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REVIEW ARTICLE

Prosthetic joint infections: diagnosis, management, and complications of the two-stage replacement arthroplasty

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Abstract

Despite improved strategies to prevent prosthetic joint infection, as the total number of joint replacements increases, so does the absolute number of infections. Radiography serves as the first-line imaging modality for the assessment of a suspected prosthetic joint infection. Additionally, serial radiographs acquired after a surgery to eradicate a prosthetic joint infection are an important clinical tool. Prosthetic joint infections are often treated with a 2-stage replacement arthroplasty utilizing a prosthesis with antibiotic-loaded acrylic cement. While complications are uncommon with this procedure, imaging may demonstrate periprosthetic fractures, as well as spacer migration, joint dislocation, and spacer fracture. We describe the classification of prosthetic joint infections, the clinical and imaging diagnosis, and treatment strategies. Familiarity with the hardware utilized in the management of the prosthetic joint infection, and its potential complications is fundamental to accurate imaging interpretation.

Keywords Prosthetic joint infection · PROSTALAC · Two-stage replacement arthroplasty · Joint replacement · Arthroplasty

Introduction

Joint replacement is a life-enhancing procedure, aimed at providing pain relief, restoration of function and independence, and overall improvement in quality of life [1]. Orthopedic surgical hardware is increasingly being used for fracture reduction, arthrodesis, and arthroplasty. Although infection rates for prosthetic implants have dropped in recent years as a result of perioperative antibiotic prophylaxis, improved surgical techniques, and laminar airflow in operating rooms, as the use of implants rises, so does the absolute number of infections [2–4]. In 2010, in the USA alone, there were 332,000 total hip and 719,000 total knee arthroplasties performed. These numbers are projected to reach 572,000 and 3.48 million by 2030 for hips and knees, respectively [1].

Prosthetic joint infection (PJI) refers to an infection involving the prosthesis and tissues surrounding the implant, with any joint susceptible [1, 4]. Periprosthetic infection is the leading cause of revision total knee arthroplasty, and third most common cause for total hip arthroplasty revision, with an estimated incidence of primary total knee or hip arthroplasties complicated by periprosthetic infection of 0.2–3% [2–6]. PJIs are associated with a 1-year mortality rate of 8–25.9% [4].

On initial contact with blood, plasma proteins are adsorbed onto the surface of the prosthesis forming a "conditioning film" for which microorganisms can adhere. Some microorganisms, such as *Staphylococcus epidermidis*, are capable of synthesizing glycoproteins, transforming the conditioning film into a biofilm, or glycocalyx, protecting the microorganism from the body's immune response and from antibiotics [1, 3]. The biofilm is a complex, highly organized community, with a well-hydrated extracellular matrix. The bacteria in the biofilm are up to 1000 times more resistant to antibiotics than systemic bacteria [2].

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PJIs can occur through direct contamination during surgery, hematogenous spread as a result of bacteremia related to a remote site of infection, or as a contiguous infection due to contact with an adjacent site of infection or open wound [2]. PJIs that occur within the first few months of joint implantation are most likely related to microorganisms acquired at the time of surgery, such as *Staphylococcus aureus*, while late infections are often related to chronic infection from indolent microorganisms such as coagulase-negative staphylococci, or hematogenous seeding of bacteria from a distant site [5]. Additional causative microorganisms include streptococci, enterococci, and gram-negative bacteria, among others [1, 4].

While imaging plays a minor role in acute infections, or those that occur within 2 weeks postoperatively, it may be useful for those with chronic infection where clinically overt and systemic manifestation are rare [2]. Radiographs are acquired to assess for osteolysis or hardware loosening that might suggest infection, among other features detailed in the section of "Diagnosis of prosthetic joint infections", and are most effective when studied serially over time [4, 7–9] (Fig. 1). Advanced imaging techniques play a limited role in the diagnosis of the PJI, being both time-consuming and expensive [7].

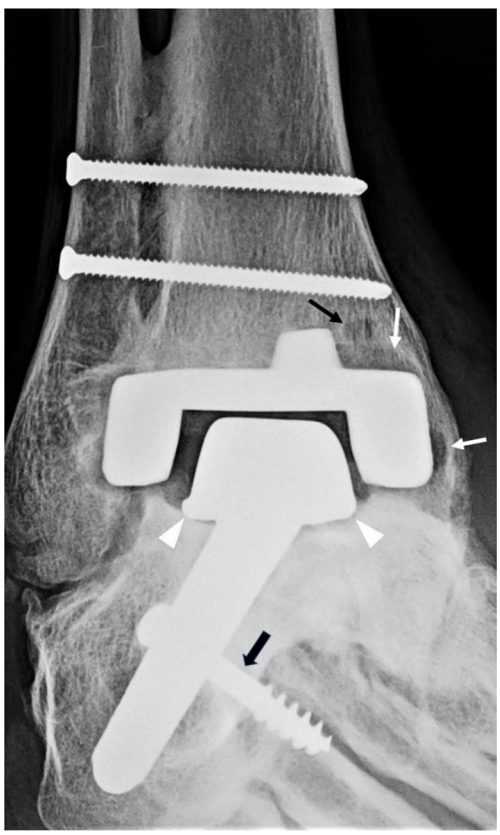


Fig. 1 53-year-old man with late-onset prosthetic joint infection 7 years after an Agility total ankle arthroplasty with a custom stemmed talar component. Mortise radiograph of the ankle demonstrates periprosthetic lucency (white arrows) and osteolysis (black arrow) adjacent to the tibial component (arrowheads: subsidence of the talar component; block arrow: retained screw from a remote triple arthrodesis)

Classification of prosthetic joint infections

The clinical classification frequently used for PJIs is based on the time of onset. The basis for this classification was proposed by Coventry et al. in 1975 and modified by Fitzgerald et al. in 1977 [10, 11]. Classification by time of onset can be early, delayed, or late. The distinction of these categories varies within the literature, such as defining an early onset infection as within 1 month [12]; however, most studies define an early onset PJI as occurring within 3 months of surgery [13]. There is no consensus whether a period of 3 months has a worse outcome than 1 month [14]. A delayed infection has been defined as occurring after early onset, but before 12 months or 24 months, with most studies stating within 24 months [13]. Lastly, a late onset infection occurs after the delayed period, usually beyond 24 months. The utility of classifying infection by time is that it provides clues as to the causative organism and route of infection, helping to guide clinical management [15] (Table 1).

Early-onset infections are due to virulent pathogens, which most commonly are *Staphylococcus aureus* or gram-negative bacilli [16]. The infection is acquired during the implantation or secondary to wound dehiscence. The typical patient presentation includes wound drainage, joint pain, effusion, and fever. At the site of the implant, there is edema, erythema, and induration [17].

Delayed-onset infections are due to less virulent pathogens, which are usually coagulase negative staphylococci or more rare isolates such as *Propionibacterium acnes* [16]. The infection is acquired typically during implantation. The patient often presents with persistent joint pain with or without implant loosening. Notably, loosening of an implant related to infection may be difficult to differentiate from aseptic loosening. With septic loosening, there is persistent pain, while aseptic loosening typically generates pain with motion or weight-bearing, but overall the two are difficult to distinguish clinically [13].

Late-onset infections are usually acquired by hematogenous spread from a distant source of infection. A source of infection is identified in about 50% of cases [1]. Clinically, the patient may present with an acute onset of infectious symptoms in a previously well-functioning joint [17].

