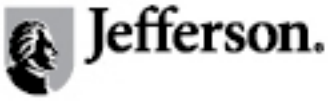

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Management of periprosthetic joint infection: the current knowledge: AAOS exhibit selection.

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Exhibit Selection

Management of Periprosthetic Joint Infection: The Current Knowledge

AAOS Exhibit Selection

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Abstract: Periprosthetic joint infection continues to frustrate the medical community. Although the demand for total joint arthroplasty is increasing, the burden of such infections is increasing even more rapidly, and they pose a unique challenge because their accurate diagnosis and eradication can prove elusive. This review describes the current knowledge regarding diagnosis and treatment of periprosthetic joint infection. A number of tools are available to aid in establishing a diagnosis of periprosthetic joint infection. These include the erythrocyte sedimentation rate, serum C-reactive protein concentration, synovial white blood-cell count and differential, imaging studies, tissue specimen culturing, and histological analysis. Multiple definitions of periprosthetic joint infection have been proposed but there is no consensus. Tools under investigation to diagnose such infections include the C-reactive protein concentration in the joint fluid, point-of-care strip tests for the leukocyte esterase concentration in the joint fluid, and other molecular markers of periprosthetic joint infection. Treatment options include irrigation and debridement with prosthesis retention, one-stage prosthesis exchange, two-stage prosthesis exchange with intervening placement of an antibiotic-loaded spacer, and salvage treatments such as joint arthrodesis and amputation. Treatment selection is dependent on multiple factors including the timing of the symptom onset, patient health, the infecting organism, and a history of infection in the joint. Although prosthesis retention has the theoretical advantages of decreased morbidity and improved return to function, two-stage exchange provides a lower rate of recurrent infection. As the burden of periprosthetic joint infection increases, the orthopaedic and medical community should become more familiar with the disease. It is hoped that the tools currently under investigation will aid clinicians in diagnosing periprosthetic joint infection in an accurate and timely fashion to allow appropriate treatment. Given the current knowledge and planned future research, the medical community should be prepared to effectively manage this increasingly prevalent disease.

Background

Periprosthetic joint infection is a devastating complication of total joint arthroplasty. In the United States, periprosthetic joint infection is currently the most common indication for revision total knee arthroplasty and the third most common indication for revision total hip arthroplasty, with an estimated prevalence of between 1% and 3%[1-3]. Because of the ease with which periprosthetic joint infection can develop, it is not an uncommon complication. Pathogen proliferation can easily occur in the joint space, with the implanted prosthesis as the growth surface, following the introduction of a small pathogen population into the systemic circulation or a wound in the joint.

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Periprosthetic joint infection is typically classified according to the timing of symptom development and the mechanism of infection as acute postoperative, acute delayed (hematogenous), or chronic. Treatment algorithms are typically dependent on such a classification. Presently, the increase in the burden of periprosthetic joint infection is outpacing developments in prevention[4].

Our institution has maintained prospective joint arthroplasty databases over the past decade. The use of these databases has allowed identification of 821 cases of periprosthetic joint infection among 3308 total revision cases. A substantial amount of research has been performed with use of these databases to better understand the care of patients following joint replacement—specifically prevention, diagnosis, and treatment of periprosthetic joint infection. Based on that work, this review explores the recent advancements in diagnosis of periprosthetic joint infection and provides guidance in the selection of a surgical treatment. In spite of the depth of this review, it will only touch on the oft-described aspects of periprosthetic joint infection management and will provide the reader with a complete understanding of the current findings that have the greatest potential to substantially change patient care.

Current Methods for Diagnosis

Since no highly accurate diagnostic method exists, clinicians have yet to agree on a "gold standard" for the diagnosis of periprosthetic joint infection. Currently, diagnosis rests on a combination of clinical suspicion, serological tests, culture results, histology, and basic molecular techniques. In large part, current modalities fall short in providing necessary and accurate information on both the existence and the virulence of microorganisms in an infected prosthetic joint. Many groups have attempted to increase the accuracy of diagnosis by providing definitions of periprosthetic joint infection that are dependent on criteria from multiple individual tests[5-10]. These diagnostic criteria sets, however, have compounded the problem of diagnosing periprosthetic joint infection since the results provided by different criteria sets are often not unanimous regarding the diagnosis[11].

