Review Article

Periprosthetic Infection in Patients With Multiple Joint Arthroplasties

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ABSTRACT

The number of total joint arthroplasties performed in the United States is increasing every year. Owing to the aging population and excellent long-term prosthesis survival, 45% of patients who undergo joint arthroplasty will receive two or more joint arthroplasties during their lifetimes. Periprosthetic joint infection (PJI) is among the most common complications after arthroplasty. Evaluation and treatment of PJI in patients with multiple joint arthroplasties is challenging, and no consensus exists for the optimal management. Multiple PJI can occur simultaneously, synchronous, or separated by extended time, metachronous. Patient risk factors for both scenarios have been reported and may guide evaluation and long-term management. Whether to perform joint aspiration for asymptomatic prosthesis in the presence of suspected PJI in patients with multiple joint arthroplasties is controversial. Furthermore, no consensus exists regarding whether patients who have multiple joint arthroplasties and develop PJI in a single joint should be considered for prolonged antibiotic prophylaxis to reduce the risk of future infections. Finally, the optimal treatment of synchronous joint infections whether by débridement, antibiotics and implant retention, and one-stage or two-stage revision has not been defined. This review will summarize the best information available and provide pragmatic management strategies.

Total joint arthroplasty is considered one of the most successful surgeries of the past 50 years, relieving pain and improving function with 88% and 93% of patients achieving a meaningful improvement after primary total knee arthroplasty (TKA) and primary total hip arthroplasty (THA), respectively.[1] In the United States, the annual THA volume is projected to reach 909,900 surgeries by 2030, whereas TKA volume is estimated to be 1.68 million.[2]

The survival rate of THA is reported to be 89% at 15 years.[3] High survival rate is also reported for TKA showing 93% survivorship at 15 years.[3] These excellent outcomes combined with a high rate of multijoint involvement in patients with osteoarthritis result in high rates of further joint arthroplasty in patients who undergo an initial hip or knee arthroplasty; indeed, a second THA

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or TKA is performed in 45% of patients at an average time interval of 4 years.[4] Consequently, the number of patients with more than one prosthetic joint has risen.

Despite available technologies and existing clinical countermeasures, periprosthetic joint infection (PJI) risk remains steady over the last decade at 0.8% to 1.2% and 0.9% to 1.4% at 5 years for primary THA and TKA, respectively.[5,6] PJI is one of the most common reasons for hip revision surgery accounting for 26% of all hip revisions in 2020.[1] In addition, 27% of all revision knee surgeries performed in 2020 were attributable to knee PJI.[1]

The burden of PJI is undeniable on a personal and societal economic scale. The 5-year patient survival rates after PJI are 67% for THA and 72% for TKA.[5] In addition, PJI remains a notable burden to the US healthcare system, and the combined estimated annual hospital cost for hip and knee PJI is estimated to reach $1.85 billion by 2030.[7]

Recent studies have evaluated the risk of developing PJI of a subsequent primary THA in patients with previously surgically treated THA or TKA PJI; the 2% risk at 10 years was markedly higher than for patients without previous PJI.[8] Similar studies evaluated the risk of PJI for subsequent primary TKA after being treated for THA or TKA PJI; the estimated risk of 6.1% at 10 years is a threefold higher compared with matched cohorts without previous PJI.[9]

Considering that PJI can occur anytime during a lifetime, patients with multiple joint arthroplasties are at higher risk for PJI than those with a single joint arthroplasty.[10] Although uncommon, a second-site PJI can lead to notable morbidity and higher mortality, reaching 27% at 1 year[11] compared with a mortality of 10% within the first year for a single PJI.[12] In the situation where more than one existing joint develops infection, the PJI can occur simultaneously, labeled synchronous PJI, or at a different time and called metachronous PJI. The purpose of this review is to summarize the current literature related to[1] the prevalence of PJI in patients with multiple joint arthroplasties[2], the risk factors for synchronous and metachronous PJI[3], the diagnosis of PJI in the subsequent joints, and[3] the management of synchronous and metachronous PJI.

