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Outcome of patients over 80 years of age on prolonged suppressive antibiotic therapy for at least 6 months for prosthetic joint infection

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SUMMARY

Objectives: To describe elderly patients treated with prolonged suppressive antibiotic therapy for a prosthetic joint infection (PJI) in cases where the infected prosthesis could not be removed.
Methods: All patients aged ≥80 years with a documented PJI and treated with prolonged suppressive antibiotic therapy for more than 6 months were included retrospectively in this study. The following events were noted: failure including persisting infection, relapse, new infection, treatment discontinuation due to severe adverse events, and related death, and also unrelated death.
Results: Thirty-eight patients with a median age of 84 years (80–95 years) were included; there were 24 hip infections, 13 knee infections, and one shoulder infection. The main causative organisms were *Staphylococcus aureus* (39%) and *Streptococcus agalactiae* (16%). The most commonly prescribed antibiotics as prolonged suppressive therapy were penicillins. The median follow-up duration was 24 months; 60% of the patients were event-free at 24 months and were still on prolonged suppressive antibiotic therapy. Fifteen events (six failures and nine unrelated deaths) were observed. Hypoalbuminaemia, the presence of a sinus tract, and a staphylococcal PJI were associated with an increased risk of an event.
Conclusions: Prolonged suppressive antibiotic therapy is an alternative therapy in elderly patients with PJI when surgery is contraindicated and when the bacteria are susceptible to well-tolerated oral antimicrobial therapy such as beta-lactams.

1. Introduction

Infection is the most dramatic complication of arthroplasties, which are used widely nowadays, especially in the elderly.[1–3] In France, approximately 100 000 total hip arthroplasties (THA) and 40 000 total knee arthroplasties (TKA) are implanted every year, with an infection incidence of 1–2% for THA and 3% for TKA.[4] In the USA, over 500 000 primary arthroplasties are implanted every year and over one million people currently live with a prosthetic joint.[5] It is anticipated that by 2030 more than four million primary THA and TKA replacements will be done per year.[3] Sixty percent of individuals with a THA in the USA are over 65 years of age and 5% over 85 years; further, 17% of patients with revision hip replacements have at least three comorbidities.[2]

Treatment strategies to cure prosthetic joint infections (PJIs) require removal, one- or two-stage replacement of the prosthesis, and prolonged systemic antibiotic therapy for a total of 3 months.[1,6] Patients with a well-fixed prosthesis, without a sinus tract, and who are within 30 days of prosthesis implantation or <3 weeks of onset of infectious symptoms should be proposed the 'DAIR' strategy of debridement, antibiotics, irrigation, and retention of the prosthesis.[6] Other patients who do not meet these criteria may also be proposed DAIR, or a minimal surgical strategy, or no surgery at all, for example when a prosthesis exchange strategy is unacceptable because of the risks involved and/or patient refusal. In these cases, where relapse of infection is more

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likely, prolonged suppressive antibiotic therapy (PSAT), which is defined as an oral antibiotic therapy prescribed for a duration longer than a curative treatment, may be used for palliative purposes. Its aim is to inhibit bacterial growth around the prosthesis and avoid the dissemination of infection.

Studies on this subject are few and of limited size.[7–10] Most of them included patients treated surgically and did not describe the oldest and frailest patients. Moreover, they did not provide patient demographics including age and treatment indications.

The objective of this study was to describe patients aged 80 years and older for whom surgical excision was contraindicated as a result of medical and surgical conditions or patient refusal, who received PSAT for a PJI for at least 6 months, and to describe their treatment and outcome.

2. Methods

2.1. Study design and population

This retrospective observational study was carried out in a French regional referral centre for osteoarticular infections at the Groupe Hospitalier Diaconesses Croix Saint Simon in Paris. All patients treated from January 2004 to December 2011 were eligible. Cases were identified retrospectively using the registry and medical charts of the orthopaedic department. Patients were included if they were aged ≥80 years and had a microbiologically confirmed PJI, either by joint aspiration or by intraoperative culture. Their prosthesis was not removed and they were treated with suppressive antibiotic therapy for at least 6 months.