The currently available sets of diagnostic criteria incorporate serological tests (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP] concentration), histological analysis of tissue, the appearance of the joint, culture of intraoperative tissue samples on a solid medium, and preoperative aspirate analysis including fluid culture, white blood-cell (WBC) count, and WBC differential. The utility of these tools has been investigated repeatedly, and the American Academy of Orthopaedic Surgeons (AAOS) recently provided evidence for the use of each tool in their guidelines for diagnosing periprosthetic joint infection[12]. The use of these individual tools, updates in the definition of periprosthetic joint infection, and the development of new tools for its diagnosis will be discussed here.

Currently Recommended Diagnostic Tests for Periprosthetic Joint Infection and the AAOS Algorithm

ESR and serum CRP are very sensitive to the presence of periprosthetic joint infection, and they are used as initial tests even when there is a low suspicion of such infection[12,13]. However, their specificity is relatively low because elevated levels can also be caused by other inflammatory diseases[14]. The thresholds for ESR and serum CRP concentration have previously been cited as 30 mm/hr and 10 mg/dL, respectively[10]. However, receiver operating characteristic (ROC) curve analysis identified the optimal thresholds for ESR and serum CRP concentration as 31 mm/hr and 2 mg/dL, respectively, in a study at our institution[13]. These thresholds provided a sensitivity of 96% and a specificity of 59% when both the ESR and serum CRP concentration were above these thresholds.

When the ESR or serum CRP concentration is above the threshold for periprosthetic joint infection in the absence of a known etiology, continued investigation is warranted. Aspiration of the joint (under fluoroscopic guidance in the case of the hip) will often provide a definitive answer to questions raised by elevated serological test results. This is the next step recommended by the AAOS guidelines, and it is inexpensive[12]. Cultures from the aspirated fluid may identify a pathogen for which tailored treatment can be initiated. However, there is a potential for false culture results, as will be discussed more thoroughly later in the section on culture of intraoperative tissue samples. In addition to culture, the cell count and differential in aspirated fluid should be determined. A substantial amount of work has been done in the past decade to identify WBC counts that are predictive of periprosthetic joint infection[5,15-18]. That work suggests that a WBC count of >1700 cells/μL or a polymorphonuclear neutrophil (PMN) percentage of >65% after the acute postoperative period is predictive of an infected knee joint[12,15,17]. Schinsky et al. performed an investigation involving these markers in hip joint aspirate and recommended threshold values of >4200 cells/μL for the WBC count and >80% for the PMN percentage[19]. Diagnosis of periprosthetic joint infection during the acute postoperative period is complicated by the natural increase in inflammatory markers during this time. Bedair et al. provided threshold values of 10,700 cells/μL for the synovial WBC count and 89% for the PMN percentage for the diagnosis of periprosthetic joint infection during this time period[20].

When suspicion of periprosthetic joint infection remains following initial aspiration and repeat aspiration, yet infection has not adequately been confirmed, the clinician may utilize imaging modalities if surgical intervention is not planned. Our institution participated in a multicenter investigation of the utility of ^{18}F-labeled fluorodeoxyglucose-positron emission tomography (FDG-PET) for differentiating between aseptic and septic causes of pain in the hip following total hip arthroplasty[21,22]. That study found that FDG-PET had a sensitivity of 85% and a specificity of 93% for diagnosing periprosthetic joint infection in the hip. Love et al. found a similar utility for FDG-PET in an analysis of periprosthetic joint infection in both the hip and the knee[23]. Other imaging modalities, including imaging of labeled leukocytes and gallium imaging, have been recommended in the AAOS guidelines, but these recommendations are based on weak to moderate evidence[12]. There is no evidence that magnetic resonance imaging (MRI) and computed tomography (CT) serve a purpose in diagnosing or characterizing a periprosthetic joint infection.