Prevalence of a Subsequent Periprosthetic Joint Infection in Patients with Periprosthetic Joint Infection and Multiple Joint Arthroplasties

Multiple studies have investigated the prevalence of a subsequent PJI in patients with multiple joint arthroplasties. Luessenhop et al[13] conducted a retrospective review of 145 patients with ≥2 hip, knee, or shoulder prostheses and a history of one PJI. Of those 145 patients, a subsequent infection occurred in a different arthroplasty in 27 patients (19%). Komnos et al[10] retrospectively studied 197 patients at a single institution who had >1 hip or knee arthroplasty at the time of presentation of an initial PJI. The authors identified 37 patients (19%) who developed a PJI in a second joint. Eleven patients had a synchronous PJI (6%), and 26 (13%) had a metachronous PJI. The causative organism was the same in eight of the 11 patients in the synchronous group, and in eight of the 26 patients in the metachronous group. In this study, cultures were negative in 38% of the cases of the presumed second PJI in the metachronous group. Moreover, Thiesen et al[14] retrospectively reviewed 644 patients who had >1 prosthetic joint at the time of the index PJI and who had aspirations of all their prosthetic joints; these prosthetic joints included hips, knees, shoulders, six ankles, two elbows, and one wrist. Twenty-six patients (4%) had a culture-positive synchronous PJI. Interestingly, 12 (2% of the total cohort) of these 26 patients did not demonstrate any clinical sign of PJI. Abblitt et al[15] reviewed 76 patients with multiple joint arthroplasties limited to hips, knees, and shoulders who were treated for PJI. Ten patients (13%) developed a subsequent PJI; 4 cases of PJI (5%) were synchronous, and 6 (8%) were metachronous. Lee et al[16] identified 96 patients diagnosed with PJI and multiple prosthetic arthroplasties. After excluding synchronous infections, 19 patients (19.7%) developed metachronous PJI when followed up for a minimum of 10 years from the time of the index PJI with 36% occurring within the first 3 months. In addition, 63% of the cases had the same microorganism at different sites. Jafari et al[17] found that 11 patients (20%) of 55 patients who presented with PJI and multiple coexisting joint arthroplasties subsequently developed PJI in a second joint; two patients had synchronous PJI (3.6%) and nine patients had metachronous PJI (16.3%). Zeller et al[18] found 16 patients (1.4%) with synchronous PJI among 1,185 patients who had multiple joint arthroplasties. Their findings were similar to Gausden et al[11] who identified 34 synchronous PJI (1.3%) in 2,671 PJIs. In the series by Haverstock et al,[19] 206 patients presented with PJI after multiple joint arthroplasties. Only 13 patients (6.3%) acquired a second site PJI. The authors attributed the low rate of subsequent metachronous PJI (3.4%) to the greater number of patients treated by a 2-stage revision of the initial PJI and fewer patients with rheumatoid arthritis (RA) in their series.

In summary, there seems to be a higher risk of developing a second PJI in patients with a history of PJI and multiple joint arthroplasties compared with the risk of PJI in a single joint arthroplasty. This risk ranges between 3%-19% for metachronous PJI and 1.3% to 6% for synchronous PJI. Table-1 summarizes the prevalence and percentages of synchronous and metachronous PJI as well as the same-organism infection rates.

Risk Factors for Synchronous Periprosthetic Joint Infection

The increasing number of patients with multiple joint revision arthroplasties increases the population at risk for synchronous PJI (SPJI). Multiple risk factors have been identified favoring SPJI. Komnos et al[10] noted that positive blood cultures and RA are more likely in patients diagnosed with SPJI. Thiesen et al[14] noted a history of neoplasia, the use of immunomodulating therapy, the presence of systemic inflammatory response syndrome (SIRS) or sepsis and having ≥3 prosthetic joints as risk factors for SPJI; furthermore, these authors identified the same bacteria in 25 of 26 patients diagnosed with SPJI, suggesting a hematogenic spread of the bacteria. Jafari et al[17] reported that the risk of SPJI is higher in immunocompromised patients. Moreover, bacteremia has been identified as a risk factor for SPJI in multiple studies.[11,18,19] Although bacteremia is defined as the presence of bacteria within an individual's bloodstream, sepsis is the clinical condition that involves the symptoms resulting from bacteremia.[20] It is important to note that bacteremia and sepsis have been used interchangeably in the literature.