Although most studies use the conventional classification governed by time of onset of infection, a few alternative classifications have been proposed. One classification by Tsukayama et al. places PJIs into four categories, three of which are based on clinical presentation: early postoperative, late chronic, or acute hematogenous. Early postoperative is defined as a wound infection that develops within 1 month

Table 1 Classification of the prosthetic joint infection by time of onset. Although alternative classifications of the prosthetic joint infection exist, time of onset is the most often used in studies [1, 4, 6, 10–17]

Time of onset	Definition	Causative organism	Acquisition	Management
Early	Within 1–3 months of surgery	Virulent pathogens; i.e., *S. aureus* or gram-negative bacilli	During implantation or secondary to wound dehiscence	Surgical debridement with replacement of prosthetic components not anchored to bone combined with antibiotics
Delayed	After early onset, but before 24 months	Less virulent pathogens; i.e., coagulase negative staphylococci or P. acnes	During implantation	Removal or revision of prosthesis with antibiotics
Late	After the delayed period/24 months		Hematogenous spread from distant source of infection	Removal or revision of prosthesis with antibiotics

of the surgery. Late chronic develops after 1 month with an insidious clinical course. Acute hematogenous is associated with a documented or suspected antecedent bacteremia and characterized by an acute onset of symptoms. Lastly, a fourth clinical setting is defined as having positive intraoperative cultures. An obvious advantage of this classification is greater emphasis on the clinical presentation rather than categorical placement based on time of onset alone, which does not always guide treatment decisions, in particular with regard to indications for prosthesis removal [12].

Another alternative classification utilizes three of the categories from Tsukayama et al., early postoperative, late chronic, and acute hematogenous, which are referred to as types I, II, or III. In addition, the systemic host status is graded using a number of patient factors, and the involved limb is also graded on several factors, which include active infection, soft tissue necrosis, or the presence of a fistula or abscess. This system attempts to provide a more specific description of PJIs [18, 19].

A study by Romano et al. proposed an all-encompassing bone and joint infection (BJI) classification, including PJIs, based on 10 previously proposed classifications using a seven-point scale: clinical presentation, etiopathogenesis, anatomopathological findings, host type, microorganism, bone defect, and soft tissues [20].

Currently used diagnostic algorithms, such as those proposed by the Infectious Disease Society of America and Musculoskeletal Infection Society (MSIS), detailed further under "Diagnosis of prosthetic joint infections", place a heavy emphasis on cultures and laboratory findings, and broadly stratify patients into acute and chronic categories using 6 weeks as a cutoff [21, 22].

Diagnosis of prosthetic joint infections

The MSIS standardized criteria for PJIs in 2011 [23]. This original classification defined PJI as having either one of the major criteria of (1) presence of a sinus tract communicating with the prosthesis, or (2) a pathogen isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint, or (3) if four of the following six minor criteria are present: (a) elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration, (b) elevated synovial leukocyte count, (c) elevated synovial neutrophil percentage (PMN%), (d) presence of purulence in the affected joint, (e) isolation of a microorganism in one culture of periprosthetic tissue or fluid, or (f) greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at × 400 magnification [23]. This "gold standard" definition was universally applied by all physicians, surveillance authorities such as the Centers for Disease Control, research community, and others involved in the management of PJI [23]. The criteria largely resulted in clinicians being more confident in their diagnosis and in providing appropriate treatment, as well as improved research collaboration and consistency [24].

The emergence of new diagnostic tests and lessons learned following the institution of the original MSIS criteria resulted in an updated version of the criteria published in 2018 [24]. The emergence of new techniques, such as serum D-dimer, synovial leukocyte esterase, synovial alpha-defensin, and synovial C-reactive protein, as well as molecular techniques, such as next-generation sequencing, resulted in modification of the original diagnostic criteria to an evidence-based scoring system for knee and hip PJIs [24–27]. The modified system judges the relative weights of each test and takes into account pretest probability to determine a score that can be used to diagnose patients in the preoperative period [24].

The new criteria emphasize that elevated CRP > 1 mg/dL, D-dimer > 860 ng/mL, and ESR > 30 mm/h are the most important variables associated with PJIs. The most significant synovial markers associated with PJIs are elevated white blood cell (WBC) count > 3000 cells/μL, alpha-defensin signal-to-cutoff ratio > 1, leukocyte esterase ++, polymorphonuclear (PMN) percentage > 80%, and CRP > 6.9 mg/L [24].

Although advances in laboratory testing and imaging modalities help to facilitate the diagnosis of PJI, a high clinical suspicion and a thorough history and physical examination

remain the mainstay in the initial diagnosis of a patient with a painful joint arthroplasty [8]. Risk stratification as high or low probability for infection is crucial, and assessing for risk factors that increase the likelihood for infection such as male gender, alcohol/drug/tobacco use, previous joint surgery, depression, inflammatory arthropathy, immune suppression (to include corticosteroid and immunosuppressive therapy), diabetes mellitus, obesity, prolonged surgery time, megaprostheses, malnutrition, early implant loosening (< 5 years), early osteolysis (< 5 years), and postoperative complications such as hematoma, superficial surgical site infection, wound drainage, and wound dehiscence, is important [1, 2, 4, 5, 28].

Serologic testing, in particular, ESR and CRP are useful screening modalities. If both tests are negative, there is a low risk of PJI. Conversely, if both tests are positive, this raises suspicion for PJI and aspiration of the joint is suggested according to the American Academy of Orthopaedic Surgeons (AAOS) clinical guidelines [28].

Joint aspiration may be performed at the bedside, intraoperatively, or with image guidance. The synovial fluid should be analyzed for WBC count, differential (% PMNs), and aerobic and anaerobic cultures [28]. The International Consensus on PJI recommends WBC > 3000 cells/μL and > 80% neutrophils as highly suspicious for PJI [29]. Culture is the best means to diagnose infection, but has poor sensitivity [30]. If no fluid is obtained, also referred to as a "dry tap," performing lavage of the joint with sterile saline is not universally recommended, as no high-quality studies exist supporting the diagnostic value of this method, which may dilute microorganism concentration, be unrepresentative of joint fluid, and with the technique posing a potential risk of causing infection in an aseptic arthroplasty [28, 31]. A dry tap does not exclude infection, and repeat aspiration may be indicated.

Aspiration can be achieved by the radiologist with fluoroscopic guidance; however, this is without direct visualization of the soft tissues and fluid [32]. Nevertheless, the fluoroscopic imaging provides the radiologist with a roadmap of osseous landmarks that are utilized to place the needle into the joint, which is ultimately confirmed with the injection of a small quantity of iodinated contrast. Ultrasound and computed tomography (CT) provide needle guidance into the joint space with the added advantage of visualization of the surrounding soft tissues and joint. Ultrasound-guided aspiration of the prosthetic joint has demonstrated a 69% sensitivity, 94% specificity, and 83% accuracy, while CT has demonstrated a 70% sensitivity, 100% specificity, and 84% accuracy for the diagnosis of infection in previous studies [32]. Ultimately, the accessibility of a given modality and operator proficiency in the use of the various modalities available plays a large role in the decision to use one approach versus another.

Intraoperative testing can be used for the diagnosis of PJIs, particularly if the diagnosis is indeterminate. Cultures are the most reliable way to identify organisms, and obtaining multiple tissue samples for culture is recommended within the AAOS guidelines. Frozen section can be useful when the diagnosis is uncertain although it depends on the surgeon's specimen samples, the skilled interpretation of the pathologist, and the threshold of the WBCs [28]. The use of intraoperative gram stain is not recommended by the AAOS as it has poor sensitivity [33].

