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The Diagnosis of Periprosthetic Joint Infection

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ABSTRACT

Periprosthetic joint infection remains one of the most common failure modes following total hip and total knee arthroplasty. As such, a systematic and cost effective approach to the evaluation and work-up of a patient with a suspected periprosthetic joint infection should be undertaken in every patient with a painful total joint. Although we have many diagnostic tools, a history and physical remain the most important. Many of the current laboratory tests are indirect measure of infection, lack specificity for diagnosis of infection, but serve as sensitive and cost effective screening tools. In addition, a new definition of periprosthetic infection helps to standardize the diagnosis. Biomarkers hold the promise of improved specificity and are becoming increasingly popular as a diagnostic tool.

Periprosthetic joint infection (PJI) remains a significant challenge and common mode of failure following total hip and total knee arthroplasty. PJI is the leading cause of revision for failed total knee arthroplasty (16.8% of all knee revisions) and the 3rd leading cause of failure of total hip arthroplasty (14.8% of all hip revisions) [1,2]. The economic impact of treating a patient with an infection after total joint replacement is staggering. It is associated with higher costs in the range of $60,000 to $100,000 per treatment, longer hospital stays and higher complication rates [3–5].

Because the treatment of a patient with PJI is so drastically different from those without an infection, it is imperative that the diagnosis of infection be ruled out or definitively established prior to surgery. Historically, there have been no standardized definitions of PJI and no standardized algorithm to approach a patient with a suspected infection following total joint arthroplasty. This often times leads to a lengthy and costly work up with the addition of unnecessary tests and procedures that can delay or misdiagnose the condition.

Recently, several helpful documents have been put forth to create a standardize definition and approach to the patient with a suspected PJI. These should be familiar to all physicians who care for and evaluate patients with a painful total joint replacement. These documents include: (1) The American Academy of Orthopaedic Surgeons Clinical Practice Guidelines on Diagnosis of Periprosthetic Joint Infection (2) The Musculoskeletal Infection Society (MSIS) modified definition of periprosthetic joint infection (3) The Proceeding of the International Consensus Meeting on Periprosthetic Joint Infection [6,7]. This review article will incorporate these finding and review a standardized approach to the patient with a suspected periprosthetic joint infection.

The Definition of PJI in the Hip and Knee

Despite the multitude of test available to diagnose PJI, what exactly defines PJI remains controversial. The diagnosis of PJI can be challenging as most tests do not evaluate specifically for the presence of PJI but rather are indirect measures of infection. The recently proposed modified Musculoskeletal Infection Society (MSIS) definition of PJI provides a standardized method to aid in the diagnosis of infection. (Table 1) [8]. To establish the diagnosis, one of two major criteria or three of five minor criteria must be met.

The Diagnosis of PJI in the Hip and Knee

History and Physical

Despite the wide array of tests that are at our disposal to diagnosis PJI, it is the initial history and physical exam that remain the most crucial. A clinical suspicion for PJI should be high in every patient that presents with a painful total joint arthroplasty. As a general rule, because the treatment of PJI is so drastically different, every patient that presents with a painful total joint should be considered infected until that diagnosis can be effectively ruled out.

The history often times will provide important clues and raise the suspicion of PJI. First, the presence of any known risk factors that may place the patient at higher risk for the development of PJI should be noted. It is important to ask these questions, as patients often will not volunteer this information or associate them with PJI. These include a history of prior infection, diabetes, smoking, obesity, malnutrition and other medical comorbidities. In addition, any bacteremic events such as other surgeries or dental work should be noted. It is also important to ascertain the events around the time of initial surgery that could be risk factors. These can include prolonged operative time, excessive

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Table 1
Modified MSIS definition of PJI.

Based on the proposed criteria, definite PJI exists when:
(1) There is a sinus tract communicating with the prosthesis; or
(2) A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or
(3) Three of the following five criteria exist:
a. Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein CRP) concentration
b. Elevated synovial leukocyte count OR ++ result on leukocyte esterase test strip
c. Elevated synovial neutrophil percentage (PMN%)
d. Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or
e. Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at 9400 magnification.

wound drainage or wound healing problems, need for blood transfusions, and use of additional antibiotics around the time of surgery.

The clinical history should also ask about the location of the pain to rule out other sources of referred pain such as the hip and the lumbar spine. The timing of onset of the patient's pain is important. Has it been persistent since surgery or did they have a pain free interval? What are the severity and the character of the pain? Do they have redness or erythema around the joint? Do they have changes associated with activity? The physical exam should focus on the appearance of the joint, noting the presence of warmth, swelling, erythema and wound healing issues. Pain with range of motion should be noted. A thorough examination adjacent joints and spine should also be conducted to rule out potential sources of referred pain.

Laboratory Test for Diagnosis of Periprosthetic Joint Infection

Blood tests provide a useful screening tool in the initial evaluation of a patient with suspected PJI. In all cases of suspected PJI, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) should be obtained as an initial screening tool. These tests have been shown to have a high sensitivity, good negative predictive value and are a cost-effective screening tool [9,10]. If either ESR (>30) or CRP(>10 mg/L) are elevated in a patient with a possible PJI, aspiration of the joint should be performed as the next step.