In summary, bacteremia and immunocompromised patients are common risk factors for SPJI. Patients with these risk factors presenting with PJI in one of many joint arthroplasties are at a higher risk of SPJI. The other prosthetic joints in these individuals need special attention and may be considered for aspiration considering

Table 1. Prevalence of Synchronous and Metachronous PJIs and Rates of Infection With the Same Organism

Study	N	MPJI	Synchronous PJI	Same Organism	Metachronous PJI	Same Organism	Comments
Komnos[10]	197	37/197 (19%)	11/197 (6%)	8/11 (72%)	26/197 (13%)	8/26 (30%)	38% culture-negative in metachronous PJI Average follow-up: 3.6 years
Thiesen[14]	644	N/A	26/644 (4%)	25/26 (96%)	N/A	N/A	Study limited to synchronous PJI
Abblitt[15]	76	10/76 (13%)	4/76 (5%)	3/4 (75%)	6/76 (8%)	3/6 (50%)	Average follow-up: 3.8 years
Lee[16]	96	N/A	N/A	N/A	19/96 (19.7%)	12/19 (63%)	Synchronous PJI excluded Average follow-up: 11.2 years
Jafari[17]	55	11/55 (20%)	2/55 (3.6%)	2/2 (100%)	9/55 (16%)	2/9 (22%)	—
Zeller[18]	1,185	N/A	16/1185 (1.4%)	16/16 (100%)	N/A	N/A	Only culture-positive PJI are included
Gausden[11]	2,671	N/A	34/2671 (1.3%)	21/22 (95%)	N/A	N/A	11/33 (32%) culture-negative 1 patient had unavailable culture
Haverstock[19]	206	13 (6.3%)	6/206 (2.9%)	4/6 (66%)	7/206 (3.4%)	2/7 (29%)	Low percentage of metachronous PJI recognized by authors Minimum follow-up: 12 months

PJI = Periprosthetic joint infection, MPJI = metachronous periprosthetic joint infection
N: Total number of patients with PJI and multiple joint arthroplasties. MPJI: Multiple periprosthetic joint infection including synchronous and metachronous infections when available, N/A: Not Available Data.

that there is a moderate rate of asymptomatic PJI in the other involved joint arthroplasties.

Risk Factors for Metachronous Periprosthetic Joint Infection

Considering the notable morbidity and higher mortality associated with multiple PJI, several studies investigated the risk factors for metachronous PJI (MPJI) to avoid a second episode. Luessenhop et al[13] identified RA as a risk factor for a second prosthetic infection, whereas diabetes mellitus and corticosteroid use were not considered as risk factors. Komnos et al[10] noted that female sex and RA are risk factors for MPJI; additionally, in the same study, an initial PJI caused by methicillin-resistant *Staphylococcus Aureus* (MRSA) was observed as an independent risk factor for a MPJI. Lee et al[16] reported that SIRS, MRSA, and ≥3 stages of resection arthroplasty, defined as the need of three or more surgeries for resection and débridement of joint before reimplantation because of ongoing infection or positive cultures, as risk factors for MPJI. The authors attributed the lower rate of eradication of MRSA estimated at 40 to 80%,[21] even in a two-stage resection arthroplasty, to the increased risk of developing a second PJI. Clesham et al[22] identified MRSA and longer hospital length of stay as risk factors for MPJI; the authors also noted that an index infection of a knee prosthesis was associated with a higher risk of developing a second site infection compared with an index hip prosthesis infection. The authors found no correlation between diabetes, chronic obstructive pulmonary disease, hypertension, atrial fibrillation, RA or ischemic heart disease, and the risk of a second MPJI. In this latter study, the fact that RA had no correlation with a higher risk of a second PJI was attributable to the improvement of controlling the inflammatory process of the disease using disease-modifying therapies. Abblitt et al[15] stated that there is a higher risk of a MPJI when the initial PJI microorganism is MRSA; in their database, MRSA was the causative microorganism in 40% of patients with multiple PJI, whereas it was detected in just 13% of patients with multiple joint arthroplasties and a single PJI.

In summary, early identification of risk factors for MPJI can help identify patients who would require closer observation and a higher index of suspicion of a second-site PJI. RA, MRSA, SIRS, index knee prosthesis PJI, longer length of stay in the hospital, and ≥3 stages resection arthroplasty of the index PJI are all risk factors for MPJI in patients presenting with an initial PJI and multiple joint arthroplasties. The risk factors for SPJI and MPJI are summarized in Table 2.