If a concrete diagnosis remains elusive after these tools have been used, the only remaining options are histological analysis of frozen tissue sections and culture of periprosthetic tissue, both of which require surgical intervention to examine the surroundings of the joint. The presence of a sinus tract in communication with the joint is a well-accepted indicator of periprosthetic joint infection and would merit immediate surgical intervention without the need for further investigation. On the other hand, purulence in the joint, which has long been well accepted as a marker of periprosthetic joint infection[11,14], should not be taken as an absolute indicator of the presence of infection. We have determined, in research that has not yet been published, that the sensitivity of the presence of gross purulence is low (<50%). Although the false-positive rate for gross purulence could logically be expected to be low, recent case reports have shown that gross purulence can be present in patients with a metal hypersensitivity reaction following metal-on-metal total hip arthroplasty[24,25]. These reports raise the suspicion that the presence of purulence in a joint (hip or knee) may be associated with an aseptic allergic reaction to a foreign material. For this reason, restraint should be exercised when diagnosing periprosthetic joint infection solely on the basis of purulent material in the joint.

Our institution does not perform histological analysis of frozen tissue sections from intra-articular samples. There are several reasons for this, including the complexity of the test and high variability of the results between reviewers. Although this tool has been promoted by many clinicians[5,6,8-10,14] and is supported by the AAOS guidelines[12], we question its addition to the work-up for periprosthetic joint infection in light of the recent advent of less expensive, more reliable tests such as aspirate analysis. It can be postulated that the association between the synovial PMN percentage and the neutrophil concentration in frozen tissue sections is very high. This hypothesis is unproven, but if it is true, frozen sections would have little utility in the diagnosis of periprosthetic joint infection after aspirate analysis had given ambiguous results, as they would probably neither confirm nor exclude periprosthetic joint infection but only mimic the aspirate results. Furthermore, it has been demonstrated by researchers at our institution and others that Gram stain is not an effective tool in diagnosing periprosthetic joint infection[26,27].

Tissue culturing of intraoperative intra-articular tissue samples on solid medium has historically been used as the gold-standard test in diagnosing periprosthetic joint infection. Nevertheless, numerous patients have a culture-negative periprosthetic joint infection, with an inability to isolate an organism from cultures reported in 2% to 18% of cases[28-33]. Inability to identify the infecting pathogen complicates diagnosis and treatment. Researchers at our institution have found culture-negative periprosthetic joint infection to be predictive of treatment failure in patients undergoing irrigation and debridement[34]. This knowledge has led us to investigate mechanisms to improve the sensitivity of tissue specimen culturing. False-negative results may be due to selection of inappropriate growth medium for the pathogen, biofilm formation, current use of antimicrobial therapy, or an inadequate culture incubation period. The AAOS guidelines recommend withholding antimicrobial agents until after tissue sampling for culture has been performed when there is a high suspicion of periprosthetic joint infection. Our institution retrospectively investigated the effect of preoperative antibiotic administration on intraoperative tissue specimen cultures in patients with previously confirmed periprosthetic joint infection, and it was found that administration of prophylactic antibiotics did not reduce the accuracy of tissue specimen culture results[35]. Schäfer et al. and Neut et al. showed that a longer culture incubation period improved the sensitivity of tissue specimen culture (from 63% to 64% after one week to 77% after two weeks)[36,37]. One concern with increasing the culture incubation period is the risk of false-positive results due to contamination. However, Schäfer et al. showed that >50% of contaminants were isolated in the first week of a two-week culture[36]. More importantly, their analysis showed that nonstandard pathogens were more likely to be isolated during the second week of incubation. Contamination of tissue specimen cultures resulting in a false-positive result occurs in 5% to 37% of periprosthetic joint infection cases[38-43]. Contamination is a real concern for the surgeon as it may subject the patient to unnecessary or more complicated surgery.

