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Medical versus surgical treatment in native hip and knee septic arthritis

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Keywords: arthritis, arthrocentesis

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Abstract

Objective. Antibiotic treatment and arthroscopic or open drainage is the gold standard for septic arthritis. Full recovery takes time after surgery and hospital stay is longer than for arthrocentesis at the bedside. We aimed to evaluate the effectiveness of arthrocentesis (medical approach) versus a surgical approach.

Method. We retrospectively included 97 cases of native joint arthritis (hip and knee) between 2010 and 2017. The primary outcome was treatment failure of medical and surgical approaches (defined as surgical intervention within 7 days following diagnosis). Risk factors of failure were identified by univariable and multivariable logistic regression.

Results. We included 72 cases of knee arthritis, of which 43 and 29 were treated medically and surgically, respectively; 25 cases of hip arthritis, of which 8 and 17 were treated medically and surgically, respectively. Failure was observed in 39.2% of cases in the medical group and in 30.4% in the surgical group (p=0.2) (37.5% vs 52.9% and 39.5% vs 17.2% for hip and knee, respectively). The univariate analysis identified age and male sex as risk factors for failure (p=0.048 and p=0.02, respectively), but only age was independently associated with failure (p=0.04). Hospital length of stay was 12 days shorter in the medical group (21 vs 33 days, p=0.02), sequelae were less frequent and less important in the medical group (31.7% vs 60%).

Conclusion. The medical treatment seems to be as effective as the surgical treatment for native joint septic arthritis with a shorter hospital stay and better functional outcome. Further prospective studies are warranted.

Introduction

Septic arthritis is a rare but serious infection requiring appropriate and rapid management to lower the burden of case fatality and morbidity. The estimated case fatality is 10% for native joint infections and 20-30% for prosthetic joint infections and elderly patients with comorbidities [1–4]. The estimated morbidity is 25-50% of irreversible functional sequelae such as joint pain, stiffness, secondary osteoarthritis, and even amputation in 5% of cases [5–8].

There is no standardized management of septic arthritis on native joints. British guidelines for management of the hot swollen joint in adults [1] suggest managing septic arthritis as follows: rapid and adequate antibiotic treatment (after microbiological sampling), mechanical treatment (*i.e.*, washing of the joint either by surgical drainage or iterative punctures), and short immobilization (mainly for analgesic purposes followed by physiotherapy to avoid stiffness) [6,9–12].

Arthritis drainage is known to reduce bacterial inoculum and to limit functional sequelae due to inflammation [9,13]. Although the protocol is clearly defined concerning the joint puncture to be systematically and rapidly performed (before antibiotic therapy initiation), the type and timing for surgical procedure is still unclear. Literature data is rather poor on the timing of surgery and on the most effective type of drainage (surgical drainage or iterative punctures).

Despite a lack of reliable data in published studies [14–16], iterative punctures (*i.e.*, medical treatment) is a very appealing approach because of its numerous theoretical

advantages: shorter length of stay, shorter antibiotic treatment, less sequelae, shorter time to recovery, etc.

On the basis of our experience, medical treatment is safe and successful. We therefore aimed to compare outcomes of surgical and medical treatment in our hospital.

Patients and method

We performed a retrospective study of medical records at the University Hospital of Amiens, France, between January 2010 and December 2017. Files were retrieved by the department of medical information using CIM10 coding for joint infections.

The study was approved by the CER-MIT ethnic community.

Inclusion criteria were patients aged above 18 years with septic arthritis of the hip or knee on a native joint, presence of septic arthritis based on identification of a bacterium in the joint fluid or on blood culture. All cases of septic arthritis on prosthesis or presence of intra- or periarticular material (osteosynthesis) were excluded.

Forty-two variables for each episode were evaluated, including demographic characteristics, clinical symptoms, microbiology, type of treatment (medical or surgical), failure, antibiotic duration, relapse, functional sequelae at 3 and 6 months, length of stay, and death.

The primary endpoint was medical or surgical treatment failure after adequate management. Medical treatment failure was defined as the need for surgery despite adequate antibiotic treatment after 7 days. Surgical treatment failure was defined as the

need for a second surgery after 7 days for the same episode. Patients for whom the surgery was delayed after one or two needle aspirations were included in the medical group, unless they had surgery during the first 7 days − in that case they were included in the surgical group. Surgery after 7 days was then considered a treatment failure. The occurrence of death or amputation was considered a treatment failure.