Diagnosis of Periprosthetic Joint Infection in the Subsequent Joint

The diagnosis of a second-site PJI can be a challenge because the serum markers, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), and D-Dimer, may not be reliable in this specific situation. These markers, which are usually used for screening for PJI, or as minor criteria for the diagnosis of PJI, are elevated because of the index PJI. Joint aspiration of the second site for suspected multisite PJI is proposed as the sole method for diagnosis in this circumstance. Although joint aspiration is the most important test in the investigation of PJI, there are potential morbidities associated with this diagnostic procedure; it can be painful and carries a small but real risk of causing a PJI when one does not already exist.[23] Identifying the correct indications for aspiration of a second-site potential PJI is crucial in limiting the morbidity of unnecessary investigations. Bakker et al[24] evaluated 108 concomitant prosthetic joints in 91 patients with hematogenous PJI, 13/108 joints were symptomatic at the time of presentation,

Table 2. **Risk Factors for Synchronous and Metachronous Periprosthetic Joint Infection**

Risk Factor	Synchronous PJI	Metachronous PJI
Bacteremia	+	–
Rheumatoid arthritis	+	+
History of neoplasia	+	–
Immunomodulating therapy	+	–
Sepsis or SIRS	+	+
≥3 prosthetic joints	+	–
Immunocompromised	+	–
MRSA	–	+
≥3 stages resection arthroplasty	–	+
Longer LOS in the hospital	–	+
Index knee prosthesis PJI	–	+

LOS = length of stay, MRSA = methicillin-resistant *S. aureus*, SIRS = systemic inflammatory response syndrome

whereas 95/108 were asymptomatic; 10 of the 13 symptomatic joints (77%) were diagnosed as a second PJI during follow-up, whereas four of the 95 asymptomatic joints (4.2%) were identified with a *Staphylococcus aureus* PJI at a median time of follow-up of 52 months. After analyzing the four asymptomatic cases that were diagnosed as PJI, the authors classified only one case (1.1%) as an unrecognized PJI at the time of the presentation. Further analysis of these cases showed that the infected prosthetic joints had been performed more recently than the noninfected joints (median prosthesis age: 4.5 versus 6.7 years). Bakker et al[24] concluded that in asymptomatic prosthetic joints, performing additional diagnostic work-up is not indicated, provided these prosthetic joints are carefully examined. Komnos et al[10] evaluated 10 of their 197 patients who had an aspiration of a prosthetic joint other than the index PJI. Four of the 10 aspirates were positive, three of which had a clinical suspicion of infection, whereas the fourth was asymptomatic. The authors concluded that given that one of the asymptomatic prostheses developed a subsequent PJI, patients presenting with risk factors for MPJI or SPJI may benefit from additional investigation with aspiration. Therefore, according to these authors, symptomatic joints should be aspirated and consideration should be given to aspirating an asymptomatic prosthetic joint in patients with risk factors for multijoint PJI. Thiesen et al[14] in their series of 644 patients who underwent aspiration of all their prosthetic joints after being diagnosed with one-site PJI, noted that 12 of 26 (46%) SPJI showed no clinical signs of infection; furthermore, eight of the 26 (30%) had no risk factors. Based on these numbers, the authors recommend aspirating all other prosthetic joints in the same patient if a PJI is present. In his comment on the study by Thiesen et al, Zhu[25] raised concerns about aspirating all prosthetic joints considering the low percentage of asymptomatic PJI (12 of 644 patients: 1.8%). The author noted the possibility of false-positive results, introduction of bacteria into the joint, patient pain and discomfort, and the cost of the procedure as concerns; he concluded that universal joint aspiration is not indicated, but the issue warrants further investigation. Zeller et al[18] suggested aspirating all symptomatic joints, joints that have positive radiographic findings, and those in patients with positive blood culture. It is important to note that in this particular setting, aspiration of a second potential PJI site, the cultures are limited by poor sensitivity. In fact, Gausden et al[11] reported 11 culture-negative results in 34 patients (32%) diagnosed with SPJI. The administration of antibiotics before aspiration for treating the index PJI is the most likely reason for this high rate of culture-negative subsequent PJI. A 2-week antibiotic-free interval has been suggested before obtaining culture samples to minimize this false-negative rate.[26] Unfortunately, this may not be possible in patients in the middle of a treatment protocol to treat the index acute PJI. In this circumstance, a break in treatment may compromise salvage attempts for the proven PJI.