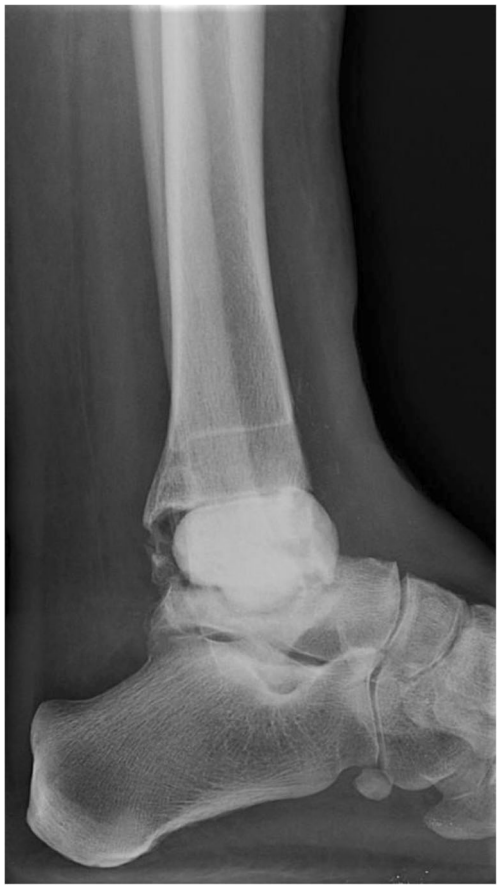


Fig. 2 64-year-old woman with delayed infection after ankle arthroplasty. Lateral ankle radiograph after first stage of two-stage replacement arthroplasty demonstrates implantation of a static antibiotic-impregnated cement spacer

Imaging

Imaging of suspected PJI is primarily by radiographs, despite their lack of sensitivity and specificity. Radiographs are most helpful when studied serially after implantation and compared with prior studies [7, 8]. Notably, radiographs are often normal in the early stages of infection [8, 9].

The rapid migration of a prosthesis, defined as at least 2 mm within 6–12 months, rapidly progressive periprosthetic osteolysis, and irregular appearing or multifocal periprosthetic osteolysis reflect features highly suspicious of PJI on radiographs. Periprosthetic lucency can occur at the metal-bone or cement-bone interface (Fig. 1).

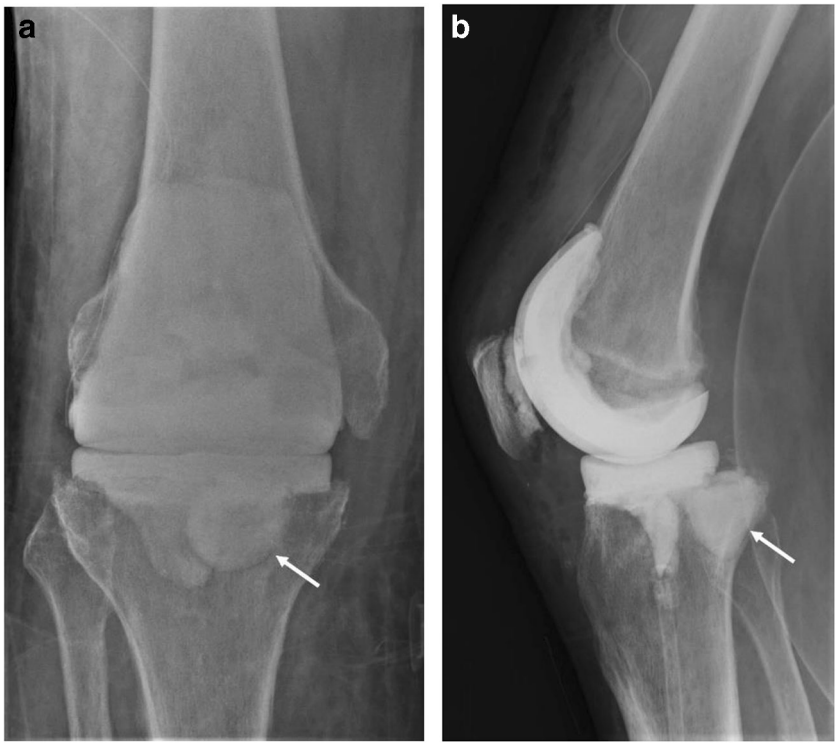


Fig. 3 62-year-old woman with an infected right knee prosthesis. Anteroposterior (**a**) and lateral (**b**) radiographs of the right knee after explant of the infected prosthesis and placement of PROSTALAC (the femoral and tibial components were constructed using StageOne™ Knee Cement Spacer Molds by Zimmer Biomet). Cement has also been placed in a pre-existing medial tibial plateau defect (arrow)

Additional features of PJI apparent on radiography include osseous erosions and new bone formation apparent within 3–6 months postoperatively, generalized bone resorption, transcortical sinus tracts, periosteal reaction, cement fracture, and sclerosis. Unfortunately, there is considerable overlap in the imaging features of PJI, aseptic loosening, and particle disease. Rarely apparent, but also suggestive of infection, is the presence of a sequestrum or gas about the prosthesis/soft tissue emphysema [4, 8, 9].

CT, magnetic resonance imaging (MRI), and ultrasound play limited roles in the diagnosis of PJIs, and the AAOS clinical practice guidelines do not recommend the routine use of these imaging modalities [8]. Both CT and MRI are prone to artifact related to the metal implant [4]. CT can detect abscesses around the arthroplasty, bone erosions, periprosthetic lucency, fistulae/sinus tracts, and communications between fluid collections. In addition to those findings apparent on CT, MRI can also detect bone marrow signal abnormalities. Ultrasound can detect collections of fluid within or adjacent to the joint, as well as subcutaneous fistulae [7, 9].

Although MRI is limited by artifact, more recent prostheses are made with less ferromagnetic alloy materials, such as titanium. Ferromagnetic alloy materials are the primary driver of metal-related susceptibility artifacts on MRI. Additionally, technologic advancements in metal reduction sequences, to include metal artifact reduction sequences (MARS), slice encoding for metal artifact correction (SEMAC), and multi-acquisition with variable-resonance image combination