Secondary endpoints were functional outcome at 12 weeks, antibiotic duration, and length of stay.

Relapse was defined as the reoccurrence, after antibiotic treatment completion for septic arthritis with the same bacterium as before.

Functional sequelae were evaluated by a clinical score (from 0 [excellent] to 4 [poor]): excellent functional outcome was defined as the absence of sequelae and normal walking, good functional outcome as the presence of mild pain and/or stiffness with no or little effect on daily life; moderate functional outcome as frequent moderate pain and/or stiffness significantly affecting daily life; poor functional outcome was defined as permanent severe pain and/or stiffness with severe impact on daily life.

Due to the absence of a radiological sequela score in the literature, we defined a radiological score as follows: destruction of articulation measured by the interlinear narrowing of the joint (from 0 [no joint nip] to 4 [complete joint nip], destruction of the bone (from 0 [no destruction] to 4 [complete destruction]) and finally, occurrence of ossification bridges (from 0 [no ossification signs] to 4 [complete ossification]).

Quantitative variables were expressed as means and standard deviations when the distribution was normal and median and interquartile ranges otherwise. Normality was

measured by the Skewness test. Qualitative variables were expressed as percentages. A proportion comparison test was used to determine the primary endpoint and to analyze the other qualitative variables. Fisher's exact test was used to compare the quantitative variables. A *p*-value below 0.05 was considered significant. A logistic regression model was used to determine risk factors for failure and to account for selection bias. A propensity score analysis was also performed. All statistical analyses were performed using STATA 13.1 (StataCorp, College Station, TX).

Results

Out of 488 patient files analyzed, 97 were included (Figure 1). Fifty-one patients (52.6%) underwent initial medical treatment, while the remaining 46 (47.4%) underwent initial surgical treatment (arthroscopy was used in 23 patients: 9 arthroscopic lavages, 14 arthroscopic synovectomies), open synovectomy in 14 patients, and joint resection in 9 patients. Patient characteristics are detailed in Table I. Medically treated patients were older (median [IQR]) than those surgically treated (67 [53-75.5] versus 59.5 years [59.5-67.7], respectively). There were 2.23 times more men than women, but sex distribution was homogeneous in both treatment groups. Surgically treated patients presented more risk factors and severity signs at admission than those medically treated, but the propensity score showed that the groups were well balanced. The more frequently affected joint was the knee with 74.2% (n=72) of our sample. *S. aureus* was found in 40.2% (39/97) of cases, of which six cases were methicillin-resistant staphylococci. Among non-*S. aureus* bacteria, there were 19 Gram-negative bacilli (8 *Pseudomonas aeruginosa*, 6 *Escherichia coli*, 1 *Klebsiella* sp., 1 *Enterobacter cloacae*, 1 *Morganella morganii*, 1 *Pantoae* sp., and 1 *Acinetobacter* sp.), 32 Gram-positive cocci including 22 streptococci et 10 coagulase-

negative staphylococci. No pathogen was identified in joint fluid for seven episodes (7%, 7/97), but blood cultures were positive (6 streptococci, 1 *Campylobacter* sp.) and were considered causative agents of arthritis. At admission 55 patients had bacteremia, but none had endocarditis.

Fourteen patients (30.4%) experienced failure after their first surgery versus 20 patients (39.2%) after medical treatment. Thus, the global proportion of treatment failure was slightly higher after medical treatment than after surgical treatment, but this difference was not significant (p=0.2). However, the affected joint significantly impacted treatment outcome. Indeed, the rate of failure was significantly greater in septic arthritis of the hip than of the knee (48% vs. 30.6%, respectively [p=0.05]). This difference was even more important for surgical treatment (52.9% of failures in hip treatment vs 17. 2% in knee treatment [p=0.01]). Conversely, medical treatment equally performed for both articulations (37.5% of failures in hip treatment vs 39.5% in knee treatment [p=0.46]). Thus medical treatment seemed to perform better than surgical treatment for hip infection, although not significantly (p=0.4), and significantly worse for knee infection (p=0.04).

Amongst the 14 patients who needed a second surgery, 10 patients required a second lavage, two had to be amputated, and two died due to septic shock.

Of the 51 medically treated patients, anatomical landmarks were left on the knees while hips were punctured guided by ultrasound. Successfully treated patients underwent an average of 2.1 iterative punctures (108/51, median: 2, min: 1, max: 5) during their treatment: six patients only had one puncture, nine had two punctures, two had three punctures, two had four punctures, and one had up to five punctures. Amongst the 20

patients who experienced medical treatment failure, two patients died in the first 14 days of management, 18 subsequently required surgical intervention.

