Journal of Infection (2015) **70**, 30—36

BIAM British Infection Association

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Factors related to outcome of early and delayed prosthetic joint infections

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Accepted 16 July 2014
Available online 28 July 2014

KEYWORDS
Prosthetic joint infections;
Surgical implant;
Infection;
Diagnosis;
Treatment

Summary In this prospective study, we evaluate the impact of adherence to a diagnostic and therapeutic protocol on prosthetic joint infections (PJI) diagnostic accuracy and outcome.
Patients and methods: Patients with early or delayed PJI referred over a 5-year period were included. Diagnosis was based on characteristic clinical signs, radiographic findings and microbiological evidence. Antibiotics were chosen on the basis of microbiological findings, and drugs active against methicillin-resistant staphylococci were administered if no microbiological evidence had been obtained.
Results: Inclusion criteria were met in 159 cases (median age 64 years, males 45%). 56 were early infections and 103 delayed infections. Comorbidities were reported in 99 (62%) cases. Positive cultures were obtained in 122/159 (77%), coagulase-negative staphylococci were cultured in 20%, *Staphylococcus aureus* in 28%, and *Pseudomonas aeruginosa* in 7%. In early infections, cure rate after debridement and antibiotic therapy was 80%. In delayed infections, cure rate after two-stage exchange was 85%. Of 28 patients with delayed infection treated with antibiotics without surgery, only 8 (29%) infections were suppressed 48 weeks after treatment discontinuation. Rifampin afforded a better outcome.
Conclusion: Appropriate diagnostic and surgical procedures and microbiologically driven antibiotic therapy including rifampin are recommended to improve diagnostic accuracy and outcome.

Abbreviations: CI, confidence interval; CoNS, coagulase negative staphylococci; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MIC, minimal inhibitory concentration; MRSA, methicillin resistant *Staphylococcus aureus*; PJI, prosthetic joint infection; RR, relative risk.

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http://dx.doi.org/10.1016/j.jinf.2014.07.008

Introduction

Infections involving surgical implants are difficult to treat because they require a long period of antibiotic therapy and repeated surgical procedures.[1,2] The number of people living with prosthetic joint implants will increase in the next few years and, consequently, the total number of prosthetic joint infections (PJI) will be higher, considering that implants can become infected not only in the perioperative period but also during the spread of bacteria from other sites of infection.[3]

PJI are associated with considerable individual disability and significant costs to the patients and to the public health authorities.[4] They are currently distinguished on the basis of the time of acquisition in early (those that develop within 3 months after surgery), delayed (3—24 months after surgery) and late (more than 24 months after surgery).[1] Currently, it is estimated that, despite the universal use of perioperative antimicrobial prophylaxis, the rate of PJI is just under 1% after hip replacement and 2% after knee replacement.[5,6]

The failure rate of PJI treatment can be high and patient characteristics, difficult-to-treat organisms, and inappropriate management choices are the main reasons for an unfavourable outcome.[7—10] It is advisable that treatment schedules be based on widely accepted published expert opinions and precise guidelines to avoid inappropriate non-standardized procedures and expensive treatments.[6,11,12] Only a few data are available on the effective cure rate obtainable with these therapeutic protocols and on the factors influencing the outcome after an appropriate treatment.[13,14]

In this prospective cohort study, we investigated the diagnostic accuracy and the factors related to outcome of patients with early and delayed PJI treated according to a previously established diagnostic and therapeutic protocol based on the available expert opinions (reviewed in [1,15,16]). Patients considered were referred over a 5-year period to our centre for an infectious disease (ID) consultation and therapeutic management.

Patients and methods

All patients observed in four orthopaedic centres of Campania region (Italy) because of suspected early or delayed PJI and referred to our observation between June 2007 and June 2012 for an ID consultation were considered. The research was conducted in accordance with the Declaration of Helsinki and national and institutional standards and patients gave their informed consent prior to be included in the study.

A diagnosis of PJI had to be defined by at least three of the following: (i) characteristic clinical signs and symptoms (i.e. persistent bone pain, local tenderness, sinus tract), (ii) two positive microbiological cultures with phenotypically identical organisms obtained from intraoperative specimens or joint aspirates, or from removed implant sonication, (iii) presence of acute inflammation on histopathologic examination (as determined by the pathologist), (iv) synovial fluid leucocyte of more than 1700 per cubic millimetre or a finding of more than 65% neutrophils, (v) radiographic evidences obtained by standard X-ray, bone CT scan, or nuclear methods.[1]

The inclusion criteria were: (i) diagnosis of PJI as established above; (ii) age >18 years; (iii) absence of implant loosening due to early infections (these patients were referred for two-stage exchange but were not included in the study because constitute a different population in respect to those with delayed PJI undergoing two-stage exchange). The exclusion criteria were: (i) post-therapy follow-up of less than 48 weeks; (ii) HIV infection.

Microbiologic studies

Cultures for aerobic and anaerobic had to be attempted in all cases. Antibiotics were not administered during a 2-week period, before specimens were obtained for microbiological analysis. Synovial fluid aspirate was collected in all cases for neutrophil count evaluation and microbiological cultures. At least 3 intraoperative specimens from purulent tissues surrounding prosthetic implant were collected for microbial examinations in the cases undergoing surgery. Fluid from implant sonication was cultured for cases undergoing two-stage exchange. Synovial fluid volumes of 0.5—3 ml were inoculated in Bactec Peds Plus/F bottles and incubated in a Bactec 9240 instrument for 14 days.[17] Tissue specimens were homogenized in 3 ml of brain—heart infusion broth for 1 min, and the homogenate was inoculated in aliquots of 0.5 ml, as described for synovial fluid. Implant sonication was performed as described by Pitt et al.[18] An isolate obtained by implant sonication was judged to be the causative agent according to Piper et al.[19] Susceptibility to antimicrobials was evaluated by E-test. Minimal inhibitory concentration (MIC) was related to CLSI breakpoints until 2010 when EUCAST breakpoints were used as interpretative criteria.

Treatment

Study protocol considered: (i) conservative strategies consisting of debridement, irrigation and prosthesis retention (DAIR) followed by antibiotic treatment for ≥10 weeks in the cases with early PJI, if no implant loosening was reported and periprosthetic tissues were not badly damaged and the duration of symptoms was less than 3 weeks (ii) two-stage exchange, consisting of infected implant removal and spacer placement followed by an antibiotic treatment course between 10 and 12 weeks prior to prosthetic implant replacement, for the cases with delayed infection; (iii) prolonged antibiotic therapy administered for at least a 4-week period after C-reactive protein (CRP) normalization for patients with a delayed infection for whom surgery was not performed due to patient's refusal or severe life-threatening co-morbidity.[20] One-stage exchange was not considered, as the procedure is not routinely performed in the referring orthopaedic centres. Empiric antibiotic therapy was started for each patient after surgery with parenteral antibiotics for 2 weeks until the microbiological culture results were available. The following therapy was based mainly on oral drugs selected on the basis of the susceptibility tests. For cases