Accepted Article

Journal of Research and Practice on the Musculoskeletal System

JRPMS

Review Article

# Current treatment of infected arthroplasties

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**Abstract**

Total hip and knee arthroplasties are among the most popular and common orthopaedic surgical interventions. Despite the very high success rate of those operations and the ongoing technical improvements, they still carry the risk of various complications, with the deep infections being among the most serious ones. The periprosthetic joint infection is defined as the presence of bacteria in the joint space of the artificial joint and the surrounding tissues, which is significantly associated with laboratory and histological findings and clinical signs of inflammation. Those infections, according to the time of their occurrence are characterized as acute -early postoperative, delayed and chronic. The most common microorganisms responsible for their cause are the coagulase-negative Staphyloccocal species and Staphylococcus aureus. Treatment of those infections involves a variety of combinations of procedures, both conservative and operative; the best treatment is the one which combines the elimination of the infection with the least possible complications for the patient. Debridement with retention of the prosthesis, one stage arthroplasty exchange and two stage arthoplasty exchange are the most commonly accepted surgical procedures for the treatment of this complication, whereas arthroplasty resection without reimplantation and arthrodesis are salvage procedures in order to avoid the unfortunate, but at least very rare solution of the amputation of the limb.

**Keywords:** Arthroplasties, Infection, Joint, Prosthetic, Treatment

## Introduction

Total hip and knee arthroplasties are among the most popular and common orthopaedic surgical procedures. In the U.S.A. alone, 332.000 total hip replacements and 719.000 total knee replacements were done in the year 2010, and the projection of those numbers by the year 2030 is estimated to be 572.000 and 3.5 million respectively[1]. Despite the very high success rate of those operations and the ongoing technical improvements, they still carry the risk of various complications, with the deep infections being the most serious ones. Additionally, the growing numbers of total joint arthropasties also brings the increase of the absolute number of the infections.

The prosthetic joint infection (PJI) is defined as the presence of bacteria in the joint space of the artificial joint and the surrounding tissues, which is significantly associated with laboratory and histological findings and clinical signs of inflammation[2]. The criteria of the Infectious Diseases Society of America (IDSFA) for prosthetic joint infections include the evidence of inflammation on the histological examination of the periprosthetic tissue, the presence of fistula, the presence of purulent discharge around the prosthesis and the positive for microbes intraoperative cultures of the periprosthetic tissues[2]. The early diagnosis of this serious complication is crucial, since delayed intervention can lead to severe functional loss, high rates of morbidity and mortality and the need for extensive and complicated surgical procedures.

## Epidemiology

During the first and second year after the operation there is the highest risk for a prosthetic joint infection, with the cumulative risk being in the area of 0.5% after the first year and 1.4% after ten years[4]. It seems that total knee

*The authors have no conflict of interest.*

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***Edited by:*** *Konstantinos Stathopoulos*

***Accepted*** *30 March 2022*

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| **1. Obesity** |
| **2. Diabetes mellitus** |
| **3. Chronic treatment with immunosuppressive medications** |
| **4. Malignancy** |
| **5. Autoimmune diseases** |
| **6. Revision Arthroplasty as a procedure** |
| **7. Perioperative factors such as**<br>Prolonged operative time<br>Allogenic blood transfusion<br>Increased intraoperative hematoma<br>Perioperative urinary or respiratory infections |

**Table 1.** Risk Factors of Infected Arthroplasties.

arthroplasties are more prone to infections, most probably due to the much lesser soft tissue coverage of the prosthesis; PJI is the most common indication for revision after a total knee arthroplasty, whereas it is the third indication after a total hip arthroplasty[4]. Shoulder arthroplasty seems to share the same rates of PJI as the hip and the knee, whereas the elbow arthroplasty has greater risk, up to 3.3%[3]. It is expected that in the near future the incidence of PJI will further increase due to the greater number of arthroplasties done to older patients and of course to the improvement of the diagnostic methods. PJIs treatment has serious economic consequences, with the annual cost in the U.S.A. estimated in the area of 1.7 billion dollars[3].

