 months after the end of treatment; and infections occurring after spinal surgery. Co-pathogens were accepted only if the *Staphylococcus spp* outnumbered them by at least three-fold in intraoperative microbiological specimens.

Since infections of total joint arthroplasties might be different from those following other orthopedic implant procedures, all analyses were repeated for arthroplasty infections and fracture fixation devices separately. Arthroplasties were defined as total hip, total knee, and total ankle prostheses. The fracture fixation device group encompassed intramedullary nails, plates/screws, screws alone, external fixation, wires, and pins.

Cure was defined as complete clinical and microbiological resolution of the former infection after a minimum follow-up time of 1 year following the end of treatment. This follow-up was active, e.g., regular postoperative controls. There was also a passive follow-up by analysis of patient medical records during the last visit to the Geneva University Hospitals, independent of orthopedic reasons. This passive follow-up had no upper time limit, unless there was general censoring on 30 September 2009, the date of closure for data sampling. Recurrence of infection meant new clinical signs of infection with the same microorganism at least 2 weeks after the end of treatment for the first episode. A pseudarthrosis without proof of the formerly infecting *Staphylococcus spp* according to study definitions was interpreted as sequelae, but not as recurrent infection. The duration and modalities of antibiotic treatment concomitant to surgery were undertaken according to expert opinion.[5]

2.5. Statistical analyses

Comparisons of the groups of staphylococcal infections were performed using the Pearson Chi-square test, Fisher's exact test, or the Wilcoxon rank sum test, as appropriate. Logistic regression analyses determined associations with cure. Independent variables with a p-value of ≤ 0.2 in univariate analysis were added stepwise in the multivariate analysis. The following variables were introduced into the final model independently of their association in univariate analysis: sex, age, duration of antibiotic treatment, number of surgical interventions, and methicillin resistance. All variables were checked for confounding, collinearity, and interaction; the latter by Mantel–Haenszel estimates. p-Values of ≤ 0.05 (two-tailed) were considered significant. STATA software (v. 9.0; STATA Corp., USA) was used.

3. Results

3.1. Patient populations

A total of 205 episodes of staphylococcal orthopedic implant infection were retrieved. Of these, 42 were excluded due to: follow-up shorter than 3 months or lost to follow-up ($n = 32$); substantial co-infection with *Pseudomonas aeruginosa* ($n = 2$), *Enterobacter cloacae* ($n = 2$), *Escherichia coli* ($n = 1$), *Propionibacterium acnes* and *Streptococcus constellatus* ($n = 1$), and *Enterococcus faecalis* ($n = 1$); infection of spondylodesis material ($n = 2$). One schizophrenic patient with MSSA infection was excluded because of very poor compliance.

In the final evaluation, a total of 163 primary surgical site infections in 157 patients (73 females; median age 69 years, interquartile range (IQR) 50–80 years) underwent further analysis. The median follow-up time was 2.3 years (IQR 1.1–4.3 years).

3.2. Implants

The infected implants in the arthroplasty group included total hip ($n = 52$), total knee ($n = 29$), and total ankle ($n = 1$). In the fracture fixation devices group, the infected implants included plates/screws ($n = 40$), intramedullary nails ($n = 16$), external fixation ($n = 13$), hip screws ($n = 4$), other screws ($n = 4$), patellar cerclage wire ($n = 3$), and pins ($n = 1$).

3.3. Staphylococci

There were 44 episodes due to MRSA, 58 due to MSSA, and 61 due to CoNS. Community-acquired MRSA was not encountered.[14] The species of CoNS were *Staphylococcus epidermidis* ($n = 36$), *Staphylococcus lugdunensis* ($n = 3$), *Staphylococcus capitis* ($n = 2$), *Staphylococcus hominis* ($n = 2$), and one episode each of *Staphylococcus intermedius*, *Staphylococcus simulans*, *Staphylococcus xylosus* and *Staphylococcus schleiferi*. The CoNS were not further identified to the species level for 14 episodes.

