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Staphylococcal orthopaedic device-related infections in older patients

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ABSTRACT

Introduction: Staphylococci are the most common pathogens causing orthopaedic device-related infections (ODRI). The treatment of these infections often involves multiple surgical procedures combined with systemic antibiotic therapy to treat the infection and restore functionality. Older patients frequently present with a compromised health-status and/or low bone quality, and despite growing importance their outcomes are not well described to date. The primary aim of the current study is to describe outcomes in older patients with ODRIs and to determine if they demonstrate lower cure rates and greater risk for complications in contrast to younger patients.

Patients and methods: Patients treated with an ODRI of the lower extremity at our institution were included in this study. Demographic data, comorbidities and infecting organisms were recorded. Older adult patients were defined as those aged 60 and older. At two-year follow-up post-discharge, we recorded the clinical course, the Lower-Extremity-Functional-Score, the patient reported general health status (SF-12-questionnaire) and the status of infection. The antibiotic resistance pattern of the disease causing pathogens was analysed and compared between the two age groups.

Results: In total, 163 patients (age: 19–94 years) with a staphylococcal ODRI were included. Sixty-four of these infections occurred in older patients, which showed a significantly higher mortality rate (9%). Within follow-up period recurrence of infection occurred significantly more frequently in younger patients (41%) than in older patients (17%). At two-years follow-up cure, which was defined as eradication of infection and terminated therapy, was achieved in 78% of younger and 75% of older patients. However, an ODRI resulted in older patients in a significantly worse functional outcome and impaired physical quality of live, as well as more frequently in an on-going infection, such as a persisting fistula (14% versus 3% in younger patients). Disease causing staphylococci, isolated from older patients showed more frequently a methicillin or multi-drug resistance than those associated with infections in younger patients.

Conclusions: ODRIs in older patients demonstrated higher morality rates rate, poor functional outcome and higher rates of persistent infections. A compromised health status and a poor bone quality may play a crucial role in this specific patient cohort.

Introduction

Implant-associated infections following fracture fixation or joint replacement are uncommon, but pose a significant challenge to patients, treating physicians and the health care system [1–3]. *Staphylococcus aureus* and *Staphylococcus epidermidis* are the most common pathogens associated with orthopaedic device-related infection [4–7]. Multiple surgical procedures as well as long-term systemic and local antibiotics are needed to cure infection and to restore the function of the limb [8]. Despite such prolonged and comprehensive therapy, infection recurs in approximately 12–38% of the cases [9,10]. Therefore a complete recovery can be difficult to achieve and significant functional deficits may remain in some cases [1,9]. It remains unclear if older patients, who often have a

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compromised health-status and a lower bone density, will experience a more prolonged course, greater functional impairments and higher complication rates than the rest of the population. A growing older population, with high functional expectations, will inevitably lead to a worldwide increase in joint replacements and fragility fractures [11–13]. Consequently, a rising prevalence of orthopaedic device-related infections (ODRI) in older adults is expected. Despite the predicted importance of ODRIs in older patients, there is limited published data analysing infectious complications and outcome in this population.

The primary aim of this study was to investigate the clinical course and the two-year outcomes in ODRIs caused by staphylococci in older patients, and to determine if this cohort has a greater risk for re-infection and lower cure rates than younger patients. The secondary aim was to analyse the antibiotic resistance pattern of the infecting pathogens to determine if older patients experienced different antimicrobial resistance patterns.

Patients and methods

This prospective study was performed from 2011 until 2013 at a level-one trauma centre with a high volume unit for septic and reconstructive surgery.

Inclusion criteria were patients with deep *S. aureus* or *S. epidermidis* infections after fracture fixation (fracture fixation infection, FFI) or prosthetic joint surgery (prosthetic joint infection, PJI) of the major joints or long bones of the lower extremity. Therefore, FFIs and PJIs involving the hip-, knee- and upper ankle-joint as well as femur, tibia and fibula were included in the study. Implant-associated infections were defined according to published guidelines: bacterial growth at the site of interest in combination with pseudarthrosis, implant-loosening/failure or local and systemic signs suggesting a surgical site infection. Bacterial growth was defined as detection of bacteria in at least one tissue sample, collected from the affected site of interest [1,14]. These criteria reflect the standard institutional requirement for diagnosis of infection and commencement of surgical and medical treatment at our centre. Osteomyelitis without the presence of an implant and infections around an external fixation pin were excluded. The presence of bacterial growth around an implant without any clinical signs of infection was defined as contamination and these patients were excluded [14].