## Risk factors

Several risk factors have been proposed for the occurrence of PJI; among them are the following[1]. First of all, obesity – with the value of body mass index (BMI) >35 being the cut-off value and it is correlated with wound complications[18]. Diabetes mellitus – most probable due to the increased formation of biofilm on the prosthetic material when the levels of blood glucose are high[5]. Furthemore, chronic treatment with immunosuppressive medications, malignancy and autoimmune diseases. Revision arthroplasty as a procedure has greater risk for PJI than the primary procedure, due to the longer surgical time, and the abnormal soft tissue envelope caused from the primary operation.

The last risk factors are the perioperative. Prolonged operative time, allogenic blood transfusion, increased intraoperative hematoma due to the surgical technique and perioperative urinary or respiratory tract infections, can all increase the risk for PJI (Table 1).

## Classification

PJIs are classified into three categories according to the time of the occurrence of the symptoms and this classification is important in determining the treatment[18]:

1. *Acute – early postoperative infection*: occurs in the first three months after the arthroplasty.
2. *Delayed-subacute infection*: the symptoms occur after the 3rd month and up to the 24th month postoperatively.
3. *Chronic infection*: the infection occurs 24 months after the arthroplasty.

The cause of the infection can be the surgical procedure or concomitant infection of the urinary tract or teeth. Another type of prosthetic infection has been reported, the asymptomatic bacterial colonization of the surface of the prosthesis[5]. The most common microorganisms responsible for the cause of PJI are the coagulase-negative Staphyloccocal species (CNS), and Staphylococcus aureus, which supports the hypothesis of the perioperative infection. The bacteria, having succeeded a stable adhesion, multiply, forming a stable biofilm on the surface of the prosthesis. This biofilm can be seen as a special form of bacterial life, being very resistant to antibiotic treatment and most of the times treated only surgically. While S. aureus and CNS account for between 50-60% of the PJI cases, streptococci and enteroccoci together are involved in the 10% of the incidents and gram – negative bacilli in less than 10%. Very interestingly relative large number of cultures (from 5% up to 34%) prove to be negative for microbes[6].

## Diagnosis

The diagnosis of PJI is based upon clinical, microbiological, radiological and histological criteria. The Musculoskeletal Infection Society (MSIS) takes into account the following criteria[7]:

*Major Criteria*: Diagnosis can be confirmed if only one of those is present.

1) Skin fistula which communicates with the prosthesis
2) Pathogen positive culture grown from at least two different fluid or tissue samples of the joint.

*Minor Criteria*: Diagnosis can be confirmed if four out of six of the criteria are present.

1) Elevated Erythrocyte Sentimentation Rate (ESR): >30 mm/h, and C-Reactive Protein (CRP) >10 mg/L
2) Elevated WBC in the synovial fluid: >1.100 cells/ul for Knee arthroplasty, >3.000 cells/ul for Hip arthroplasty.
3) Elevated neutrophils in the synovial fluid: >64% for Knee arthroplasty, >80% for Hip arthroplasty.
4) Occult pus in the joint.
5) Pathogen positive culture.
6) Acute inflammation on the histologic examination of periprosthetic tissue sample.

Several specific synovial fluid tests, like leukocyte esterase, a-defensin and nucleic acid amplification techniques for bacteria can play important role in diagnostic process[16]. Moderate evidence supports obtaining these tests without administrating any antimicrobial treatment. This will happen provided that the patient is not septic and his

life is not threatened. If a patient is suspected of having periprosthetic joint infection and previous antimicrobials have already been initiated, the sunovial fluid cultures have to been taken after two weeks to maximize the yield in the culture results[16].

Further diagnostic procedures such as Computed Tomography, Magnetic Resonance Imaging, Bone Scan and PET Scan should not be done as routine investigation tests.