Table 1
Characteristics and comparisons between three groups of staphylococcal orthopedic implant-associated infections

All types of implant infections ($N = 163$)	MRSA ($n = 44$)	Comparison MRSA vs. MSSA p-Value[a]	MSSA ($n = 58$)	Comparison MSSA vs. CoNS p-Value[a]	CoNS ($n = 61$)
Patient population					
Female sex	23 (52%)		23 (40%)		29 (48%)
Median age	74 years	0.003[a]	60 years	0.001[a]	71 years
Chronic immunosuppression[b]	11 (25%)		14 (24%)		17 (28%)
Infection					
Median time delay between previous implantation and infection onset	21 days	0.001[a]	125 days		129 days
Bacteremia	9 (20%)		19 (33%)	0.000[a]	0 (0%)
Treatment					
Median duration of antibiotics	10 weeks		6 weeks		9 weeks
Use of rifampin	20 (45%)		32 (55%)		39 (64%)
Median No. of surgical interventions	2		2		1
Removal of infected implant	29 (66%)		46 (79%)		46 (75%)
Re-implantation of a new implant	9 (20%)		13 (22%)	0.017[a]	27 (44%)
Outcomes					
Recurrence of infection	5 (11%)		9 (16%)		6 (10%)
Cure	25 (57%)		42 (72%)		50 (82%)
Median length of hospital stay	57 days	0.026[a]	29 days		39 days

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; CoNS, coagulase-negative staphylococci.
Group comparisons were performed with the Wilcoxon rank sum test, Fisher's exact test, or the Pearson Chi-square test, as appropriate.
[a] Only statistically significant p-values of ≤ 0.05 (two-tailed) are displayed.
[b] Diabetes mellitus, transplantation, chronic alcoholism, neoplasia, Child's class C cirrhosis, AIDS, steroid medication. Polytrauma did not count as chronic immunosuppression.

Eighty-seven staphylococci (53%; MRSA and CoNS) were methicillin-resistant. Three staphylococci (all CoNS) were resistant to rifampin. Five MSSA patients, four MRSA patients, and two patients with CoNS were co-infected with other pathogens, with the *Staphylococcus spp* outnumbering these by at least three-fold in microbiological specimens; pathogens included *Klebsiella pneumoniae* ($n = 2$), *Proteus mirabilis* ($n = 2$), CoNS ($n = 2$), and one case each of *Enterococcus faecalis*, *Streptococcus pyogenes*, MRSA, *Streptococcus constellatus*, and *Enterobacter cloacae*.

3.4. Clinical presentation of all implant infections

Table 1 summarizes the differences in clinical presentation among the three groups of staphylococci for all types of implant infections. Statistically significant differences included the following: MRSA infections had shorter incubation times; patients with MSSA infections were younger than patients with methicillin-resistant staphylococci; and bacteremia was witnessed only in *S. aureus* (MRSA and MSSA), but not in CoNS infections.

3.5. Treatment

All patients received systemic antibiotic therapy directed towards the causative pathogen for a median duration of 7 weeks (IQR 6–12 weeks). There were no significant differences in duration of treatment between the staphylococcal groups (Table 1) or between arthroplasty and fracture fixation device infections (8 vs. 7 weeks, $p = 0.21$). There were no clear preferences for the choice of antibiotic agents. MRSA and CoNS were treated with vancomycin, doxycycline, and combinations of ciprofloxacin–rifampin or fusidic acid–rifampin. For MSSA, clindamycin, vancomycin, floxacillin, rifampin, and ciprofloxacin were used in the majority of cases. In 91 infections (56%, 91/163), rifampin was used in combination therapy.

All but two patients underwent surgery, and the median number of interventions to cure was two (IQR 1–2). There were no significant differences in terms of number of surgical interventions between the staphylococcal groups or between the groups of arthroplasty vs. fracture fixation device infections (median number two vs. two interventions, $p = 0.65$). In contrast, a revision arthroplasty was more frequently performed in patients with CoNS infections than those with *S. aureus* infections (Table 1).

3.6. Overall outcomes for all implant infections

Two patients died of septic shock due to MSSA and MRSA, respectively. They were not included in the final analysis as they were among the 32 patients excluded because of insufficient follow-up time.