Definition of Periprosthetic Joint Infection

Despite their shortcomings, multiple tools for differentiating between periprosthetic joint infection and other diseases are at the disposal of the medical community. Although the AAOS guidelines provide direction in utilizing these tools, a definition of periprosthetic joint infection is necessary to permit comparisons among research studies and to provide the clinician with a definitive diagnosis when investigating a suspected periprosthetic joint infection. For this reason, multiple academic researchers have taken it upon themselves to provide a definition of periprosthetic joint infection based on the previously discussed diagnostic tools[5-10]. To date, these definitions have not incorporated the synovial aspirate cell count and differential. For this reason, we proposed a new definition of periprosthetic joint infection that incorporated aspirate analysis and attempted to improve the definition of a positive tissue specimen culture[11]. As no gold-standard definition of periprosthetic joint infection exists, our proposed definition was analyzed by comparison with the existing definitions. In addition, the results based on existing definitions were compared among themselves. That analysis found that in 24% of cases, at least one existing definition resulted in diagnosis of a periprosthetic joint infection while another well-accepted definition resulted in a diagnosis involving an aseptic etiology. This suggests that a diagnosis of periprosthetic joint infection may often be dependent on which well-regarded definition is being utilized, complicating comparisons among research studies that utilize different diagnostic definitions of periprosthetic joint infection. Our proposed definition of periprosthetic joint infection had an accuracy of 53% to 100% compared with existing definitions.

As previously discussed, our institution does not utilize histological tissue analysis, and this has therefore not been incorporated into our proposed definition of periprosthetic joint infection. Furthermore, as discussed above, it is suggested that

DEFINITION OF PERIPROSTHETIC JOINT INFECTION

Based on the proposed criteria, a definite PJI exists when:

1) There is a sinus tract communicating with the prosthesis; or
2) A pathogen is isolated by culture from two or more separate tissue or fluid samples obtained from the affected prosthetic joint; or
3) When four of the following six criteria exist:
   a. Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration,
   b. Elevated synovial white blood cell (WBC) count,
   c. Elevated synovial polymorphonuclear 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 5 high power fields observed from histological analysis of periprosthetic tissue at 400 times magnification.

Please note that a PJI may be present if less than 4 of these criteria are met.

The panel also acknowledged that in certain low-grade infections (e.g., *P. acnes*), several of these criteria may not be routinely met despite the presence of PJI.

Fig. 1

The Musculoskeletal Infection Society's new algorithm for diagnosis of periprosthetic joint infection (PJI)[44]. P. acnes = *Propionibacterium acnes*.

purulence serves a limited purpose and may result in misdiagnosis of periprosthetic joint infection. The Musculoskeletal Infection Society recently released a definition of periprosthetic joint infection[44]. It is hoped that this definition will be adopted as the gold-standard definition of periprosthetic joint infection and will provide uniformity in this field (Fig. 1).

As improvements continue to be made in the uniformity and accuracy of definitions of periprosthetic joint infection based on current diagnostic tools, other diagnostic tools continue to be developed. The tools investigated at our institution are discussed below and, if and when their efficacy is proven, their incorporation into the definition of periprosthetic joint infection will further improve the ability to diagnose periprosthetic joint infection in an accurate and timely fashion.

Leukocyte Esterase

As reported above, the combination of synovial fluid leukocyte count and neutrophil differential has been reported to have high sensitivity and specificity in the diagnosis of infection after total knee arthroplasty. It is therefore reasonable to expect an increase in the synovial concentration of enzymes specific to these white blood cells and to neutrophils in particular. Our institution conducted a prospective study that revealed one of these enzymes, leukocyte esterase, to be a highly accurate predictor of periprosthetic joint infection[45]. Synovial fluid was collected intraoperatively, prior to arthrotomy, in knee revision arthroplasties performed over a period of three years. At the time of collection, the synovial fluid was applied to a colorimetric strip test that is commonly used to test for urinary tract infection (Fig. 2). The results were stratified into four separate categories on the basis of the degree of color change in the strip (representing the concentration of leukocyte esterase in the sample). Periprosthetic joint infection was defined in the study according to a modification of our diagnostic criteria incorporating aspirate cell count analysis[11]. Compared with these criteria, the highest category of leukocyte esterase concentration (++) was 81% sensitive and 100% specific. Alternatively, when the two highest categories of leukocyte esterase concentration (+ and ++) were considered positive, the strip was 94% sensitive and 87% specific. Similar results were seen when aspiration was performed in