Therefore, at the time of initial presentation, careful clinical evaluation and aspiration of all joint arthroplasties in each patient may be considered to try to accurately diagnose all involved joints; once treatment is started for one acute PJI, it may compromise the ability to identify other joints that are involved in a timely manner. As successful salvage of acute PJI seems to be somewhat time dependent, any delay in diagnosis may lead to notable morbidity.

Management of Synchronous Periprosthetic Joint Infection

Synchronous PJI are rare and articles discussing the management of this condition are scarce with usually small series. Wolff et al[27] evaluated 21 patients with bilateral infected TKAs; the mean age of the patients was 71 years, and the time between the onset of symptoms and presentation was less than 3 weeks for all the patients. Ten patients (20 knees) were treated initially with bilateral resection arthroplasties; seven patients (14 knees) had bilateral reimplantation at a mean interval of 3 months using antibiotic impregnated cement; and the other three patients (six knees) did not undergo reimplantation because of low functional demands and medical comorbidities. Nine patients (18 knees) underwent débridement, antibiotic therapy and implant retention (débridement, antibiotics and implant retention (DAIR)) with tibial polyethylene insert exchange followed by oral chronic suppressive antibiotics, and the remaining two patients (four knees) had DAIR without polyethylene exchange followed by oral chronic suppressive antibiotics. Two patients died within 2 years, and one patient was lost to follow-up. The remaining 18 patients were followed for a mean of 5 years. Nine of the 11 patients treated with DAIR and chronic oral suppressive antibiotics had a recurrence of the infection and required revisions in both knees. Of the seven patients who were treated initially with 2-stage revision arthroplasty, none required a revision. The authors concluded that despite the early presentation after initial symptoms in their patients, the preferred treatment for

medically stable patients is bilateral 2-stage revision with reimplantation at different timing using antibiotic-impregnated cement spacers in the interval. This conclusion needs to be interpreted with caution because multiple factors can contribute to the success rate of DAIR, among these factors are the type of organism and the time of surgery relative to the onset of symptoms. Zeller et al[18] retrospectively reviewed 16 patients with concomitant PJI and proposed a therapeutic strategy. Patients with an acute postoperative infection or hematogenous infection lasting less than 2 weeks are treated with bilateral DAIR. Bilateral successive one-stage revision arthroplasty is the authors' treatment of choice for patients with symptoms lasting more than 2 weeks; those patients are to receive pathogen-targeted antibiotic therapy preoperatively. Prolonged suppressive antibiotic therapy with occasional palliative surgical intervention is the treatment of choice for patients at high surgical risk or who refuse surgery. A study by Gausden et al[11] evaluated 34 patients with SPJI with a mean age of 72 years at the time of infection. Joint aspiration cultures remained negative in 11 patients. Blood cultures were positive in 14 patients at the time of SPJI. The choice of treatment was made by the orthopaedic surgeon in collaboration with infectious disease specialists on a case-by-case basis. DAIR was performed for all involved joints in 23 patients; implant resection of all involved joints in 10 patients and one patient received a combination of DAIR for one joint and implant resection for the other joint. Most patients were treated with a minimum of 6 weeks of intravenous antibiotics, and 23 patients received long-term oral antibiotic suppression. Four patients were lost to follow-up before 2 years, and the rest had a mean follow-up of 6 years. The authors noted that mortality was very high in this patient population, 18% within 30 days and 27% within 1 year; RA and liver disease were risk factors. Incidence of reinfection was 13% at 1 year and 27% at 5 years, and the authors stated that the risk of reinfection was not associated with the initial treatment method, DAIR versus resection arthroplasty. In addition, the incidence of any surgical revision including recurrent infection, implant loosening, extensor mechanism reconstruction, and osteolysis were high; 6% at 1 year and 20% at 5 years. Furthermore, it is important to note that intensive care unit was required perioperatively for 35% of patients. The authors concluded that SPJI is associated with bacteremia and immunocompromised patients. They also noted that despite TKAs being more prone to SPJI compared with THAs, mortality risk is higher with THAs. Although this series was not able to associate early resection and 2-stage revision with lower recurrence of infection, the authors consider that the high rate of reinfection at 5 years should encourage surgeons to consider this therapeutic strategy in treating these high-risk patients when clinically appropriate.