In most of the times the clinical condition is characteristic, with the early manifestations being fluid discharge from the surgical wound along with the acute onset of fever, pain, erythema and oedema in the joint area; if untreated, the infection can lead to the fistula formation. Bacteremia and sepsis are very serious and life-threatening complications of condition. Chronic infection can present with gradually worsening joint pain and restraint mobility, radiological findings of prosthesis loosening and even fistula formation in the neglected cases.

## Treatment

As soon as the diagnosis of prosthetic joint infection has been confirmed, a decision must be taken regarding the appropriate treatment for the patient. Treating this kind of infections involves a variety of combinations of procedures, both conservative and operative, with the final decision depending upon the patient's wishes and the advice of the orthopaedic surgeon along with the infectious diseases specialist. The best treatment is the one which combines the elimination of the infection with the least possible complications for the patient. The selection of the appropriate surgical treatment depends on a number of criteria, such as the symptoms of the patient, the presence or the absence of a fistula, the possibility of wound closure at the end of the surgical procedure, the microorganism responsible for the infection, the antibiotic route (per os or iv), the general clinical condition of the patient along with his willingness to undergo one or two surgical procedures. The three basic aims of PJI's treatment is to: 1) Treat definitely the infection, 2) Restore full range of movement and pain-free the joint which was affected and 3) Minimize the side effects, the morbidity and the mortality of the patient; unfortunately, most of the times those three goals cannot be achieved altogether[1]. The various surgical and conservative treatment options are described in the following paragraphs.

### *1. Debridement with prosthesis retention*

This procedure, often described as Debridement, Antibiotics and Implant Retention (DAIR) is performed with open arthrotomy through the prior surgical incision, irrigation, removal of any obvious necrotic tissue, hematoma or infected soft tissue and most of the times replacement of the polyethylene liner of the joint prosthesis. The overall success rate of this procedure is around 50-55%[8], with the main indications being the following:

- Acute infection (less than three weeks after the initiation of the symptoms).
- Acute hematogenous infection (ideally, just 48 to 72 hours after the initiation of the symptoms).
- No fistula found in the soft tissues surrounding the affected joint.
- The prosthetic joint is stable, with no signs of loosening.
- The quality of the soft tissues surrounding the joint is acceptable.
- There is availability of antimicrobial therapy for the pathogen responsible for the infection.

After the surgical debridement and the wound closure, intravenous broad-spectrum antibiotic therapy is immediately commenced until the responsible for the infection microbe is identified from the intraoperative cultures and then the specific, antibiogram-based antibiotic treatment is administered intravenously for a period of 2-6 weeks. In the majority of the patients this first period of the intravenous antibiotic treatment is followed by oral antibiotic therapy, which would last up to six months for the infected total knee arthroplasties and up to three months for the infected total hip arthroplasties. This oral treatment should always include rifampicin in order to cover stap. species infections. According to Byren et al (2009)[8] the failure rates after the DAIR procedure are higher if the debridement is done arthroscopically, for prosthesis which have already been debrided at least once and when the responsible for the infection microbe is Staphylococcus aureus; although the risk of failure increases after discontinuation of the antibiotics, it seems that antibiotic treatment just postpones and does not prevent the recurrence of the infection – if this recurrence is going to occur.

### *2. One stage arthroplasty exchange*

Also referred as direct exchange procedure, involves open arthrotomy with irrigation, debridement and removal of the prosthetic material along with the orthopaedic cement used in the primary operation. After thorough irrigation of the surgical wound, a new prosthesis is fixed in place, using orthopaedic cement containing the specific against the microbe responsible for the infection antibiotic which was identified by the antibiograms. The direct exchange procedure is much more popular in Europe in comparison to the U.S.A., when treating infected total hip, in comparison to total knee arthroplasties, and when the microorganism responsible for the infection is already known. Its success rate is in the area of 75-100%, having the benefits (in comparison to the two-stage procedure), of a single anaesthetic, shorter time in the hospital, less cost and definitely preserving much more function to the patient; the main indications for performing it are the following[9]:

- There is no fistula present in the surrounding the joint soft tissues.
- Patient with no major co-morbidities.
- Relative healthy soft tissues surrounding the joint.