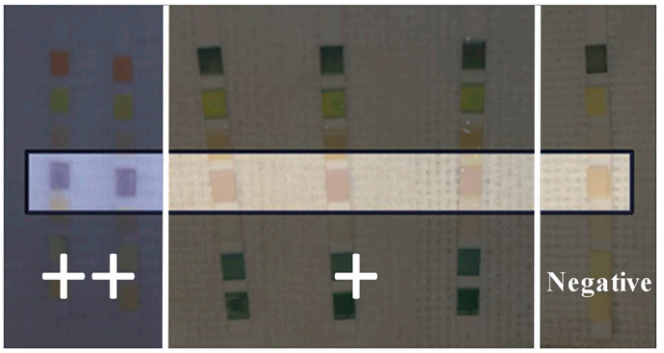

Fig. 2
Leukocyte esterase strip test showing purple ++, dark pink +, and light yellow negative results.

the clinic prior to surgery. The leukocyte esterase concentration also showed a high correlation with the ESR, CRP, synovial WBC count, and synovial PMN percentage.

Although this research is in its infancy, there is great promise that the use of colorimetric strips will provide the surgeon with another tool for accurately diagnosing or ruling out joint infection. This strip test has the advantages of being inexpensive and providing immediate results. Instant results are invaluable to the clinician and to the surgeon intraoperatively, and other instant-result tests have failed to prove to be useful to date[26,27].

Other Molecular Markers of Periprosthetic Joint Infection

As leukocyte esterase has proven itself to be a useful tool in diagnosing periprosthetic joint infection, the addition of other molecular markers has the potential to further increase the accuracy of diagnosis. For this reason, commonly known proteins in inflammatory pathways were also investigated. Identification of additional molecular markers in the synovial fluid that are predictive of periprosthetic joint infection has the potential to lead to the development of other rapid tests similar to the pregnancy and urinary tract infection dipstick tests.

A study was performed at our institution to assess the utility of forty-six well-known inflammatory proteins in samples of synovial fluid obtained prior to arthrotomy in seventy-four revision arthroplasty procedures, thirty-one of which were classified as septic and forty-three as aseptic according to our institutional criteria[46]. A proteomics analysis was conducted to determine the concentrations of the inflammatory proteins in each sample, and ROC curve analysis was used to establish the optimal threshold of each potential marker for diagnosing periprosthetic joint infection. This analysis indicated that five proteins could be considered highly accurate indicators of periprosthetic joint infection: interleukin-6 (IL-6), IL-8, CRP, α-2 macroglobulin, and vascular endothelial growth factor (VEGF). Using the optimal threshold of 4270 pg/mL, IL-6 was the most accurate predictor of periprosthetic joint infection, with a sensitivity of 87% and a specificity of 100%[46]. This work confirmed similar findings by Deirmengian et al., who studied a series of twenty-three potential biomarkers of periprosthetic joint infection[47]. In both analyses, IL-6 was the most accurate predictor of periprosthetic joint infection.

Our research remains under way, with plans for an increased sample size and the inclusion of multiple institutions. The long-term potential for development of a quick, accurate diagnostic test for periprosthetic joint infection, supplementing the existing diagnostic criteria and the leukocyte esterase test, represents an enormous opportunity to improve management of patients, decrease cost, and relieve the ambiguity currently involved in treating a failed total joint arthroplasty.

Synovial CRP Concentration

The CRP concentration in serum is a well-accepted tool in the investigation of suspected periprosthetic joint infection[13,48]. However, as previously described, serum CRP has low specificity as a marker of periprosthetic joint infection. It was postulated that this inflammatory marker, which is a known marker of periprosthetic joint infection, would be more definitively elevated at the arthroplasty site. For this reason, an investigation of the synovial CRP concentration as a predictor of periprosthetic joint infection was undertaken at our institution.