Among the remaining 163 infections, cure was achieved in 57% (25/44) of all episodes of MRSA, in 72% (42/58) of MSSA, and in 82% (50/61) of CoNS (Table 1). These differences were not statistically significant. Forty-three patients (27%, 43/157) had sequelae of former infection, including: Girdlestone hip ($n = 8$), arthrodesis ($n = 8$), amputation ($n = 4$), and other functional handicaps and/or incapacitating pain ($n = 23$). MRSA-infected patients had significantly more sequelae than MSSA or CoNS patients (13/44 vs. 93/119, odds ratio (OR) 3.4, 95% confidence interval (95% CI) 1.3–8.9, $p = 0.004$).

Recurrence of infection always occurred locally and was seen in 20 episodes (12%, 20/163) with a median delay of 94 days after the end of treatment. The number of recurrences were not statistically different between arthroplasty vs. fracture fixation device infections (12 vs. 8 recurrences, $p = 0.36$).

The median length of hospital stay for all staphylococcal infections was 36 days (IQR 16–82 days). Patients with methicillin-resistant infections (MRSA and resistant CoNS) stayed significantly longer (Table 1).

3.7. Subgroups of patients

Upon stratification of the results into the staphylococcal groups, for arthroplasty infection, cure was achieved in 39% (7/18) of MRSA episodes, in 60% (15/25) of MSSA episodes, and in 77% (30/39) of CoNS episodes. These differences were statistically significant (Pearson Chi-square test between MRSA and CoNS, $p = 0.008$). Patients with arthroplasty infections ($n = 82$, 50%) were significantly older than those with fracture fixation device infections ($n = 81$, 50%; median age 73 vs. 55 years, $p < 0.001$), were more immunosuppressed (28/82 vs. 14/81, $p = 0.014$), had a longer incubation time (median delay 176 vs. 50 days, $p < 0.034$), had significantly lower cure rates (52/82 vs. 65/81, $p = 0.017$), a significantly shorter recurrence time to infection (median delay 71

Table 2
Characteristics and comparisons between three groups of staphylococcal arthroplasty infections

Arthroplasty infections ($N=82$)	MRSA ($n=18$)	Comparison MRSA vs. MSSA p-Value[a]	MSSA ($n=25$)	Comparison MSSA vs. CoNS p-Value[a]	CoNS ($n=39$)
Patient population					
Female sex	11 (61%)		9 (36%)		19 (49%)
Median age	80 years	0.043[a]	71 years		71 years
ASA score of 1	0 (0%)		2 (13%)		3 (11%)
ASA score of 2	5 (50%)		11 (69%)		13 (48%)
ASA score of 3	5 (50%)		3 (19%)		11 (41%)
Chronic immunosuppression[b]	7 (39%)		8 (32%)		13 (33%)
Infection					
Median time delay between previous implantation and infection onset	16 days	0.001[a]	361 days		196 days
Bacteremia	3 (17%)	0.026[a]	12 (48%)	0.000[a]	0 (0%)
Treatment					
Median duration of antibiotics	8 weeks		7 weeks		8 weeks
Use of rifampin	8 (44%)	0.033[a]	17 (68%)		24 (62%)
Median No. of surgical interventions	2.5		2	0.037[a]	2
Removal of infected implant	14 (78%)		18 (72%)		30 (77%)
Re-implantation of a new implant	4 (22%)		10 (40%)		22 (56%)
Two-stage revision	4 (100%)		9 (90%)		19 (86%)
Median delay between stages	208 days		69 days		98 days
Outcomes					
Recurrence of infection	2 (11%)		5 (20%)		5 (13%)
Cure	7 (39%)		15 (60%)		30 (77%)
Median length of hospital stay	66 days		44 days		51 days

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; CoNS, coagulase-negative staphylococci.
Group comparisons were performed with the Wilcoxon rank sum test, Fisher's exact test, or the Pearson Chi-square test, as appropriate.
[a] Only statistically significant p-values of ≤ 0.05 (two-tailed) are displayed.
[b] Diabetes mellitus, transplantation, chronic alcoholism, neoplasia, Child's class C cirrhosis, AIDS, steroid medication.

vs. 129 days, $p = 0.011$), and a longer hospitalization (median duration 52 vs. 24 days, $p < 0.001$), and were more likely to receive a new implant (34/82 vs. 15/81, $p = 0.001$). In contrast, the proportions of implant removal were similar (62 vs. 59, $p = 0.69$). Table 2 summarizes the characteristics of arthroplasty patients stratified by staphylococcal infection. Of note, MRSA infections occurred at a significantly higher patient age, had shorter incubation times, and benefited less from the use of rifampin.