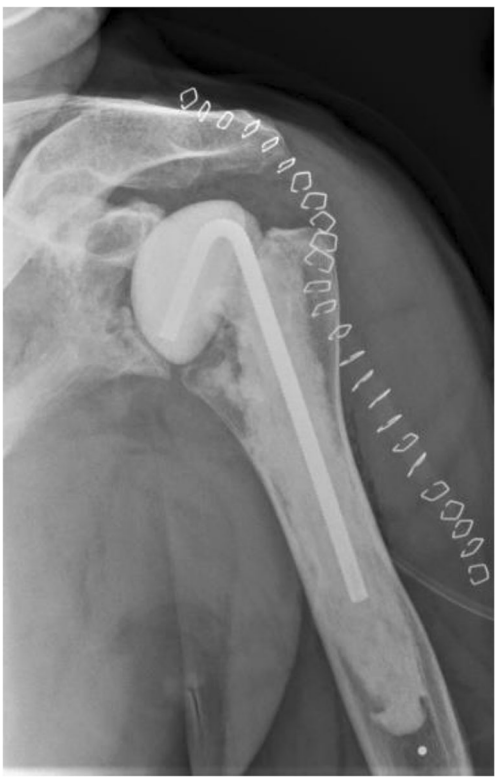
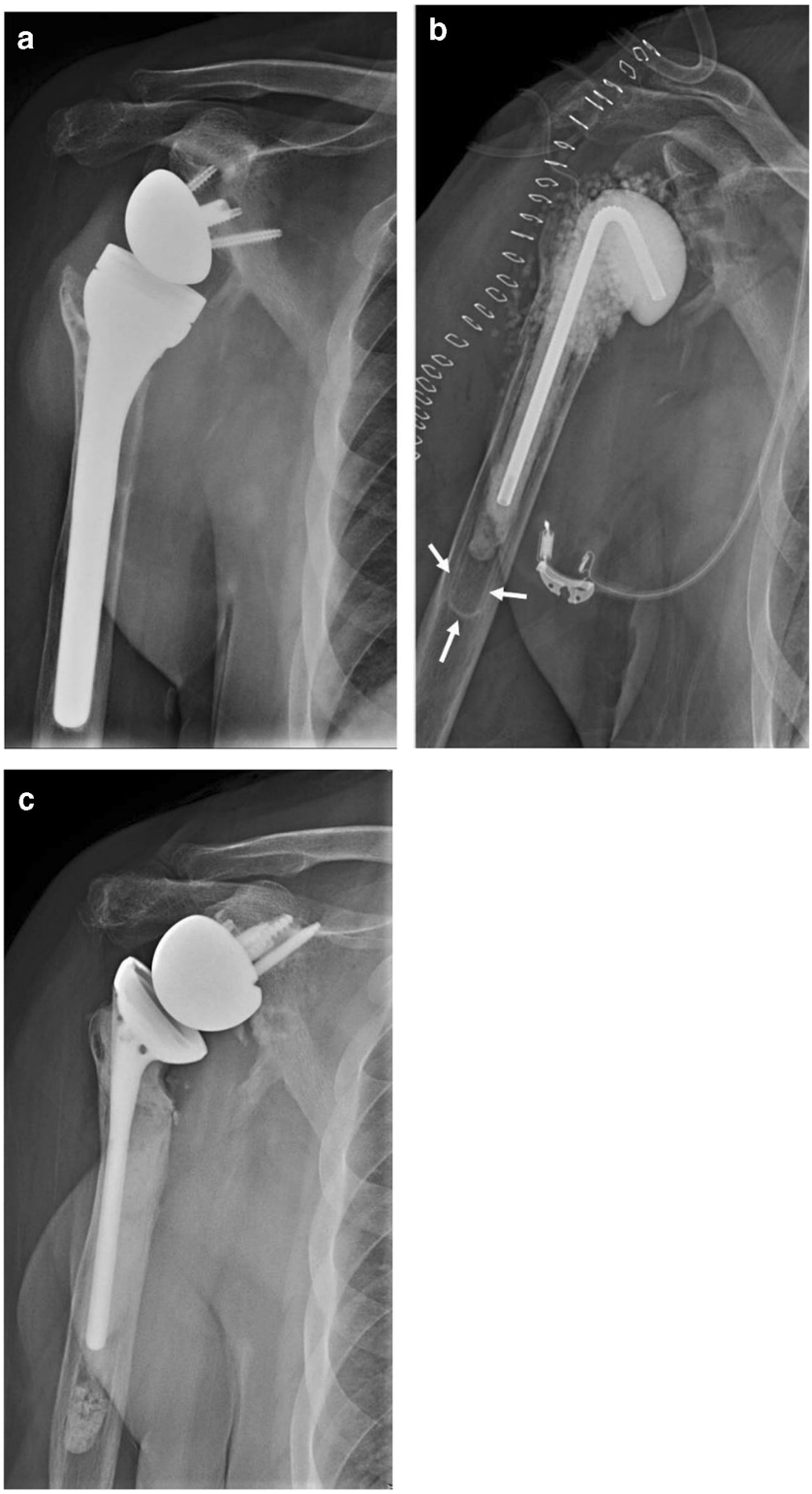


Fig. 4 49-year-old man with a postoperative anteroposterior shoulder radiograph after the first stage of a two-stage revision demonstrating an articulating shoulder spacer (InterSpace Shoulder)*. *The InterSpace Shoulder is a preformed unipolar hemiarthroplasty made of gentamicin-impregnated polymethylmethacrylate (PMMA) bone cement and a stainless-steel core (https://www.exac.com/spacers/. InterSpace®: Trust the Science. Accessed: 9/5/2019. 2018)



(MAVRIC), have made MRI a more feasible option in the diagnostic work-up of the suspected PJI. Prior studies have demonstrated 65–92% sensitivity and 85–99% specificity for infection at the knee, and 94% sensitivity and 97% specificity at the hip [32, 34].

Radionuclide imaging has low specificity, but may predict the absence of infection with a negative scan when the diagnosis of PJI is indeterminate, for instance in the case of failed attempts to retrieve synovial fluid [9, 35]. The "triple-phase scan" (Tc-99 bone scan, In-111 white blood scan, and sulfur

◀ **Fig. 5** 57-year-old man with a chronically infected polymicrobial right reverse total shoulder arthroplasty treated with seven debridement and irrigation procedures with retention of the implant in the span of 6 years. He had a persistent draining sinus with grossly purulent discharge, ultimately warranting a two-stage replacement arthroplasty. Anteroposterior radiograph of the right shoulder (**a**) demonstrates a reverse total shoulder arthroplasty. Postoperative anteroposterior shoulder radiograph (**b**) after the first stage of a two-stage revision procedure demonstrates an articulating shoulder spacer (InterSpace Shoulder) and placement of antibiotic beads. Radioluceny (arrows) distal to the stem of the spacer is normal and represents the cavity left from the original implant. He was treated with 6 weeks of intravenous antibiotics and chronic oral suppression with doxycycline. Five months after revision to antibiotic spacer, the patient was cleared for a second-stage implantation by the multi-disciplinary managing team. Anteroposterior shoulder radiograph (**c**) after the second stage of the revision procedure demonstrates conversion to a reverse total shoulder arthroplasty

colloid scan) may improve the sensitivity and specificity of an isolated 3-phase bone scintigraphy study, and is generally recommended over a single nuclear test alone [9, 32, 36]. The routine use of FDG-PET/CT in patients with suspected PJI is not supported [9].

Pathogenesis, surgical management, and complications of the two-stage replacement arthroplasty

In the majority of cases, the successful management of a PJI requires surgical intervention and medical therapy [1]. Treatment strategies vary depending on the clinical scenario, and include open or arthroscopic debridement without removal of the prosthesis, resection of the prosthesis without reimplantation, resection of the prosthesis with reimplantation of a new prosthesis either at the time of removal (one-stage or direct arthroplasty exchange) or delayed by weeks to months (two-stage arthroplasty exchange), arthrodesis, amputation, or antimicrobial suppression without surgery [1].

In cases of an acute infection, or those detected and treated within 2–4 weeks of the beginning of the infection, a biofilm has not fully formed. While the microorganisms are protected by mucus created from extracellular polymeric substances that limits the efficacy of antibiotics and the host's immune response, the film is still treatable. Therefore, in the acute infection, treatment is aimed at rupture of the biofilm. An attempt at prosthesis-preserving treatment is justifiable if the infection is acute, the implant is well anchored, soft tissues are intact, and the pathogen is easily treatable. Management may include surgical debridement with replacement of prosthetic components not anchored to bone, such as the polyethylene liner or modular femoral head, combined with antibiotic therapy for 6 weeks to 6 months, beginning with intravenous and transitioning to oral. With appropriate therapy, prosthesis preservation is achieved in 35–90% of cases [1, 4]. Debridement with prosthesis retention is commonly referred to as debridement, antibiotics, and implant retention (DAIR). Open debridement has a lower rate of treatment failure when compared with arthroscopic debridement [1].