Synovial fluid samples were collected intraoperatively during aspiration prior to arthrotomy in sixty-six revision knee arthroplasties performed over the course of a single year[49]. Again, revisions were classified as septic or aseptic according to our institution's set of diagnostic criteria[11]. ROC curve analysis indicated the optimal CRP threshold to be 3.7 mg/L in the joint fluid compared with 16.5 mg/L in the serum in the same subset of patients. The sensitivity of the CRP concentration in the synovial fluid was 84%, the specificity was 97%, and the accuracy was 96%. The synovial CRP concentration was a superior predictor of periprosthetic joint infection compared with the serum CRP concentration, which had a sensitivity of 76%, a specificity of 93%, and an accuracy of 91%[49].

These findings, although preliminary, provide yet another avenue for improving the early diagnosis of periprosthetic joint infection and decreasing false-negative diagnoses. As with the previously mentioned work, this research is continuing at additional centers and the expectation is that synovial CRP will prove itself and become incorporated into the diagnostic algorithm for periprosthetic joint infection. The advantage of testing for synovial CRP is that this marker can be readily measured in all hospital clinical laboratories and can be easily utilized without development of novel technologies or training of additional staff. In addition, the outcome of this test is not heavily dependent on the operator and can be universally compared among clinics.

Current Methods for Treatment

Accurate and timely diagnosis of periprosthetic joint infection is essential as its treatment is an urgent matter. Furthermore, the treatment for aseptic failure of an arthroplasty varies greatly from that required for eradication of periprosthetic joint infection. Once the diagnosis of periprosthetic joint infection is confirmed, the characteristics of the infection must be elicited. These include the duration of symptoms, patient immune status and overall health characteristics, history of