Looking at the global failure rate depending on the causative bacteria, we observed no difference (*S. aureus* [35.9%] vs. non-*S. aureus* bacteria [37.3%], p=0.3). The seven patients, for whom joint fluid did not grow any bacteria, were excluded from this analysis.

Medical treatment failure rate was slightly higher with non-*S. aureus* bacteria (55%) than with *S. aureus* (45%), although not significantly (p=0.38); the same was observed for surgical treatment (64.3% vs. 35.7%) (p=0.45). Similarly, antimicrobial resistance did not impact treatment outcome (Table II). Only two patients relapsed at 12 weeks of *Pseudomonas aeruginosa* infection.

Univariate analysis identified age, hip localisation, and male sex as risk factors for failure (p=0.048, p=0.03, and p=0.02, respectively), but only age was independently associated with failure on multivariable analysis (p=0.04).

At the end of Week 12, 7 of 97 patients died (7.2%): five patients in the medical group and two in the surgical group. Four deaths were directly attributable to septic arthritis as they died only a few days after admission: one multiple organ failure (surgical group) and three sepsis (two in the medical group). Causes of the other three deaths were cardiac arrest, hemodynamic failure, and multiple organ failure 25 days after the start of treatment. All had severity criterion or were fragile (*i.e.*, >80 years). A total of 22 patients died between 2010 and 2018 (13 patients in the medical group and nine patients in the surgical group).

Functional and radiological outcomes at 12 weeks were performed on 76 patients. Radiological score comparison between admission and three months showed lesion stability (data not shown). Only two patients (surgery group) developed greater bone destruction, regardless of the time to adequate treatment initiation (2 and 5 days, median range = 3 [2-7]). In addition, patients with significant destruction of the joint upon admission (stage 4) did not gain any improvement over time and usually required joint prosthesis later on.

Among these 76 patients, 42 (55.3%) presented satisfactory results with little or no change in quality of life at home compared with their initial status. They were significantly more numerous in the medical group (n=28 [68.3%]) than in the surgical group (n=14 [40%] (*p*=0.01)) (Figure 2).

Functional outcome was better after knee arthritis than after hip arthritis (clinical score between 0 and 1 for 34 patients [58.6%] vs 8 [44.4%], respectively), independently of the treatment group (medical: 70.4% vs 57.1%, surgical: 41.7% vs 36.4%).

The three-month functional outcome in medically treated patients was better with non-*S. aureus* bacteria than with *S. aureus* (72.2% vs 58.8%, respectively). This difference was not observed in surgically treated patients (39.1% vs 41.7%, respectively).

The median duration of hospitalization [IQR] was 22 days [13-49] with extremes ranging from 4 to 168 days in both groups. It was significantly longer in the surgical group than in the medical group (33.5 vs 21 days, respectively [*p*=0.02]).

All cases of septic arthritis were initially treated with intravenous antibiotic therapy. The median [IQR] duration of intravenous treatment was 11 days [7-16] (min: 2, max: 98) in

both groups. Due to complications and significant comorbidities during hospitalization, nine patients received intravenous treatment for the entire course of treatment.

The median total [IQR] duration of the antibiotic therapy was significantly longer in the surgical group than in the medical group (45 days [42-79] vs 42 days [41-46], respectively [*p*=0.01]).

The median duration [IQR] of IV treatment was equivalent in the two groups (medical: 13 [8-14.5] vs surgical: 10 [6.3-17.8]), but the mean duration was significantly longer in the surgical group (19.6 days [min: 4, max: 84] vs. 12 days [min: 2, max: 30]).

The antibiotic treatment was adequate in dosing and spectrum of activity in 84/88 patients (95.5%) (nine missing pieces of data). The main inadequacy was under-dosing related to the patient's weight.

Discussion

This retrospective study of 97 cases is, to our knowledge, the largest on the subject. It showed that the proportion of failures was not different between surgical (30.4%) and medical (39.2%) treatment. This lack of difference between the two groups could be explained by several factors confounding each other: a smaller number of patients with risk factors in the medical group than the surgical group (62.7% vs 95.7%, respectively) and older patients in the medical group which was an independent risk factor for failure in multivariable analysis. Moreover, advanced age was defined as a risk factor for failure by McBride [17]. Both joints combined, there was also no average difference between the two groups. However, they seem to behave very differently. Surgery seemed to work better on

knee arthritis than medical treatment (17.2% vs 39.5%, respectively), while medical treatment worked better on hip arthritis than surgical treatment (37.5% vs 52.9%, respectively). By performing a propensity score that showed that the two groups were well balanced, the inclusion bias was controlled. Thus, surgical treatment could probably work better on knee than hip because arthroscopy (rather than arthrotomy) is more often performed on knee.