With chronic infection, for which biofilm formation is presumed complete, removal or revision of the prosthesis is typically required [4]. In the single-stage procedure, the infected hardware components are removed, the field is aggressively debrided, and a new arthroplasty is placed, typically using

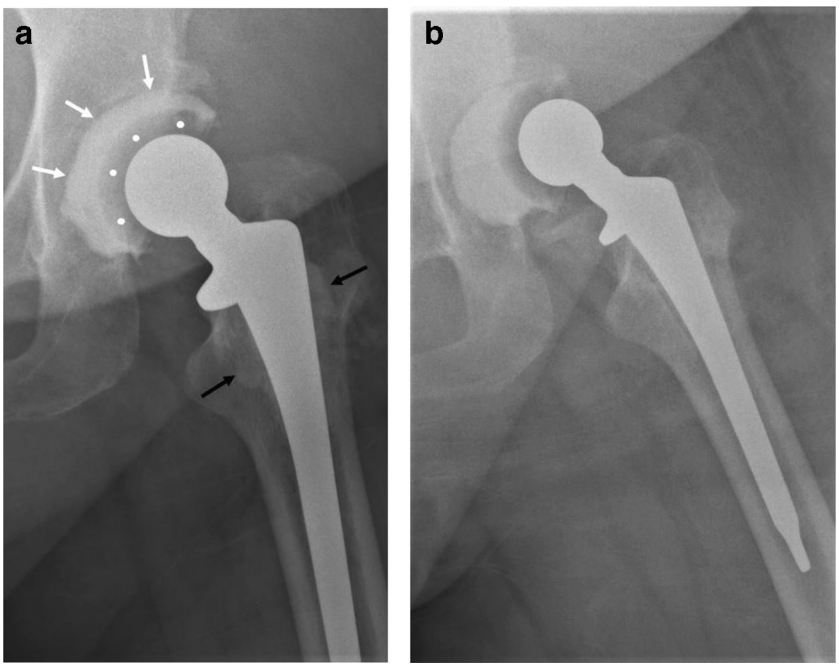


Fig. 6 58-year-old woman with recalcitrant left hip prosthesis infection status post placement of a PROSTALAC. Anteroposterior left hip radiograph (**a**) demonstrates hip PROSTALAC, composed of a polyethylene liner (white dots) cemented to the acetabulum (white arrows) as well as a modular femoral metallic core coated with cement along its proximal non-articulating surface (black arrows; antibiotic-impregnated cement was used). Anteroposterior left hip radiograph (**b**) obtained 1 month later shows loosening and vertical migration of the acetabular component of the prosthesis

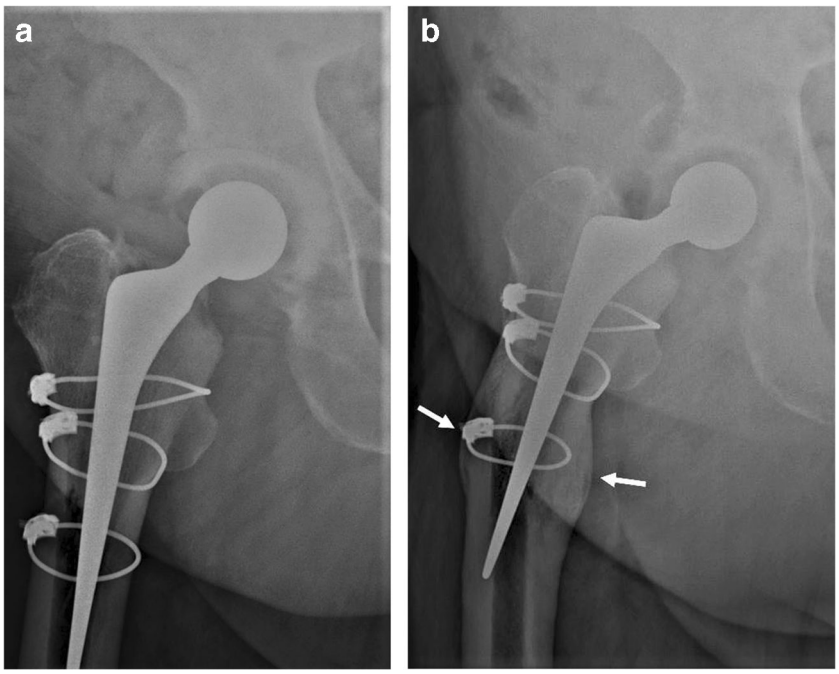


Fig. 7 65-year-old man with prosthetic joint infection and placement of PROSTALAC as well as proximal femoral wires (**a**). Hip radiograph obtained 2 years later (**b**) demonstrates hypertrophic callus formation and malunion (arrows) at the site of a healed periprosthetic fracture

antimicrobial-loaded polymethyl methacrylate (PMMA) to fix the new arthroplasty in place, followed by intravenous and long-term oral antibiotics [1, 6]. This form of direct exchange of the infected prosthesis for a new one is associated with a reinfection rate of up to 30%, presumably related to incomplete sterilization of the operative bed [6, 37]. As such, a two-stage procedure is typically preferred for the treatment of chronic PJIs in both the USA and Europe, in which the infected prosthesis is removed and replaced once the infection has been eradicated, with an intervening period of time provided for antibiotic therapy [3, 6, 37]. The successful eradication of infection is achieved in more than 90% of cases of two-stage revision [3].

Two-stage replacement arthroplasty

Surgical candidates for a two-stage replacement arthroplasty are those medically fit for multiple surgeries and with adequate bone stock. In the first stage, all foreign material is removed, bone and soft tissue debridement is performed with synovectomy, irrigation, and reaming of the medullary canal. Antibiotic-loaded cement beads and/or an antibiotic-loaded static or articulating spacer is placed, followed by closure of the soft tissues [1, 2, 6, 37].

Intravenous and/or oral antibiotics are typically administered for approximately 2–12 weeks afterwards, and delayed reconstruction is subsequently performed [1, 2, 4, 6, 37]. No specific metrics exist to determine optimal timing of reimplantation. When to reimplant should be based on clinical signs of infection, down trending of serologic markers, and, if aspiration is performed, results of synovial fluid [1, 37].

Although no conclusive evidence exists to support the practice, a 2–8-week antibiotic free interval may be given following the completion of the intravenous antibiotic regimen, referred to as a drug holiday, to allow for residual infection to reemerge. This also theoretically ensures that samples collected at reimplantation for microbial culture are not falsely negative as a result of previous antibiotic administration. During this timeframe, serologic testing and synovial aspiration are performed to identify possible persistent infection before the reimplantation procedure [1, 37].

A review of the literature performed by Aalirezaie et al. yielded limited evidence for deferring reimplantation until all serologic markers are normalized, with no single factor alone considered flawless for evaluating the success of a two-stage arthroplasty in eliminating infection. Further, the authors highlight that serologic and synovial testing may be inconsistent or misleading when used to identify persistent infection, and that deferring reimplantation to allow serologic markers to normalize can lead to prolonged disability, soft tissue contractures, and further bone loss. Aspiration of a

Table 2 Checklist for radiographic evaluation of the antibiotic cement spacer [1, 6, 38, 39]

Questions for the radiologist to address:
Has bone loss occurred about the construct?
Has the component migrated relative to the immediate post-operative imaging?
Is there joint dislocation?
Is there spacer fracture?
Is there periprosthetic fracture?

