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Periprosthetic Joint Infection Treatment in Total Hip and Knee Arthroplasty

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The cumulative incidence of periarticular joint infection is about 1.2%, and there are multiple ways to surgically manage these patients. Arthroscopy is not recommended because of poor outcomes of high infection recurrence. Open debridement and irrigation shows a success rate up to 80%, and this technique should only be considered during the very early stages of infection. For definitive treatment, one-stage or two-stage exchange arthroplasty is recommended, and the success rate after single-stage revision and two-stage revision is about 93% and 86%, respectively. However, comparative studies have not shown significant difference in the success rate of infection control comparing one-stage and two-stage surgery. Static or articulating spacers are implanted in two-stage exchange arthroplasty, and articulating spacers seem to show some advantage with regard to range of motion. Cement abrasion is considered a problem with articulating spacer placement, and there has been no significant difference in clinical outcomes between spacers reported yet.
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Introduction

Infection is one of the most challenging and devastating complications after total joint arthroplasty (TJA). A cumulative incidence of 1.2% has been reported for periprosthetic joint infection (PJI), which is slightly higher after total knee arthroplasty (TKA) (1.41%) than after total hip arthroplasty (THA) (0.92%).[1] Others have reported an overall infection rate of 1%-4% after TKA.[2,3] The incidence per prosthetic year for late PJI seems to be significantly lower than for early PJI. For TKA and THA, late PJI rates of 0.08% and 0.053% have been reported, respectively.[1]

According to the Finish joint arthroplasty registry, early infection that was defined as an infection within 3 months after surgery was found in 47% of all infected cases.[1] Delayed infection, which was defined as PJI between 3 and 24 months after surgery, was seen in 32%. This is often a result of hematogenous seeding during the first 2 years after surgery.[4] Late infection (>2 years after surgery) was seen in 21% of patients. However, the incidence of PJI in Scandinavia seems to be underestimated, which is owing to the fact that the registries are not designed for the registration of PJI.[5]

Infection is a very common reason for revision TJA. The most common reason for revision in TKA is infection (25%), followed by mechanical loosening (18.5%), and other mechanical problems (10.3%).[6,7] The New Zealand joint registry also reported that 25% of all TKA revisions are caused by infection and another 36.4% by aseptic loosening.[8]

In contrast, infection seems to be the third most common cause (15.4%) for revision after THA following dislocation (22.1%) and aseptic loosening (20.3%).[7] Interestingly, the infection rate has increased over time according to data from Dale et al[9] and Kurtz et al.[9,10] The infection rate after THA was 0.66% in 1990 and nearly doubled to 1.23% in 2004.

Readmission after TKA was reported to be approximately 2.5% and after THA was about 2%.[11] Patient readmission within 30 days after TJA was mostly due to surgical site infection (23.2%) and cardiovascular events (16.8%) in a Canadian hospital.

The most important risk factors for developing PJI are diabetes mellitus and obesity.[12] Typically diabetes mellitus

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causes impaired polymorphonuclear neutrophil cell function, reduces chemotaxis, and reduces phagocytosis.[13] An analysis of the Danish Arthroplasty Hip registry showed no difference in the rate of aseptic loosening between diabetic and non-diabetic patients.[14] However, diabetic patients showed a significant higher PJI rate after TJA. According to the Finish Arthroplasty Registry, male sex, seropositive rheumatoid arthritis, posttraumatic osteoarthritis, and a previously used semiconstrained or full-constrained TKA are typically associated with a higher risk of PJI after primary TKA.[15]

This review focuses on treatment options for PJI depending on the classification of PJI, antibiotic administration, and surgical treatment strategies.

Classification of PJI

The interval between the index surgery and PJI has a direct effect on the optimal treatment strategy. Generally, inoculation of micro-organisms on the TJA prosthesis may either occur exogenously or hematogenously.[16] Exogenous infections typically occur during surgery or the early phase of wound healing. Hematogenous infections may start at any time after TJA, but typically occurs after a symptom-free postoperative interval.