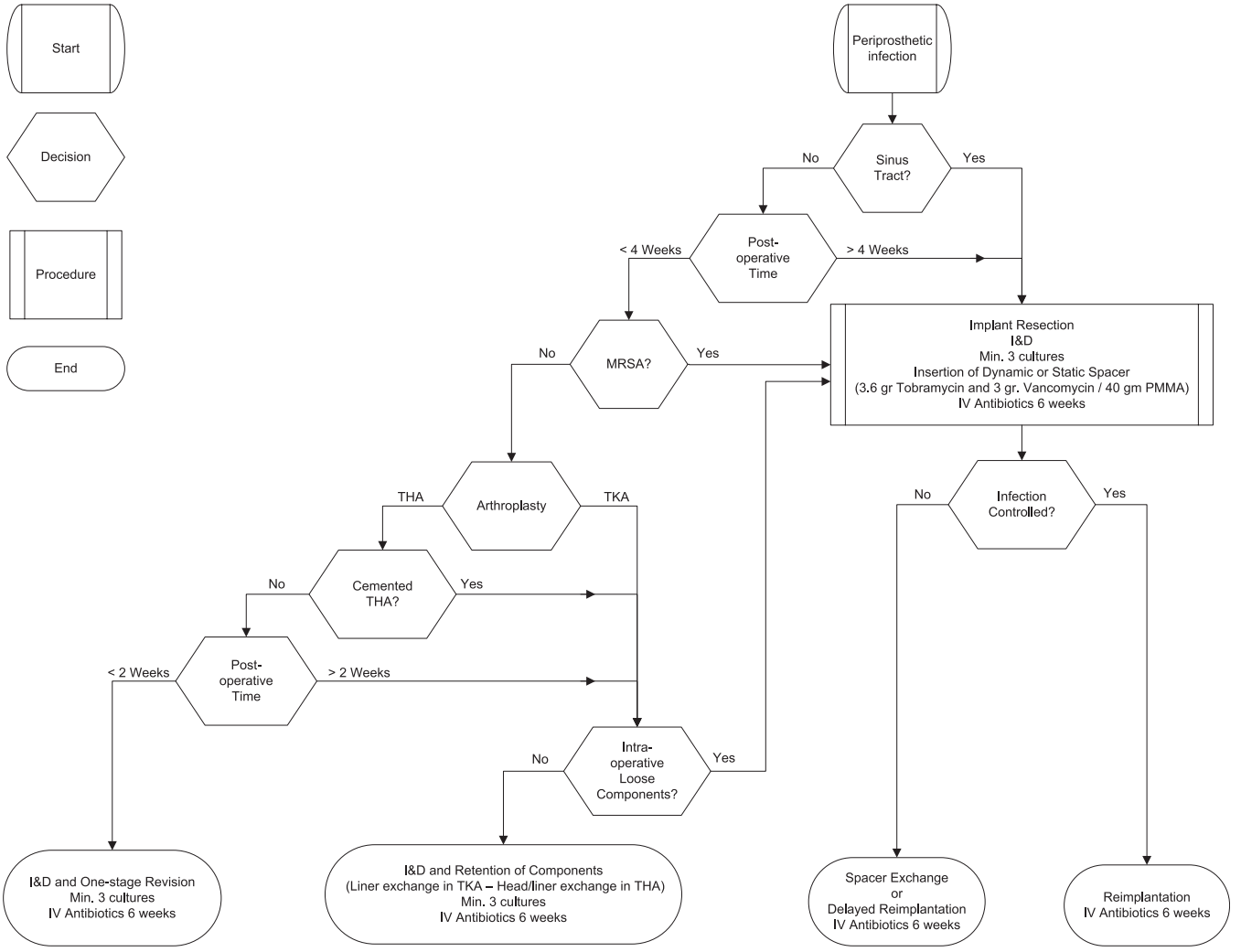

Fig. 3

Algorithm utilized for periprosthetic joint infection treatment at our institution. THA = total hip arthroplasty, TKA = total knee arthroplasty, I&D = irrigation and debridement, Min. = minimum, IV = intravenous, gr = grams, MRSA = methicillin-resistant *Staphylococcus aureus,* and PMMA = polymethylmethacrylate.

periprosthetic joint infection in the current joint and all other joints, status of any joint wound, joint function expectations, and characteristics of the infecting organism. These data will dictate the surgical treatment selection (Fig. 3).

When surgery would present a great risk to patients because of their state of health and the infection is caused by a pathogen that is of low virulence and susceptible to antimicrobial agents, antibiotic suppression alone may be the best treatment option. There is a lack of evidence for treatment of patients solely with antibiotics, without surgical intervention. Despite this lack of literature support, patients who cannot tolerate surgery are without options other than attempts to control the periprosthetic joint infection with antimicrobial agents. Chronic antibiotic suppression is also indicated in patients with persistent periprosthetic joint infection following surgical debridement if they decline or cannot tolerate subsequent surgery. Infection control has been shown to be moderately successful in this patient population[50-53].

Two-stage exchange—resection of the implants, placement of a temporary antibiotic-impregnated cement spacer, and delayed component reimplantation—is the gold-standard treatment for periprosthetic joint infection in North America. However, retention of the original prosthesis could provide decreased morbidity and improved return to function. Irrigation and debridement with retention of the prosthesis is traditionally indicated in patients with acute onset of symptoms, a well-fixed and aligned implant, an antibiotic-susceptible organism, and sufficient soft-tissue coverage[54]. Our institution has studied the outcome of this treatment method[34,55-60]. No statistically significant difference in outcome could be identified among acute postoperative, acute hematogenous, and chronic infections in multiple investigations of irrigation and debridement for the treatment of periprosthetic joint infection[34,55]. However, it is possible that these studies were underpowered and unable to detect actual differences. These analyses did identify staphylococcal infection as an independent predictor of failure of treatment involving irrigation and

debridement with implant retention. Deirmengian et al. also supported this finding[61]. Furthermore, two separate studies that included our institution indicated poor eradication rates (16% and 37%) for methicillin-resistant *Staphylococcus aureus* (MRSA) after irrigation and debridement with implant retention[58,60]. In another study, streptococcal infections—which have historically been believed to be well treated with irrigation and debridement with implant retention—had an eradication rate (65%) that was comparable with that of all other organisms (71%)[56].

These recent additions to our knowledge regarding periprosthetic joint infection treatment suggest a decreased utility for surgical intervention with prosthesis retention. Our institution's treatment algorithm provides an opportunity for irrigation and debridement with one-stage prosthesis exchange for the treatment of a non-MRSA periprosthetic joint infection occurring during the acute postoperative period (within two weeks) after cementless total hip arthroplasty. Although the effectiveness of such treatment remains unknown, the removal of the implant before it has become well fixed allows for more extensive debridement and for removal of the pathogen's growth surface.