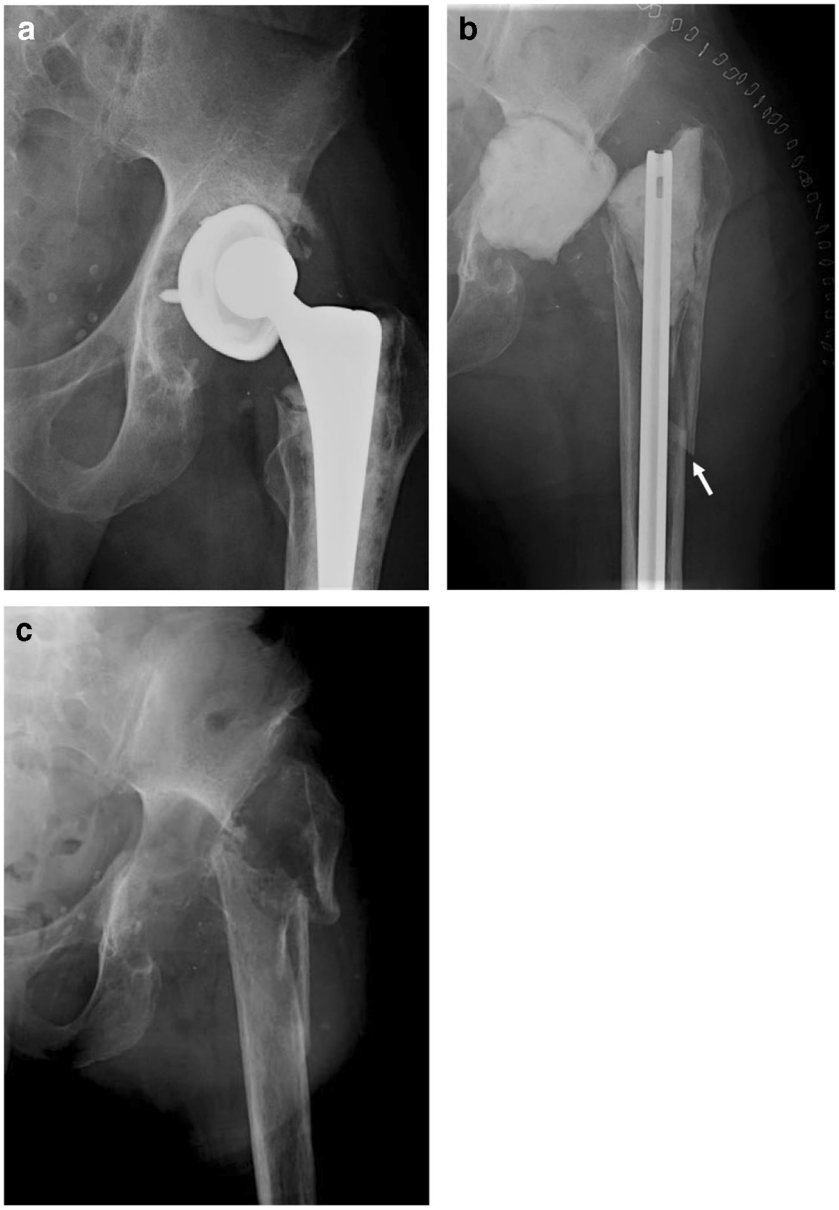


Fig. 8 52-year-old man with a failed revised left total hip arthroplasty secondary to chronic fungal prosthetic infection. Anteroposterior radiograph of the left hip (**a**) demonstrates vertical migration of the grossly loose acetabular component of the total hip prosthesis. Anteroposterior hip radiograph after Girdlestone arthroplasty (**b**) demonstrates a proximal femoral shaft fracture (sustained intraoperatively and demarcated with an arrow) transfixed with an intramedullary rod as well as packing of the acetabular and proximal femoral defects with antibiotic-impregnated cement. Anteroposterior hip radiograph obtained 4 months later (**c**) demonstrates removal of the intramedullary rod and antibiotic-impregnated cement

cement spacer, interpreted in conjunction with clinical evaluation, imaging, serologic tests, and biopsies, provides the highest diagnostic accuracy for identifying persistent infection before reimplantation [37].

Intraoperatively, frozen sections of periprosthetic tissue to identify and quantify polymorphonuclear cells per high-power field, and leukocyte esterase strip testing, can be used as a decision-making tool for reimplantation, with reimplantation held if positive results [1, 37].

A temporary antibiotic-loaded acrylic cement (spacer) is implanted locally during the first stage of the two-stage replacement arthroplasty, and remains in place during the antibiotic drug regimen, and during the drug holiday [37]. Bone cement, or PMMA, is used to affix prosthetic components to bone [6]. The concept of adding antibiotics to bone cement was introduced in 1970 by Buchholz and Engelbrecht, when they reported the efficacy of gentamicin-loaded cement in the prevention of infection following hip replacement [3]. The antibiotic-impregnated cement delivers a higher concentration of antibiotic locally than can be obtained with systemic antibiotics, with pharmacokinetic studies estimating local concentrations up to 200 times higher than those for systemic administration, while reducing the drug toxicity that may occur with high parental doses of antibiotics [1, 3, 6]. Local diffusion allows the drug to reach avascular areas that are otherwise inaccessible by systemic therapy, and at a required concentration that otherwise would not be achievable systemically [3].

PMMA cement is prepared by mixing powdered PMMA particles that contain barium sulfate with liquid methyl methacrylate and an activator. The antibiotics, such as vancomycin,

aminoglycosides, penicillins, cephalosporins, and erythromycin, are mixed in powdered form with the PMMA powder before the addition of a liquid monomer and can then be molded [1, 3, 6].

The role of the spacer is two-fold. The spacer not only acts to eradicate the infection but is also used to occupy the space previously occupied by the prosthesis, in effort to reduce scarring, to increase the ease of reimplantation, and to maintain bone quality [3]. Without a spacer, the limb is placed in either external fixation or traction, severely limiting mobility and resulting in muscle atrophy or stiffness. Debris fills the space left by the vacated components, and soft tissue contracture occurs in 80–100% [1, 6].

Antibiotic cement spacers are classified as either static, also known as nonarticulating or block spacer, or articulating [1]. Static spacers were used in the past, composed of chains of antibiotic-impregnated PMMA beads or a cement block, which pack the vacated space (Fig. 2). Their use is no longer routine, as they become surrounded by fibrotic tissue and are difficult to remove after 4–6 weeks. Additionally, the immobile joint makes ambulation challenging [3]. These spacers are typically handmade in the operating room [1].

An articulating spacer provides better mobility, decreased scarring, and better long-term range of motion relative to the static spacer, by providing a structure and function similar to the traditional arthroplasty components [3, 6]. They can be custom molded or premanufactured and commercially available preformed units [1]. The evolution of the articulating spacer has included cement-only spacers, to cement molded around metal or polyethylene, and to a prosthesis with antibiotic-loaded acrylic cement, known as a "PROSTALAC" implant, which was designed to treat infected knee and hip arthroplasties [3, 6]. The PROSTALAC was developed by Duncan and Beauchamp to treat infected hip joint replacements, with the initial design a metal femoral endoskeleton covered with antibiotic-loaded acrylic cement (ALAC) [6]. The initial design allowed the cement of the femoral head to articulate with the native acetabulum, which led to bone erosion and discomfort. This resulted in the introduction of an acetabular cement component, but this cement-on-cement interface resulted in limited motion and discomfort. As a result, the design further evolved, leading to an articulating polyethylene acetabular liner and a metal femoral head, with the nonarticular portion of the hardware coated or embedded with ALAC. The PROSTALAC implant for the knee also underwent revisions from the original design, with the implant eventually using articulating femoral and tibial components, and the nonarticulating surfaces covered with ALAC. A femoral cam and tibial post provide stability that is normally provided by the posterior cruciate ligament [6] (Figs. 3 and 4). Articulating spacers have also been used in other joints such as the shoulder and ankle.

At the second stage, the PROSTALAC implant is removed, and a preshaped, well-vascularized cavity is present which permits receipt of the final arthroplasty [6]. Antimicrobial therapy may be administered after reimplantation [1] (Fig. 5).