In a recent Spanish retrospective study [16], 50% of medically treated patients experienced failure (requiring surgical revision). The authors concluded that septic arthritis of the hip and shoulder should be preferentially treated by surgery. Conversely based on our results, septic arthritis of the hip without risk factor is as likely to heal as knee arthritis after medical treatment.

The bacterium encountered was not a risk factor for treatment failure. In our study *S. aureus* did not increase treatment failure (35.9%) compared with other bacteria (37.3%). These results are similar to those published by Kaandorp *et al.* who reported that *S. aureus* arthritis was not worse than non-*S. aureus* arthritis [7].

Only two surgically treated patients for *Pseudomonas aeruginosa* arthritis relapsed at 2 months. This reflects the good management of patients, who recovered in 98% of cases irrespective of the type of treatment. Nonetheless Gram-negative bacilli are known to be a risk factor for relapse at treatment discontinuation (odds ratio = 5.9, 95% confidence interval [1.4–25.3]) [17,18].

Case fatality at 3 months was 7.2%: this rate is close to the case fatality results (10%) reported in most studies [4,13,17]. Four deaths were attributable to septic arthritis, and

occurred in frail patients (>80 years) or with severity criteria (sepsis), same factors as in Weston and Maneiro's studies [8, 19]. Morbidity at 3 months in our study was 44.7%, quite similar to published literature data (25-50%) [6,19].

Almost twice as many patients had good functional results in the medical group as in the surgical group (28 vs 14, respectively). These results are better than those published in the Spanish study (56% medical vs 50% surgical) [16], but quite similar to those obtained by Goldenberg or Ravindran (67-69% after aspiration vs 42-53% after surgery or surgical drainage) [14, 15]. Both showed that medically treated patients had better functional outcome than surgically treated patients within three months of infection.

Antibiotic therapies prescribed for septic arthritis were effective and adapted in most of our patients. This can partly be explained by a well-known written infectious policy in our facility (available to all departments online). The median total duration of the antibiotic therapy in all groups was 44 days [42-54]. This treatment duration is longer than that reported by Flores-Robles *et al.* (30 days in the medical group vs 29.5 days in the surgical group) [16]. Most of the protocols found in the literature [1,13] suggest treatment duration from 4 to 6 weeks. The longer antibiotic treatment duration observed in our study does not seem to be related to antibiotic misuse within our facility, but rather to complicated patients with underlying chronic diseases. It is noteworthy that three non-compliant outpatients received a relatively short antibiotic treatment (15 to 30 days) and did not perform poorly compared with patients receiving longer treatment.

The median duration of hospitalization in our study was 22 days [13-49] with extremes ranging from 4 to 168 days in both groups. It was significantly higher in the surgical group than in the medical group (33.5 vs 21 days). This difference was mainly related to

post-intervention follow-up, but especially to the need for a longer period of rehabilitation in a rehabilitation center in the surgical group, confirming data published by Ravindran *et al.* [15].

The main limitation of our study is its retrospective design with major selection bias. The choice of care (medical or surgical) was primarily made at admission. Our facility does not currently have any written protocol for suspicion of septic arthritis, but it is common rule to first call the surgeon. Depending on clinical emergency and bed availability, patients can then be sent to medical wards such as rheumatology or infectious diseases. Treatment decision was thus probably influenced by the patient's overall health, although not solely. As mentioned above, surgically treated patients were more seriously ill, with more risk factors but younger. However, to account for this selection bias we performed a propensity score analysis that could properly balance the two groups. Some of our variables were based on rather subjective criteria such as limitation of motion or pain and completeness depended on file records. Lastly, despite our large sample size, the study power was very low (1-β=0.148). The absence of difference between the two treatment groups could just be due to this low study power. A prospective randomized study is therefore warranted with at least 459 patients per group (1-β=0.8) to validate the medical treatment of native hip and knee septic arthritis.

Conclusion

Our retrospective study of native joints reported no difference between medical or surgical management of treatment failure, as the rate of failure and death were comparable between the two treatment groups. However, medically treated patients had better

functional results at three months due to the less invasive nature of iterative punctures compared with surgery, as well as a shorter hospital stay.