In summary, current literature does not support a single therapeutic strategy when dealing with SPJI. The variety of patient presentations, comorbidities, timing from infection, and the causative pathogen make a case-by-case therapeutic decision the most appropriate strategy to deal with these heterogenous cases. Special care and close observation of patients with SPJI is crucial considering the high morbidity and mortality associated with this condition. Despite that, DAIR is preferred for early postoperative and acute hematogenous PJI for its role in reducing the perioperative morbidity of implant removal and reimplantation and a single DAIR is associated with high failure rate especially when MRSA is the causative pathogen[28] and might not be the best therapeutic option, especially when dealing with the complex cases of multiple joint involvement in SPJI. In these cases, a double DAIR[29] of each joint, which implements a 2-stage débridement protocol and the use of high-dose antibiotic beads between stages for the treatment of acute PJI and which seems to have a better salvage rate than a single DAIR, or 2-stage revision may need to be considered.

Management of Metachronous Periprosthetic Joint Infection

Prompt diagnosis and aggressive therapy of PJI in a patient with multiple joint arthroplasties is crucial to prevent the high risk of hematogenous spread of the infection to the subsequent prosthetic joints. DAIR, 1-stage revision arthroplasty, and two-stage revision arthroplasty are the curative surgical options, whereas chronic oral suppressive antibiotic therapy is proposed as a treatment for patients with low-functional demands and high surgical risks or for patients who refuse additional surgery. Detailed therapeutic strategy for PJI is beyond the scope of this review; however, it is important to know that despite the absence of validation studies of the McPherson classification system,[30] support exists for the use of DAIR or 1-stage revision arthroplasty for infected THA and TKA in McPherson type I/A/1 patients (acute infection, not compromised host and not compromised local factors). In addition, it is important to know that patients with positive blood cultures are

at a higher risk of hematogenous spread of the pathogen to other prosthetic joints and have been found to have lower success rates when treated with DAIR[31]; therefore, the two-stage revision should be considered.

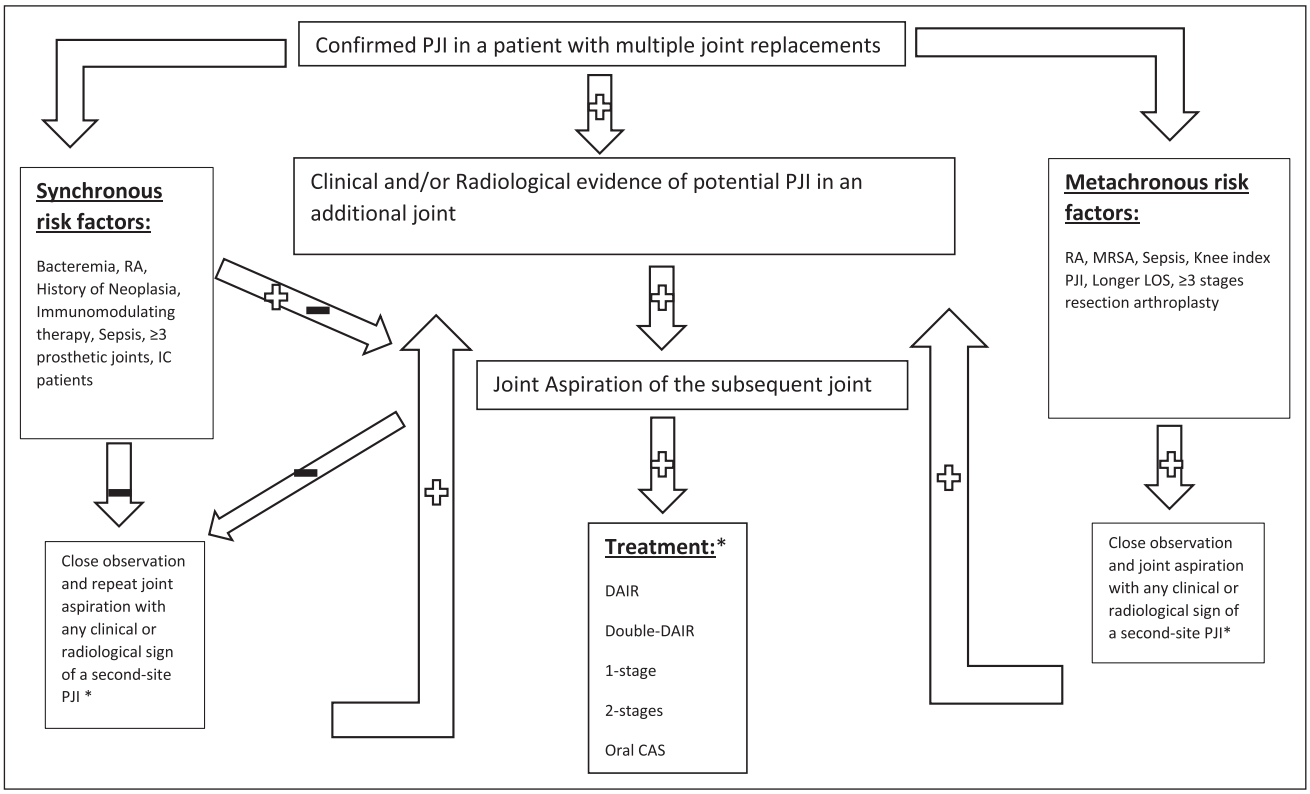
Oral Chronic Prophylactic Antibiotic in Patients with Periprosthetic Joint Infection and Multiple Joint Arthroplasties