Antibiotic cement spacers rarely exhibit complications. Prolonged implantation with the elution of subtherapeutic levels of antibiotic may result in the development of resistant organisms. Additionally, once the antibiotic elution is complete, the cement may act as a foreign body that predisposes to superinfection [3]. Bone loss with static spacers can occur, as can extensor mechanism damage and wound dehiscence with articulating spacers [1]. Mechanically, the component can migrate, the joint can dislocate, and both the spacer and surrounding bone can fracture [6, 38, 39] (Figs. 6 and 7), features that may be apparent on follow-up radiographs (Table 2).

Salvage procedures and amputation

In exceptional cases, such as very poor bone status, seriously ill patients, or at the request of the patient, salvage procedures or amputation can be performed [1, 4].

Salvage procedures include resection with placement of a spacer left in place indefinitely, the prosthesis is removed (arthroplasty resection) and no new prosthesis placed (Girdlestone) (Fig. 8), arthrodesis (Fig. 9), and implant retention with prolonged suppressive antibiotics. Arthrodesis can

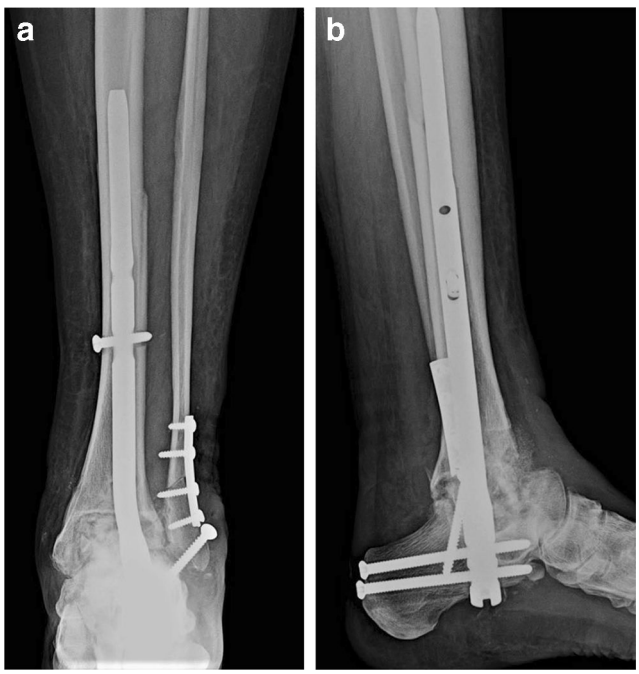


Fig. 9 67-year old woman with failed two-stage replacement left ankle arthroplasty (same patient as Fig. 2) due to prosthetic joint infection. Anteroposterior (**a**) and lateral (**b**) ankle radiographs demonstrate ankle and subtalar arthrodesis with a long stemmed retrograde hindfoot nail. Observe the distal fibula osteotomy transfixed with plate and screws as well as packing of the dorsal talar defect with bone graft

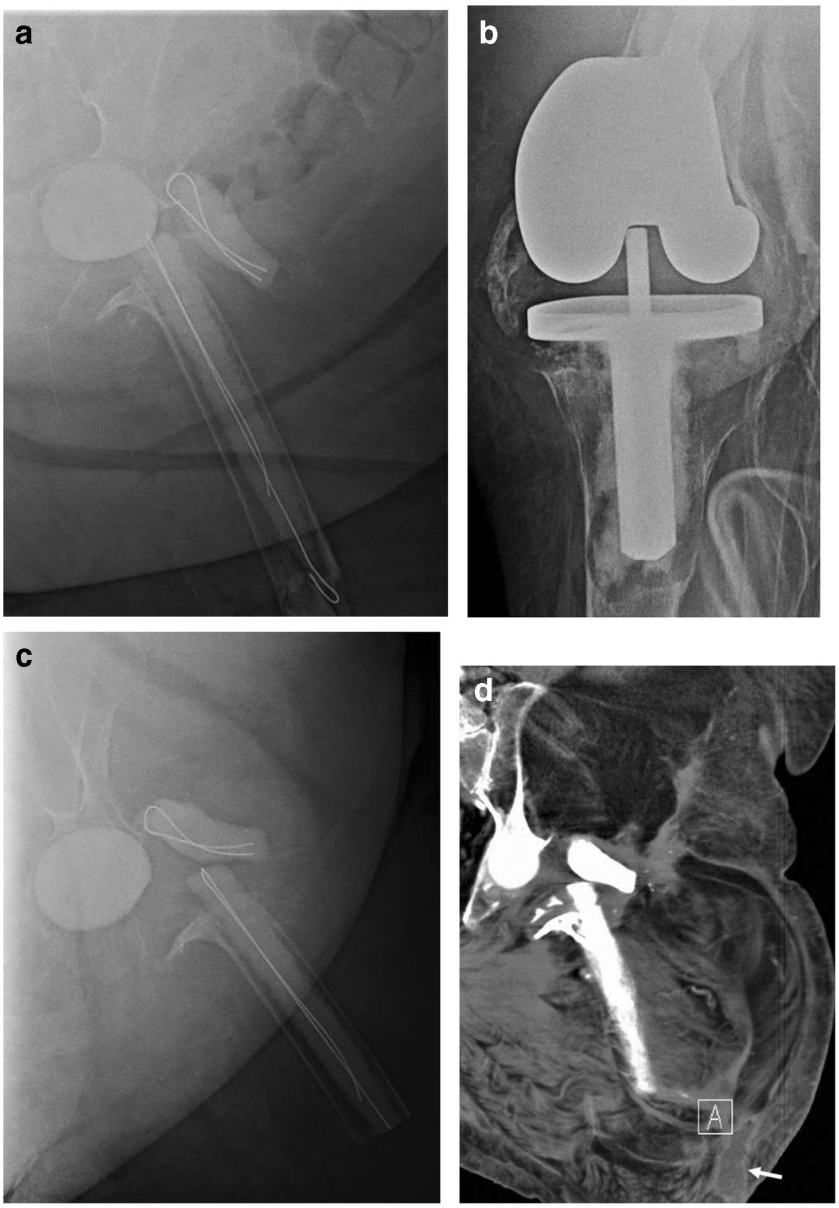


Fig. 10 62-year-old woman with failed left hip and knee replacements status post multiple failed revisions for prosthetic joint infection. She had multiple medical comorbidities including rheumatoid arthritis and insulin-dependent diabetes mellitus. Anteroposterior left hip radiograph (**a**) demonstrates a fracture of the hip prosthesis with antibiotic-loaded acrylic cement. Anteroposterior left knee radiograph (**b**) demonstrates loosening of the tibial component of the knee prosthesis seen as marked lucency and osteolysis at the cement-bone interface (on physical examination, a draining sinus was present on the anterior aspect of the patient's distal thigh). Anteroposterior left hip radiograph (**c**) demonstrates above-knee amputation. Coronal reconstructed, contrast enhanced CT scan of the left knee (**d**) demonstrates an amputation stump abscess (arrow)

be performed using either an intramedullary nail or external fixation device. Antimicrobial therapy used alone unfortunately often results in a delay in appropriate surgical management and is considered only for those who are unable to or unwilling to undergo even a single surgical procedure. As a last resort, in those who have failed all other treatment options or who have life-threatening infections in which emergent source control is required, amputation can be performed [1, 4, 6] (Fig. 10).

The treatment strategy is ultimately dictated by the joint efforts of the orthopedic surgeon, infectious disease specialist, and the patient. As noted, algorithms may be used to optimize treatment strategies, with the intent to identify those who may be candidates for less invasive options such as DAIR or a one-stage exchange, as opposed to a two-stage exchange [1].