A negative result on both tests has extremely good negative predictive value at ruling out active PJI [11]. A positive result on both tests more reliably rules in PJI compared to a positive result on just a single test and should prompt the physician to perform a joint arthrocentesis [12].

Serum interleukin 6 (IL-6) is a more recently available blood test with promise as a more specific marker of acute infection but is not readily available in all laboratories [13]. Peripheral white blood cell (WBC) counts are readily available as part of a complete blood count (CBC). Multiple studies have investigated the utility of serum WBC in diagnosis of PJI [14,15]. Despite differing thresholds among the studies, WBC count was not as consistently useful as ESR or CRP for the diagnosis of PJI and not recommended to be used as a screening tool for PJI.

Joint Aspiration and Synovial Fluid Analysis

In a patient with an elevated ESR and/or CRP or a high clinical index of suspicion for PJI, joint aspiration and synovial fluid analysis should be performed. Knee aspiration can routinely be performed in the office setting. Hip aspirations are more difficult to perform and are associated with a higher false positive rate. It is recommended that selective hip aspiration be performed based on laboratory results, plan for surgery and physician index of suspicion [16].

All synovial fluid aspirates should be evaluated for total White Blood Count (WBC), with particular attention paid to the differential (% PMN's). In addition, the fluid should be sent for aerobic and anaerobic cultures. Elevated synovial fluid WBC count is highly suggestive of PJI. Multiple recent studies have demonstrated excellent sensitivity and specificity of synovial WBC for diagnosis of chronic periprosthetic infection (Table 2). Synovial fluid white blood cell (WBC) count >1700 cells/μL and percentage of polymorphonuclear cells (%PMNs) greater than 60-65% are should be considered highly suspicious for PJI [17]. Based on the available literature, the proceedings of the International Consensus on PJI recommends the following thresholds for diagnostic tests for chronic PJI: ESR >30, CRP >10mg/L, Synovial fluid WBC >3000 cell/μL and % PMN of 80% [7].

It can be difficult to differentiate between infection and the pain and swelling that is commonly experienced in the early postoperative period, particularly following TKA. Recently, data on cell counts and WBC's differential have demonstrated values above which PJI may be present in the acute postoperative period [18]. Within six weeks of surgery, both inflammatory markers and synovial cell counts are elevated secondary to recent surgery, and must be interpreted more conservatively. Based on the available literature, the proceedings of the International Consensus on PJI recommends the following thresholds for diagnostic tests for acute PJI (within 6 weeks of surgery): ESR not reliable, CRP >100 mg/L, synovial fluid WBC >10,000 cell/μL and % PMN of 90% [7].

Gram stains lack sensitivity and specificity and is not routinely recommended in synovial fluid evaluation [19]. Cultures remain the most effective method for specific organism identification. Unfortunately, although cultures from synovial fluid and tissue have a high specificity, they have poor sensitivity and a negative culture does not rule out the diagnosis of PJI (Table 3). As such, every effort should be made to try and improve the yield of cultures from synovial fluid analysis. Routine aerobic and anaerobic cultures should be obtained. Fluid placed in blood culture vials tends to have higher yield and swabs should be avoided [20,21]. If suspicion is high or prior cultures have been negative, the addition of Acid Fast Bacilli (AFB) and fungal cultures should be added. Additionally, incubating cultures for a longer duration (21 days) may assist in identifying fastidious organisms such as p. acnes. Despite attempts to identify the infecting organism, cultures may remain negative in up to 20% of cases that are truly infected [22].

More recent evaluations of the synovial aspirate include assessment for the presence of leukocyte esterase. This simple and inexpensive test has been shown to be highly sensitive and specific for the presence of PJI [23,24]. In addition, it is a "point of service" test with the results available rapidly. Because it is a colorimetric test, the synovial fluid must be clear and not bloody in order to be accurate.

Radiographic Tests

Plain X-Rays

Plain radiographs should be obtained in every patient complaining of a painful total joint replacement. Ideally, these radiographs should be compared to prior films to evaluate for signs of loosening, malposition or osteolysis. The utility of plain radiographs for the diagnosis of PJI is limited. Early signs of failure such as unexpected bone loss (osteolysis) or component loosening should raise the clinician's suspicion for PJI. One should keep in mind however, that the sensitivity of plain radiographs to detect bone loss is low, and substantial bone resorption noted on plain radiographs can take months to develop.

In addition, the utility of Computer Tomography (CT Scans) as well as Magnetic Resonance Imagining (MRI) remains limited in the diagnosis of PJI. These expensive test lack the specificity to differential infection, and the AAOS Clinical Practice guidelines do not recommend the routine use of these imaging modalities for the diagnosis of PJI [16]. Enhanced imaging techniques, such as PET scans, however are continually being developed that may improve the sensitivity and specificity of this modality as a diagnostic tool in the future [25].