- Adequate bone stock in order to insert the new prosthesis.
- There is no prior extensive use of antibiotics.
- Low load of the organism from the microbe, with adequate sensitivity to the antibiotics.

Once more, after the operation, antibiotic treatment is mandatory, involving 4-6 weeks of intravenous antibiotics, followed by per os treatment for 3 up to 12 months.

### *3. Two-stage arthroplasty exchange*

Two-stage arthroplasty exchange (TSE) is the treatment of choice for prosthetic infections which occur in more than four weeks after the initial procedure and is regarded by many authors, as the most definite surgical option[3]. The purpose is to leave the joint cavity free of any foreign body for a transitional period to enhance the efficacy of antibiotic therapy and cure of infection, for reimplantation into an aseptic environment. The expected success rates are about 85-95%[17]. The main indications for this procedure are:

- A relative healthy patient, who is able to undergo multiple surgical procedures.
- Adequate bone stock of the area.
- Presence of fistula in the tissues surrounding the infected joint.
- Radiological signs of loosening of the prosthesis.
- Multi-drug resistant pathologic microorganism responsible for the infection (for example candida species or infection from fungal microorganisms).

The first stage of this surgical technique involves thorough surgical debridement and irrigation of the infected tissues, removal of all the prosthetic devices of the original operation, including the orthopaedic cement, collection of multiple culture specimens[3-5], deep staged samples of differing types (joint fluid, synovium, bone, cement)[17] and finally placement in the joint area a custom-made cement spacer, loaded with antibiotics. The role of this spacer is: 1) To provide a continuous supply of antibiotics to the infected area in order to treat the infection, 2) To support the joint as much as possible, maintaining even a rudimentary mobility and 3) To prevent the shrinkage of the soft tissues of the area. For the next four to six weeks the patient is treated with intravenous antibiotics, specific to the pathogenic microorganism which was isolated from the first-stage surgical procedure. This period is followed by another four to six weeks in which the patient is free from antibiotics, but is evaluated for signs and symptoms of ongoing infection; in case those signs are positive, along with elevated inflammatory markers and positive for microbes cultures of the synovial fluid, a second debridement surgical procedure has to take place and further intravenous antibiotic treatment has to follow[10].

In contrast to the two previously mentioned surgical treatment options (debridement with prosthesis retention and one-stage arthroplasty exchange), most of the times during the two-stages arthroplasty exchange, combination with rifampin antibiotic treatment is not indicated, since there is no prosthetic material left in place. When the surgeon is confirmed from both the clinical symptoms and signs and the laboratory findings that there is no on-going infection, the second stage of the revision of the arthroplasty is carried out, using antimicrobial loaded polymethyl methacrylate (PMMA, bone cement), followed again with intravenous antibiotic treatment until the cultures taken after the second operation become negative.

The success rate of this method is quite large, in the area of 87% to 100%. Lange et al (2012)[11] published a systematic review and meta-analysis including in total 929 patients who received a two-stage revision arthroplasty and 377 patients who received a one-stage revision arthroplasty for infected total knee and hip prosthesis. The re-infection risk rate, as the final outcome of those procedures was 13.1% in the one-stage group and 10.4% in the two-stage group, indicating that there seems to be a risk of three more infections per 100 patients treated with the one-stage method in comparison to the two-stage method.

### *4. Arthroplasty Resection without Reimplantation*

Arthroplasty resection without prosthesis re-implantation is a salvage surgical procedure, performed in order to prevent the amputation of the patient's limb; it is carried out in cases where the previously mentioned methods (debridement with prosthesis retention, one- and two- stage arthroplasty exchange) have failed, or in patients with severe health comorbidities and functional impairments, for whom it is estimated that the above mentioned surgical methods will greatly burden their clinical picture or will not offer the substantial improvement in the mobility and the function of the infected joint. The first mention of this surgical technique was made in 1945 by Gathorne Robert Girdlestone who, in an era before antibiotics' introduction, described this excision hip arthroplasty as a salvage procedure for the treatment of septic arthritis of the hip joint; since then this particular procedure is mentioned by most of the authors as "the Girdlestone situation" or "the Girdlestone procedure"[12].