Conclusion

As the use of arthroplasty increases, so does the absolute number of PJIs. The radiologist plays an important role in the diagnosis and management of PJIs, assisting with the interpretation of radiographs which may exhibit features of infection, providing image-guided joint aspiration to confirm the presence of infection, and interpreting post-operative imaging that is acquired once surgical management for PJI has been performed to evaluate for possible hardware-related complications. The two-stage replacement arthroplasty is commonly utilized in the management of PJIs, employing a prosthesis with antibiotic-loaded acrylic cement. Familiarity with this procedure and its complications is necessary for accurate interpretation of associated imaging.

Compliance with ethical standards

Conflict of interest The authors declare they have no conflicts of interest.

References

1. Tande AJ, Patel R. Prosthetic joint infection. Clin Microbiol Rev. 2014;27:302–45.
2. Cyteval C, Bourdon A. Imaging orthopedic implant infections. Diagn Interv Imaging. 2012;93:547–57.
3. Heffernan EJ, Alkubaidan FO, White LM, Masri BA, Munk PL. The radiology of antibiotic-impregnated cement. AJR Am J Roentgenol. 2007;189:446–54.
4. Otto-Lambertz C, Yagdiran A, Wallscheid F, Eysel P, Jung N. Periprosthetic infection in joint replacement. Dtsch Arztebl Int. 2017;114:347–53.
5. Kolinsky DC, Liang SY. Musculoskeletal infections in the Emergency Department. Emerg Med Clin North Am. 2018;36:751–66.
6. Gee R, Munk PL, Keogh C, Nicolaou S, Masri B, Marchinkow LO, et al. Radiography of the PROSTALAC (prosthesis with antibiotic-loaded acrylic cement) orthopedic implant. AJR Am J Roentgenol. 2003;180:1701–6.
7. Saeed K. Diagnostics in prosthetic joint infections. J Antimicrob Chemother. 2014;69(Suppl 1):i11–9.
8. Springer BD. The diagnosis of periprosthetic joint infection. J Arthroplast. 2015;30:908–11.
9. Diaz-Ledezma C, Espinosa-Mendoza R, Gallo J, Glaudemans A, Gómez-García F, Goodman S, et al. General assembly, diagnosis, imaging: proceedings of international consensus on orthopedic infections. J Arthroplast. 2019;34:S215–23.
10. Coventry MB. Treatment of infections occurring in total hip surgery. Orthop Clin North Am. 1975;6:991–1003.
11. Fitzgerald RH, Nolan DR, Ilstrup DM, Van Scoy RE, Washington JA, Coventry MB. Deep wound sepsis following total hip arthroplasty. J Bone Joint Surg Am. 1977;59:847–55.
12. Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. J Bone Joint Surg Am. 1996;78:512–23.
13. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. N Engl J Med. 2004;351:1645–54.
14. Pellegrini A, Legnani C, Meani E. A new perspective on current prosthetic joint infection classifications: introducing topography as a key factor affecting treatment strategy. Arch Orthop Trauma Surg. 2019;139:317–22.
15. Giulieri SG, Graber P, Ochsner PE, Zimmerli W. Management of infection associated with total hip arthroplasty according to a treatment algorithm. Infection. 2004;32:222–8.
16. Zimmerli W. Infection and musculoskeletal conditions: prosthetic-joint-associated infections. Best Pract Res Clin Rheumatol. 2006;20:1045–63.
17. Barrett L, Atkins B. The clinical presentation of prosthetic joint infection. J Antimicrob Chemother. 2014;69(Suppl 1):i25–7.
18. McPherson EJ, Tontz W, Patzakis M, Woodsome C, Holtom P, Norris L, et al. Outcome of infected total knee utilizing a staging system for prosthetic joint infection. Am J Orthop. 1999;28:161–5.
19. McPherson EJ, Woodson C, Holtom P, Roidis N, Shufelt C, Patzakis M. Periprosthetic total hip infection: outcomes using a staging system. Clin Orthop Relat Res 2002;8–15.
20. Romanò CL, Romanò D, Logoluso N, Drago L. Bone and joint infections in adults: a comprehensive classification proposal. Eur Orthop Traumatol. 2011;1:207–17.
21. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Executive summary: diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013;56:1–10.
22. Shohat N, Bauer T, Buttaro M, Budhiparama N, Cashman J, Della Valle CJ, et al. Hip and knee section, what is the definition of a periprosthetic joint infection (PJI) of the knee and the hip? Can the same criteria be used for both joints?: proceedings of international consensus on orthopedic infections. J Arthroplast. 2019;34:S325–7.
23. Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, et al. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res. 2011;469:2992–4.
24. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. J Arthroplasty. 2018;33:1309–1314.e2.
25. Patel R, Alijanipour P, Parvizi J. Advancements in diagnosing periprosthetic joint infections after total hip and knee arthroplasty. Open Orthop J. 2016;10:654–61.
26. Lee YS, Koo K-H, Kim HJ, Tian S, Kim T-Y, Maltenfort MG, et al. Synovial fluid biomarkers for the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am. 2017;99:2077–84.
27. Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, Parvizi J. Diagnosing periprosthetic joint infection: has the era of the biomarker arrived? Clin Orthop Relat Res. 2014;472:3254–62.
28. Ting NT, Della Valle CJ. Diagnosis of periprosthetic joint infection-an algorithm-based approach. J Arthroplast. 2017;32:2047–50.
29. Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014;32(Suppl 1):S98–107.
30. Parvizi J, Ghanem E, Sharkey P, Aggarwal A, Burnett RSJ, Barrack RL. Diagnosis of infected total knee: findings of a multicenter database. Clin Orthop Relat Res. 2008;466:2628–33.
31. Abdel Karim M, Andrawis J, Bengoa F, Bracho C, Compagnoni R, Cross M, et al. Hip and knee section, diagnosis, algorithm: proceedings of international consensus on orthopedic infections. J Arthroplast. 2019;34:S339–50.
32. Signore A, Sconfienza LM, Borens O, Glaudemans AWJM, Cassar-Pullicino V, Trampuz A, et al. Consensus document for the diagnosis of prosthetic joint infections: a joint paper by the EANM, EBJIS, and ESR (with ESCMID endorsement). Eur J Nucl Med Mol Imaging. 2019;46:971–88.
33. Della Valle CJ, Scher DM, Kim YH, Oxley CM, Desai P, Zuckerman JD, et al. The role of intraoperative Gram stain in revision total joint arthroplasty. J Arthroplast. 1999;14:500–4.
34. Talbot BS, Weinberg EP. MR imaging with metal-suppression sequences for evaluation of total joint arthroplasty. Radiographics. 2016;36:209–25.
35. Scher DM, Pak K, Lonner JH, Finkel JE, Zuckerman JD, Di Cesare PE. The predictive value of indium-111 leukocyte scans in the diagnosis of infected total hip, knee, or resection arthroplasties. J Arthroplast. 2000;15:295–300.

36. Ouyang Z, Li H, Liu X, Zhai Z, Li X. Prosthesis infection: diagnosis after total joint arthroplasty with three-phase bone scintigraphy. Ann Nucl Med. 2014;28:994–1003.
37. Aalirezaie A, Bauer TW, Fayaz H, Griffin W, Higuera CA, Krenn V, et al. Hip and knee section, diagnosis, reimplantation: proceedings of international consensus on orthopedic infections. J Arthroplast. 2019;34:S369–79.
38. Jung J, Schmid NV, Kelm J, Schmitt E, Anagnostakos K. Complications after spacer implantation in the treatment of hip joint infections. Int J Med Sci. 2009;6:265–73.
39. Anagnostakos K, Jung J, Schmid NV, Schmitt E, Kelm J. Mechanical complications and reconstruction strategies at the site of hip spacer implantation. Int J Med Sci. 2009;6:274–9.