As it is apparent that irrigation and debridement with prosthesis retention has become a stepping stone to two-stage exchange, it should be noted that a multicenter study including our institution found a lower eradication rate following two-stage exchange of a knee prosthesis in patients who had undergone a prior irrigation and debridement compared with patients treated directly with two-stage implant exchange[57]. A subsequent study at our institution found no difference in the outcome of two-stage exchange of a hip prosthesis depending on whether or not prior irrigation and debridement had been performed. Furthermore, our institution has reported similar functional outcomes after total knee revision for septic and aseptic causes[62].

The orthopaedic community currently lacks a concrete prognostic classification for the outcome of treating periprosthetic joint infection. Efforts have been made to fill this void, beginning with predictors of recurrent or persistent infection after two-stage knee revision[63]. That investigation found culture-negative periprosthetic joint infection, a methicillin-resistant pathogen, and increased operative time during reimplantation to be independent predictors of recurrence of the infection. In a separate study, two-stage revision to treat a periprosthetic joint infection caused by a gram-negative pathogen was found to have as low a success rate (52%) as two-stage treatment of an infection caused by MRSA (51%), whereas the success rate for treatment of methicillin-sensitive gram-positive organisms (69%) was considerably better[64]. This, combined with recent findings, illustrates the poor outcome of even the gold-standard treatment (two-stage exchange) for periprosthetic joint infection.

Because of the high failure rate of periprosthetic joint infection treatment, patients often present with recurrent infection following two-stage exchange. This presents a challenge to the treating surgeon as few surgical options, including a repeat two-stage exchange, remain. It has been our experience that repeat two-stage exchange does provide patients with a reasonable expectation of infection control. In a study of repeat two-stage exchange of a knee prosthesis at our institution, fourteen of eighteen patients remained free of infection at a minimum of two years, and two of the four failures were successfully treated with a third two-stage exchange[65]. In a separate study involving the hip, only eight of fifteen patients undergoing repeat resection underwent reimplantation, but seven of these eight patients remained free of infection. In comparison, eradication of the infection failed in seven of eleven patients treated with repeat two-stage exchange of a hip prosthesis in a study by Kalra et al.[66].

Salvage procedures must be considered in the event of repeat failure of treatment for periprosthetic joint infection in patients with a limited probability of a functional joint on reimplantation, a compromised immune system, or a quality of health that precludes multiple surgeries. Salvage procedures in the knee include arthrodesis and above-the-knee amputation. Both procedures have the potential to eradicate the periprosthetic joint infection and produce a functioning limb. A multicenter analysis including our institution indicated moderate success following above-the-knee amputation secondary to periprosthetic joint infection[67]. Although the study cohort was small, it appeared that the patient's quality of life was dependent on use of a prosthesis. It is important to understand that internal fixation during knee arthrodesis for the treatment of periprosthetic joint infection can result in the formation of a biofilm on this implant and lead to persistent infection; thus, the use of external fixation should be considered despite the higher rate of nonunion. At this time, salvage procedures for the hip are limited to arthrodesis, which requires the use of plate fixation. Surgeons should therefore be mindful of the likely need for continued chronic antibiotic suppression in these patients.

Discussion

As the burden of periprosthetic joint infection trends upward, it is likely that an increasing number of clinicians and surgeons will encounter this disease. If prevention fails, meeting this burden will require improved detection and treatment on the part of all physicians and substantial efforts by academic researchers to enhance these tools. This review has outlined many of the recent developments in the diagnosis and treatment of periprosthetic joint infection. The tools of the diagnostician are constantly changing, with addition of the highly accurate synovial fluid analysis technique during the past decade and the likely addition of other biomarkers and instant-result dipsticks in the next decade. Further work is needed to fully understand the prognostic factors associated with successful treatment of this debilitating disease. Given the current knowledge outlined in this review and the investigations planned for the future, it does not seem unrealistic to expect that the orthopaedic community and its medical partners can meet this burden. ■

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