3.8. Adjustment of risk factors

Table 3 summarizes the univariate and the multivariate results of logistic regression. In multivariate analysis including all implant infections, arthroplasty (OR 0.2, 95% CI 0.1–0.6) and MRSA infections (OR 0.3, 95% CI 0.1–0.9) were significantly associated with lower cure outcomes, whereas CoNS infection (OR 3.0, 95% CI 1.2–8.0) and the insertion of a new implant (OR 4.5, 95% CI 1.6–13.1) were significantly associated with higher cure results.

In the separate analysis for the group of arthroplasty infections only, a new implant (OR 12.8, 95% CI 2.7–61.9) showed a statistically significant association with cure, while in the group of fracture fixation device infections, no parameter reached statistical significance.

4. Discussion

Our study shows that clinical features and outcomes differ considerably in orthopedic implant infections due to MRSA, MSSA, or CoNS. Overall, cure increased from 57% for MRSA, to 72% for MSSA, and to 82% for CoNS. This tendency was also similar when considering arthroplasty infections separately, with corresponding cure rates of 39%, 60%, and 77%, respectively. In our study, the overall infection recurrence rate was only 12%, which is less than reported rates of 26%[15] and 38%[9] in the literature.

When adjusted in multivariate analysis, revision arthroplasty with insertion of a new implant (for arthroplasty infections) was the most significant protective factor for cure, followed by CoNS disease (for all types of infection). In contrast, infection due to MRSA was inversely associated with cure,[9,10] as was the case in the group of arthroplasty infections compared to the group with fracture fixation devices, which were mostly removed when infected. As previously reported by others,[15,16] patient demographics (immunosuppression, sex, age), disease intensity (bacteremia), and treatment modalities (rifampin use,[17,18] duration of antibiotic therapy, number of surgical interventions, proportion of one-stage revisions) did not influence cure.

One explanation for the lower cure rates of MRSA infections might lie in the lower proportion of new implants inserted in MRSA infections as compared to those patients with CoNS disease. This is highlighted by significantly more sequelae for patients with MRSA infections. Theoretically, a higher sequelae risk might be a sign that surgeons did not perform revision surgery and did not put in a new implant. We cannot completely exclude this decision bias.

It is clear that infection with *S. aureus* demonstrates an enhanced virulence. For example bacteremic disease, a hallmark of *S. aureus* infection, was not seen in CoNS disease. Two patients in our study died secondary to *S. aureus* septicemia. Contrary to the evidence for staphylococcal bloodstream infections,[7,8] non-prosthetic surgical site infections,[19] and community-acquired MRSA,[14] it remains unclear whether staphylococcal methicillin resistance among *S. aureus* or CoNS results in failure of treatment in localized tissue infections. While in vitro studies[20] point to this concept, in vivo studies show conflicting results. Al-Nammari et al. reported the same duration of antimicrobial therapy and the same number of surgical interventions for the treatment of septic arthritis whether due to MRSA or MSSA.[21] Volin et al. demonstrated that methicillin resistance did not influence the probability of cure in patients with two-stage re-implantation after total joint infection.[22] In contrast, Kilgus et al. showed that infection following hip arthroplasty secondary to MRSA was treated successfully in only 48% of cases, as compared to 81% with MSSA infection.[10] Salgado et al. attributed a nine-fold higher hazard ratio to treatment failure in prosthetic joint infections due to MRSA than due to MSSA.[9] In our analysis, methicillin resistance per se was not a risk factor for

Table 3
Predictors of cure in staphylococcal orthopedic implant-associated infections