In many cases this condition can occur after the first stage of the arthroplasty exchange, where the patient, for various reasons is not keen or capable of proceeding to the second stage of the arthroplasty revision; in this particular situation, the polymethyl methacrylate spacer can remain in situ permanently, providing surprisingly a reasonable degree of joint movement and function for a long period of time, especially in the hip joint. Choi et al in 2014[13] published a case series of 18 patients with prosthetic joint infections (seven total knee and eleven total hip arthroplasties), who were treated permanently, for various reasons with resection of the original arthroplasty and retention of the PMMA spacer. After a 44 months follow-up, 3 out of the 18 spacers were revised (one because of recurrent infection and two because of loosening), with the remaining 15 patients being infection-free and with an acceptable level of function of their affected joints (Harris Hip score 92 and Knee Society knee score 92) and well coping with the activities of their

daily living. The researchers therefore concluded that this salvage surgical technique may prove to be effective as a permanent solution of an infected prosthetic arthroplasty.

Antibiotic treatment following resection arthroplasty follows the generic rules described in the previous procedures: four to six weeks of intravenous, microbe-specific antiobiotics, followed sometimes from even longer per os treatment.

### 5. Arthrodesis

Arthrodesis (joint fusion), is another salvage procedure, aiming to avoid the amputation of the limb. Most of the times this procedure takes place in the knee joint, either with an intramedullary nail, or with the use of external fixation device, with the end result being an acceptable function of the patient's joint in most of the cases[14].

### 6. Amputation

Amputation will be reserved for those patients in which all the previous therapeutic interventions have failed and in those in which the infection is so severe that is becoming life-threatening. Amputation, fortunately, is performed in less than 0,1% of the total hip and knee arthroplasties[15]. An additional problem for those patients is that after the amputation or the disarticulation procedure, most probably they will need further irrigation and debridement, meaning that only a minority of them will be able to be fitted with a functional prosthesis. Antibiotic treatment usually is prescribed for one or two days after the operation, unless the pathologic situation is further complicated with chronic osteomyeliitis, meaning that the antibiotic treatment after the amputation should continue until the clinical and laboratory findings show that the infection has resolved.

## Conclusion

The infection of a total hip or knee arthroplasty, with the most common responsible pathogen being Staphylococcus aureus, is an unfavourable and very aggravating complication for the patient; while the revision rate of total knee arthoplasties has already doubled since 2015, the revision rate of total hip arthroplasties is expected to double by the year 2026. The risk factors of this devastating complication should be indentified during the preoperative period, during surgery, in the immediate postoperative period and even after the end of the patient's hospitalization, when he has returned back home. According to the patient's history, those risk factors could be diseases such as diabetes and rheumatoid arthritis or habits such as smoking, while other risk factors depend upon the condition under which the operation has been performed, such as the type of the prosthesis applied or the duration of the operation. Postoperative risk factors such as cardiovascular complications, prolonged use of non-steroidal anti-inflammatory medication (NSAIDS), and dental procedures can also lead to prosthetic infections even at a much later stage, and therefore should be identified and treated promptly.

Among the various preventive interventions that have been proposed, the most effective ones could be the following[1]:

- *Reduction of skin flora*, especially in patients who are colonized by Staphylococcus aureus species.
- *Optimal antibiotic treatment during the perioperative period.*
- *Routine use of laminar airflow in the operating rooms and body exhaust suits by the surgeons.*
- *Routine use of antibiotic loaded polymethyl methacrylate for the implantation of the prosthetic devices.*
- *Routine and thorough antibiotic treatment before any dental procedure.*

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