At the very early stages of implant colonization, micro-organisms are still in a planktonic form, which presents an active metabolic status and fast replication.[17] Planktonic bacteria adhere to the implant, but the binding is still reversible. When organisms colonize the implant surface, they form a biofilm that can effectively avoid surveillance and treatment by antibiotics. It can be interpreted as a result of the evolution of the micro-organism against the host.

Early biofilms are unstable and are still susceptible to host defense and antimicrobial agents.[18,19] Mature biofilm is formed by a high density of micro-organisms after a period of approximately 3 weeks. The biofilm develops a quorum-sensing system during that time, which is a form of interspecies and intraspecies bacterial cell-to-cell communication. The system is used by many pathogenic bacteria, including *Staphylococcus aureus* or *Pseudomonas aeruginosa*, to regulate the production and release of different virulence factors.[20] This mature biofilm can resist the host immune response, as well as antibiotics or other antimicrobial treatments. Thus, less-invasive surgical interventions may not be as successful in later stages of infection.

PJI has been classified according to the time of manifestation in early infection (within 3 months), delayed infection (3-24 months), and late infection (after 24 months).[21,22] The time frame is very important for guiding optimal treatment decision. Debridement, antibiotics, and implant retention (DAIR) might be successful within the first 4 weeks after surgery without the formation of a mature biofilm. Patients who present with well-fixed and stable implants with no sinus tracts or certain comorbidities, who are infected by micro-organisms that are susceptible to antibiotics against surface-adhering micro-organism may have an infection control rate up to 80% using this treatment method.[23-25]

Another classification proposed by Chiu and Chen[26] is also based on the timing after TKA. The authors distinguish between the following 4 types of infection:

Type 1: acute postoperative infection (<4 weeks after surgery),

Type 2: late chronic infection (>4 weeks after surgery),

Type 3: acute hematogenous infection with acute onset at the site of a previously well-functioning prosthetic joint, and

Type 4: positive intraoperative cultures, which is clinically unapparent infection with 2 or more positive intraoperative cultures.

The classification of PJI is important and helps to standardize the decision-making process. Generally, the following 3 surgical strategies are considered: (1) open debridement and exchange of the liner, (2) one-stage exchange arthroplasty, or (3) two-stage exchange arthroplasty. The last section discusses these treatment options in depth.

Antibiotic Treatment

PJI does not spontaneously resolve without the administration of antibiotics.[27,28] As the bacteria in PJI are encapsulated in a biofilm, bacteria cannot be easily phagocytized and the infection can only be cured by a combination of surgical and antimicrobial therapy.[29] Therefore, antibiotic regimens to treat PJI should last several weeks, up to 6 months or for life to suppress PJI using antibiotics.[21,30,31] Under suppressive antibiotic therapy, the goal is to mask the symptoms of infection with life-long antibiotic treatment.

Choosing the antibiotic regimen for treatment is difficult, as antibiotic treatment in the in vitro condition may not always translated to the in vivo situation.[30,31] In vitro susceptibility testing is normally done with planktonic bacteria, whereas the bacteria responsible for PJI are embedded in a biofilm. Antibiotic choice is dependent on the 2 different growth phases of bacteria—a logarithmic and a stationary one. In PJI, bacteria are in the stationary phase and bacteria are not susceptible to antibiotics that affect cell-wall synthesis, such as beta-lactams (cephalosporin, carbapenem, and penicillin) or glycopeptides (vancomycin and teicoplanin).[27,30] Thus, antibiotics that are effective against bacteria in the logarithmic phase may not be useful for treating PJI bacteria. For example, daptomycin is an excellent antibiotic against *Staphylococcal* biofilms in vitro,[32] but biofilm can only be eradicated in combination with rifampin in an established foreign body infection animal model (guinea pig).[33] The same results were found for dalbavancin.[34] Therefore, antibiotics should be tested against bacteria in the stationary phase to translate the results of in vitro observation into clinical practice.[31] For Gram-negative bacteria, quinolones are the preferred antibiotics. This has been shown in vitro, in vivo, and in clinical studies.[27,35]

An established and standardized antibiotic management plan for the treatment of PJI is shown in Table 1.[22] The initial