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*-Value[a]	OR (95% CI)	*p*-Value[a]
All implant infections				
Female sex	1.5 (0.7–3.0)		2.0 (0.8–4.8)	
Age	1.0 (1.0–1.0)		1.0 (1.0–1.0)	
MRSA	0.4 (0.2–0.8)	0.011[a]	0.3 (0.1–0.9)	0.032[a]
MSSA	1.1 (0.5–2.1)		1.2 (0.5–3.0)	
CoNS	2.4 (1.1–5.1)	0.028[a]	3.0 (1.2–8.0)	0.030[a]
Total joint arthroplasties	0.4 (0.2–0.9)	0.018[a]	0.2 (0.1–0.6)	0.002[a]
Duration of antibiotic treatment	1.0 (0.9–1.0)		0.9 (0.9–1.0)	
Number of surgical interventions	1.0 (0.8–1.2)		1.0 (0.8–1.3)	
Bacteremic disease	0.5 (0.2–1.1)		0.7 (0.2–2.3)	
Methicillin resistance[b]	0.6 (0.3–1.2)		1.0 (0.3–3.0)	
Total arthroplasties				
Female sex	0.9 (0.3–2.1)		1.7 (0.5–5.6)	
Age	1.0 (0.9–1.0)		0.9 (0.9–1.0)	
MRSA	0.3 (0.1–0.8)	0.018[a]	0.6 (0.2–2.3)	
MSSA	0.8 (0.3–2.1)		1.2 (0.3–5.4)	
CoNS	3.2 (1.2–8.3)	0.018[a]	1.9 (0.5–7.6)	
Duration of antibiotic treatment	1.0 (0.9–1.0)		1.0 (0.9–1.2)	
Number of surgical interventions	0.8 (0.5–1.2)		0.7 (0.3–1.5)	
New implant	8.9 (2.7–29.1)	0.000[a]	12.8 (2.7–61.9)	0.001[a]
Bacteremic disease	0.3 (0.1–0.9)	0.048[a]	0.6 (0.1–6.6)	
Methicillin resistance[b]	0.7 (0.3–1.8)		1.0 (0.3–3.0)	
Non-arthroplasty implants				
Female sex	4.5 (1.2–17.2)	0.029[a]	3.3 (0.7–15.6)	
Age	1.0 (1.0–1.0)		1.0 (1.0–1.0)	
MRSA	0.4 (0.1–1.2)		0.3 (0.1–1.2)	
MSSA	1.2 (0.4–3.7)		1.2 (0.3–5.0)	
CoNS	3.1 (0.6–15.0)		5.9 (0.6–58.0)	
Duration of antibiotic treatment	0.9 (0.9–1.0)		0.9 (0.8–1.0)	
Number of surgical interventions	1.0 (0.8–1.4)		1.0 (0.7–1.5)	
Bacteremic disease	0.8 (0.2–3.3)		1.2 (0.2–8.3)	
Methicillin resistance[b]	0.6 (0.2–1.8)		0.3 (0.1–1.4)	

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; CoNS, coagulase-negative staphylococci.
[a] Only statistically significant *p*-values of $\leq$0.05 (two-tailed) are displayed.
[b] MRSA and methicillin-resistant CoNS.

failure, but was related to a higher age and a longer length of hospital stay.[9] This reflects nosocomial aspects rather than damage by the pathogen itself, because methicillin-resistant infections more likely occur in the elderly population with more co-morbidities[21] and frequent healthcare contact.[4,21]

Our study has limitations: (1) It was retrospective, from a single institution, and with a small sample size, thus limiting the generalizability of the findings. (2) Patients with an infection treated in another hospital may have been undetected. However, given that the Geneva University Hospitals comprise the largest and only public hospital in the area, and given the active post-discharge follow-up of our patients, we consider this selection bias to be minimal. (3) We used databases with microbiological documentation, with another possible selection bias for infections where the microbiological cultures did not grow any staphylococci. Half of the infections were due to methicillin-resistant strains, which are unlikely to be masked by unreported pre-hospitalization antibiotic use. In the literature culture-negative prosthetic infections account for only 7% of cases, and the outcome appears to be indistinguishable from that due to cultured bacteria.[23] (4) The potential influence of small-colony variants was not investigated since it was a retrospective study and many specimens had not been stored. Small-colony variants are resistant to aminoglycosides, considered difficult to treat, and responsible for recurrence.[24] However, we consider their influence to be minimal because small-colony variants are inherent to all three groups of staphylococci independent of their methicillin resistance.[24,25] In addition, our episodes were not recurrent infections and patients were not subjected to long-term anti-staphylococcal therapy before the onset of their infection.

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Conflict of interest: No conflict of interest to declare.

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