Our results suggest that medical treatment may be sufficient for a large number of native joint septic arthritis without signs of severity and abscess, whether for hip or knee joints. Surgical treatment would be preferred when the medical treatment is ineffective or in seriously ill patients with a more difficult joint access or more severely damaged (*e.g.,* radiological damage).

These results need to be confirmed in a randomized controlled trial stratified on clinical and radiological severity. The reflection on such study protocol is currently in progress.

Disclosure of interests: the authors declare no conflict of interests.

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Figure 1. Flow chart

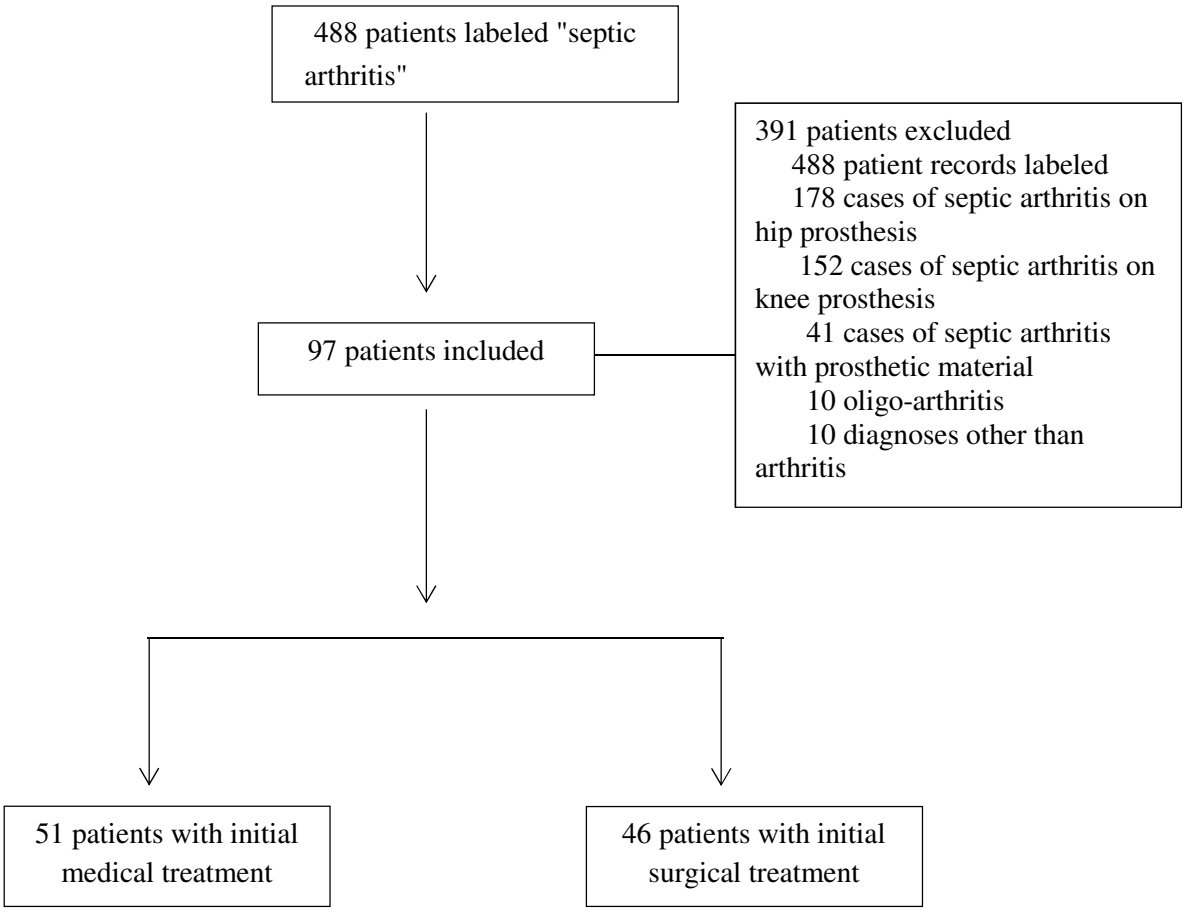

Figure 2. Functional outcome by treatment group

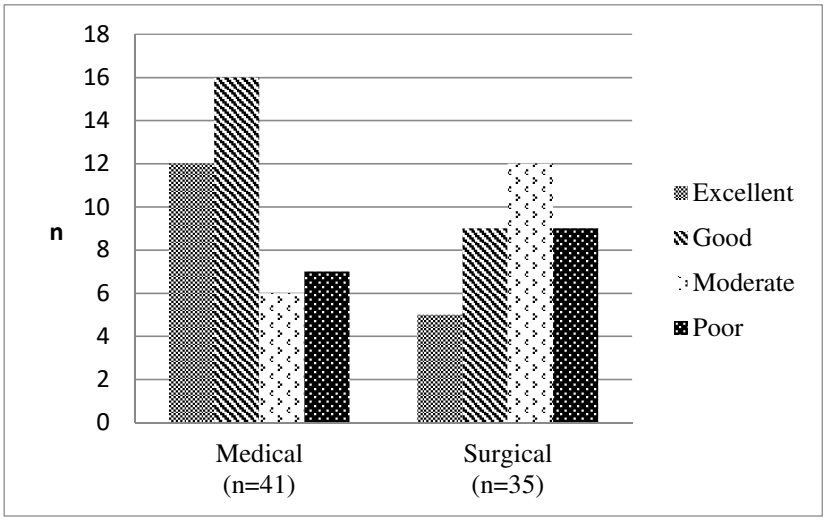

Table I. Characteristics of patients

Characteristics		Medical treatment (n=51)	Surgical treatment (n=46)	Total (n=97)
Age [IQR], years		67 [53-75.5]	59.5 [46.3-67.7]	63 [50-74]
Sex, male		35 (68.6%)	32 (69.6%)	67
Bacteremia		30 (58.8%)	25 (54.3%)	55
Risk factors	Yes	32 (62.7%)	44 (95.7%)	76
	No	19 (37.3%)	2 (4.3%)	21
Recent joint procedure		8 (15.7%)	15 (32.6%)	23
Diabetes		9 (17.6%)	3 (6.5%)	12
Skin ulceration		5 (9.8%)	13 (28.3%)	18
Immunodepression		1 (1.9%)	5 (10.9%)	6
Pre-existing joint disease		3 (5.9%)	3 (6.5%)	6
Chronic ethylism		3 (5.9%)	2 (4.3%)	5
Elderly subject (>75 years)		3 (5.9%)	1 (2.3%)	4
Intravenous drug user		0	2 (4.3%)	2