Chronic oral prophylactic antibiotherapy as a prophylaxis against metachronous infection in patients with previous PJI and multiple joint arthroplasties is an area of controversy; current literature on this topic is rare. Abblitt et al[15] suggested chronic oral antibiotherapy to be beneficial for patients with bacteremia because 20% of patients with bacteremia developed MPJI compared with only 5% of patients without bacteremia. To our knowledge, no studies have analyzed the cost-effectiveness of oral chronic antibiotherapy in preventing MPJI. However, extended oral antibiotic prophylaxis has been shown to be cost-effective in preventing infection among high-risk patients after total joint arthroplasty,[32] and patients with PJI and multiple joint arthroplasties should be considered at high-risk. However, the potential contribution of extended antibiotherapy to antimicrobial resistance must be considered. In the most recent International Consensus Meeting on Orthopedic Infections, there was a strong consensus on 3 months oral extended antibiotic after reimplantation of a 2-stage revision directed toward the initial organism,[33] but the benefit in patients with multiple prosthetic joint arthroplasties is yet to be investigated.

Summary

The incidence of PJI in patients with multiple joint arthroplasties is expected to increase considering that 45% of patients undergo more than one joint arthroplasty. The second-site prosthetic joint in patients with PJI is at a higher risk of infection compared with PJI in a patient with a single joint arthroplasty. Multijoint PJI can be

Figure 1



Suggested management strategy in patients with periprosthetic joint infection (PJI) and multiple joint arthroplasties. After completing active treatment of the first PJI, all patients with multiple joint arthroplasties should be considered for long-term oral prophylactic antibiotherapy (minimum of 3 months). PJI = periprosthetic joint infection, IC = immunocompromised patient, RA = rheumatoid arthritis, MRSA = methicillin-resistant *S. aureus*, LOS = length of stay, DAIR = débridement, antibiotherapy and implant retention, CAS = chronic antibiotic suppression.

simultaneous and designated as SPJI or occur at a subsequent time and termed MPJI. Multiple risk factors have been identified for SPJI and MPJI and should prompt particular attention when encountered. The diagnosis of a second PJI is challenging, and even joint aspiration, considered to be the only reliable diagnostic tool in this setting, can be unreliable, especially if performed after antibiotic treatment has been initiated as part of the treatment protocol for the first PJI. Higher level of evidence studies are required to demonstrate superiority of one treatment approach over another for cases of SPJI or MPJI. A single or double DAIR, resection arthroplasty, and one- or two-stage revision arthroplasty are all viable options; however, given the higher failure rates with these patients, stronger consideration for the 2-stage exchange may be indicated for certain patients. Chronic oral suppressive antibiotic is also proposed in some particular nonsurgical cases to limit symptoms while not being curative. Finally, extended prophylactic oral antibiotic after reimplantation is controversial and further clinical and cost-effectiveness studies are needed in patients with multiple joint arthroplasties. A management strategy is proposed in Figure 1.

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