The following data were collected: sex, age, medical history, past history of PJI, ASA score (American Society of Anesthesiologists), symptoms of PJI (fever, pain, fistula), type of PJI (acute or chronic, postoperative or haematogenous), and the pathogen isolated.

2.2. Prolonged suppressive antibiotic therapy

Indications for PSAT were collected and classified as very high operative risk, very complex surgical intervention, or patient refusal. The antibiotic therapy was detailed, including (1) the initial intravenous antibiotic therapy and the following oral regimen, which included the initial higher doses (considered as curative treatment) and the subsequent lower doses, (2) the duration of treatment, and (3) drug-related adverse events and reasons for drug withdrawal. The duration of PSAT included the initial intravenous treatment. Doses were prescribed according to the national recommendations of France.[11]

2.3. Surgery

Patients underwent surgery only to drain an abscess, to reduce the bacterial burden, or to perform a partial exchange in those with severe pain and loosened components. The indications and types of intervention were recorded.

2.4. Outcome

Patients were seen as outpatients every 3 to 6 months. For patients not seen for more than 1 year, they or their referring doctor was contacted by phone. The following events were noted: treatment failure including persisting infection, relapse, new infection, treatment discontinuation because of severe adverse events, or related death. Unrelated death was included in events.

2.5. Definitions

PJI was defined as a sinus tract communicating with the prosthesis or clinical (local inflammatory signs including swelling, warmth, erythema), laboratory (C-reactive protein (CRP) >5 mg/l), or radiological signs (periosteal bone formation, subchondral osteolysis) of infection, and positive cultures of joint fluid aspiration and a synovial leukocyte count $>4.300 \times 10^9$/l with a differential of >80% neutrophils in hip infection, or a synovial leukocyte count $>1.700 \times 10^9$/l with a differential of >65% neutrophils in knee infection, or isolation of the same organism from two or more cultures of intraoperative tissue specimens.

Acute infection was defined as a duration of symptoms less than 1 month. Early infection was considered if it occurred within 1 year after surgery (corresponding to time free of symptoms).

Persisting infection was defined as persistence of clinical signs of PJI. Reappearance of clinical signs of PJI after a symptom-free period led to the diagnosis of 'relapse' if the same bacterial organism was isolated as was found at inclusion, or as 'new infection' if the organism was different.

2.6. Statistical analysis

Statistical analyses were performed with R (version 2.10.1) software. A Kaplan–Meier curve was generated to assess overall survival without an event. Factors related to the occurrence of an event were analyzed with a univariate log-rank test, and the unadjusted hazard ratio (HR) was performed with Cox analysis for each factor. The level of significance was set at $p < 0.05$.

3. Results

3.1. Patients

A total of 452 patients were treated for PJI during the study period, 104 of whom were ≥80 years old. Of these, 38 patients were included in the study, i.e., 8% of all patients and 36.5% of patients aged ≥80 years. Their characteristics are detailed in Table 1. The median duration of symptoms was 99 days (range 1–1825 days). Fifteen patients had an acute infection and 15 an early-onset infection. The infection was classified as postoperative in 23 patients. Among these, the portal of entry was cutaneous in seven patients, dental in three, urinary in three, digestive in three, and undetermined in two. Two patients had endocarditis confirmed by echocardiography, including one with pacemaker-related endocarditis. The other patient had concomitant cervical spondylodiscitis.

3.2. Microbiology

The microorganisms isolated in these patients are shown in Table 2. Identification was done by joint aspiration in 29 patients (76%) and by intraoperative cultures in nine patients.

3.3. Prolonged suppressive antibiotic therapy

Indications for PSAT were a very high operative risk for 20 patients, a very complex surgical intervention for nine, and patient refusal to have surgery for nine.

Thirty-two patients initially received an intravenous (IV) antibiotic therapy for a median duration of 30 days (range 10–45 days) prior to the oral regimen. The IV agents used were beta-lactams in 24 patients (amoxicillin in 10, cefazolin in 10, ceftriaxone in two, and cloxacillin in two), clindamycin in four, and vancomycin in four. They were associated with aminosides for less than 1 week in 20 patients and with rifampin in 15 patients with susceptible *Staphylococcus aureus* infections.