Severity criteria		10 (19.6%)	23 (50%)	33
presence of fistula			4	
septic dislocation			1	
sepsis according to SOFA score		4	6	
Resistant bacteria		2	10	
GNB		4	2	
Symptom duration before treatment, median [IQR], days		3 [2-7]	3 [2-6.5]	3 [2-7]
Joint				
Knee		43 (84.3%)	29 (63%)	72
Hip		8 (15.7%)	17 (37%)	25
Biological results				

CRP (mg/l)	170 [84.5-240]	180 [101.5-250]	170 [90-250]
WBC (/mm^3)	10600 [8800-13200]	11150 [9325-14525]	10900 [9200-13800]
ANC (/mm^3)	8500 [6300-10800]	9500 [6750-12350]	8900 [6300-11600]
Microbiological results			
S. aureus	22 (43.1%)	17 (37%)	39
Non-*S. aureus*	29 (56.9%)	29 (63%)	58
Duration of hospitalization [IQR], days	21 [15-28]	33.5 [10-56]	22 [13-49]
Duration of antibiotics [IQR], days			
IV	13 [8-14.5]	10 [6.3-17.8]	11 [7-16]
Total	42 [41-46]	45 |42-79]	44 [42-54]

IQR: interquartile range, CRP: C-reactive protein, WBC: white blood cell, ANC: absolute neutrophil count

Table II. Treatment failure by treatment group, bacteria, and drug susceptibility

		S. aureus	Non-*S. aureus* bacteria
Treatment	Medical (n=20)	9 (45%)	11 (55%)
	Surgical (n=14)	5 (35.7%)	9 (64.3%)
Drug susceptibility	Susceptible (n=28)	12 (42.9%)	16 (57.1%)
	Multidrug resistance (n=6)	2 (33.3%)	4 (66.7%)
Joint	Hip (n=12)	6 (50%)	6 (50%)
	Knee (n=22)	8 (36.4%)	14 (63.6%)

Multidrug resistance was defined as bacteria resistant to several classes of antibiotics (two methicillin-resistant *Staphylococcus aureus* [MRSA], three extended-spectrum ß-lactamases [ESBL], one vancomycin-resistant enterococci [VRE])