At baseline examination, the following parameters were documented: gender, age, body mass index (BMI), smoking, type of implant, affected bone or joint, open or closed fractures and time between implantation of the orthopaedic device and onset of infection symptoms. Infections presenting within 6 weeks were considered as early onset infections and others as late onset infections. The Charlson Comorbidity Index and the immune status were documented [15]. Chronic immunosuppression was defined if the patient suffered at least from one of the following: Diabetes mellitus, chronic alcoholism, Child's class C cirrhosis, neoplasia, transplantation, acquired immune deficiency syndrome (AIDS) or steroid medication [9]. Patients aged 60 years and older were defined "older patients" according to the recommendation of the World Health Organization (WHO) [16].

Infecting pathogens were isolated from the site of interest and studied for antimicrobial resistance characteristics. Identification and antibiotic susceptibility testing of infecting pathogens (staphylococci) was performed using a Vitek2, automated microbiology system for microbial identification, and antibiotic susceptibility testing (bioMerieux Vitek Inc., Hazelwood, MO, USA) according to recommendations of the European Committee of Antimicrobial Susceptibility Testing (EUCAST). Multi-drug-resistance (MDR) was defined according to the definitions of the EUCAST [17]. Oxacillin resistance was used as an indicator for methicillin-resistant *S. epidermidis* (MRSE) or methicillin-resistant *S. aureus* (MRSA).

Patients with an ODRI were diagnosed and treated according to recent guidelines and recommendations [18–20] using an interdisciplinary approach [21]. Revision surgeries or reoperations were documented within the treatment and follow-up period.

Follow-up examination was performed for a minimum of 22 months after initial treatment with a mean follow-up time of 26 months (range: 22–28 months). The following outcome parameters were investigated: cure, persistence of infection and recurrence of infection, the Lower Extremity Functional Score (LEFS) [22] and the SF-12 score [23]. The LEFS describes the functionality of the lower extremity (maximum score of 80 equates to the best functional outcome) [22]. The SF-12 assesses the patients physical and mental state and includes the physical component summary (PCS) and the mental component summary (MCS) [23]. The authors defined cure as absence of infection after surgical and systemic therapy had ended. In cured patients, the final functional status with restoration of joint or limb function was achieved and no local or systemic signs of infection were present at follow-up. The definition of persistence of infection and reinfection were based on the IDSA guidelines [18]: local signs of infection with the presence of a fistula and/or the proof of an organism from site of interest; systemic signs of infection, such as an abnormal C-reactive protein (CRP) level and/or elevated erythrocyte sedimentation rate (ESR). Systemic signs of infection must be related to underlying bone or joint infection and a different focus of infection should be excluded. In persistent infections, one of the above-mentioned parameters has to be positive at follow-up examination. Recurrence or relapse of infection was defined as appearance of above mentioned local or systemic signs suggesting a reinfection more than 14 days after a period of culture negativity or clinical quiescence after treatment with presumed eradication of infection. Recurrence of infection could occur at any time point within the follow-up interval and can either be cured or persist at the final follow-up examination. Absence/persistence of infection is not synonymous with cure/no-cure since cure is considering the overall treatment success and not just eradication of infection. The definitions of the outcome parameters are summarized in Table 1.

All participants gave informed written consent and Institutional Review Board approval to perform this study was granted by the responsible ethical board; Approval number: 12063.

Data was tested for normal distribution and presented as mean with standard deviation. Differences between the groups were analysed for parametric data with the Student *t*-test for independent variables and for non-parametric data with the Mann–Whitney *U*-test. Binary data were tested with a regression analysis and differences between the groups analysed with a Chi-square test. Univariate logistic regression models were used to determine the influence of each prognostic factor (obesity, smoking, diabetes mellitus, chronic immune suppression, open fracture, early onset infection, methicillin-resistance, MDR and Charlson comorbidity index) on cure. A p-value <0.05 was considered to be significant. Statistical tests were performed with IBM SPSS software v. 19 (IBM, USA).

Results

Patient populations

In total, 163 patients met inclusion criteria with a *S. aureus* or *S. epidermidis* ODRI of the major joints or long bones of the lower extremity.

Of the entire study population, 69% were male and the mean age was 54 (±17) years (range: 19–94 years). The older cohort