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What Is the Optimal Criteria to Use for Detecting Periprosthetic Joint Infections Before Total Joint Arthroplasty?

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ABSTRACT

Background: The purposes of this study were to (1) test the accuracy of α-defensin and combined α-defensin-aspiration cultures in diagnosing periprosthetic joint infection (PJI) before revision total knee and hip arthroplasty and (2) evaluate Musculoskeletal Infection Society (MSIS) criteria and α-defensin as predictors of successful reimplantation (second-stage) at 1 year after surgery.
Methods: We retrospectively evaluated a total of 97 synovial fluid aspirations performed between August 2014 and September 2016 before revision due to septic or aseptic failures (n = 70) or before second-stage (n = 27) joint arthroplasty. Revisions were categorized as either septic or aseptic according to the MSIS criteria. Synovial fluid was tested for α-defensin, cell count with differential, and cultures. Reimplantations were assessed for success or failure (defined as the need for reoperation due to infection) within 1 year after surgery.
Results: For septic and aseptic revision arthroplasty, the sensitivity, specificity, positive predictive value, and negative predicted value of α-defensin was 97% while for the combined α-defensin and aspiration culture, it was 96%, 100%, 100%, and 97%. Despite being performed with negative MSIS criteria and α-defensin test results, 11% (3/27) of reimplantations (second-stage) failed within 1 year postoperatively because of infection.
Conclusion: Alpha-defensin is an accurate diagnostic test for the diagnosis of PJI before revision arthroplasty. The combination of α-defensin and aspiration cultures has higher specificity and positive predictive value. MSIS criteria and α-defensin may help predict the success of reimplantations within 1 year after surgery.

Periprosthetic joint infection (PJI) is a serious complication that is usually accompanied by a high economic burden. As the revision burden increases, we must scrutinize the accuracy of the tools currently available that aid in the diagnosis of PJIs [1,2]. A false-positive PJI diagnosis entails an unnecessary 2-stage revision while a false negative might lead to recurrent implant failure due to infection.

No single instrument or test is 100% accurate in the diagnosis of PJI [3,4]. Serology tests such as C-reactive protein and erythrocyte sedimentation rate have been reported to have a sensitivity of 95% and 88% for hips and a sensitivity of 94% and 97% for knees, respectively [5]. However, these 2 particular biomarkers may misdiagnose PJI in total joint arthroplasty [6]. A positive preoperative culture of synovial fluid obtained from joint aspiration remains valuable in the diagnosis of infection; unfortunately, a negative result does not rule it out.

The Musculoskeletal Infection Society (MSIS) criteria is a new definition for PJI from the workgroup of the MSIS. It is the result of the International Consensus Meeting on PJI [3,4]. The presence of one major MSIS criteria or at least 3 minor criteria represents a positive result, in other words, PJI (Table 1). The MSIS criteria is the most comprehensive tool available for the true identification of PJI, and in the current investigation, it was used as the “gold standard.” Unfortunately, the diagnosis of PJI remains elusive in many cases. We

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Table 1
Musculoskeletal Infection Society (MSIS) Criteria.

MSIS Criteria	
Major criteria	Two positive periprosthetic cultures with phenotypically identical organisms or a sinus tract communicating with the joint.
Minor criteria	Elevated serum C-reactive protein (CRP; >10 mg/L) and erythrocyte sedimentation rate (ESR; >30 mm/h). Elevated synovial fluid white blood cell count (>3000 cells/μl) or ++ change on leukocyte esterase test strip. Elevated synovial fluid PMN percentage (>80%). Positive histological analysis of periprosthetic tissue. A single positive culture.

PMN, polymorphonuclear.

acknowledge that a hypothetical ideal "gold standard" test should have a 100% sensitivity and specificity, but MSIS criteria is the current consensus and accepted definition of PJI, yet, it is complex and time consuming [7]. It has been shown to have a low sensitivity and a high specificity [8,9]. George et al [9] reported a 26% sensitivity while specificity (the ability to rule in infection) was high, at 94% . Certainly, the preoperative diagnosis of PJI remains challenging.

Attempts at simplifying the diagnosis of PJI have led to the identification of biomarkers with the hope that they could be used as standalone tests. These biomarkers include α-defensin, leukocyte esterase, procalcitonin, interleukin-6, tumor necrosis factor-alpha, and interferon-gamma [10,11]. Alpha-defensin is a neutrophil antimicrobial peptide. The response of neutrophils to an infection in the synovial fluid causes the release of this peptide whose role is to neutralize the offending pathogens [12]. Therefore, its identification in the synovial fluid may represent a periprosthetic infection because it is expressed by polymorphonuclear cells and lymphocytes when in the presence of proinflammatory cytokines [13]. Although not currently part of the MSIS criteria, α-defensin is being currently used as a biomarker in the detection of periprosthetic join infection with a reported sensitivity and specificity of over 96% [14].

In light of the limitations of MSIS criteria and the increasing use of α-defensin for the diagnosis of PJI, the purposes of this study were to (1) test the accuracy of α-defensin and combined α-defensin-aspiration cultures in detecting PJI before revision total knee and hip arthroplasty using the MSIS criteria as the "gold standard" and (2) evaluate MSIS criteria and α-defensin as predictors of success of reimplantation (second-stage) within 1 year after surgery.

Materials and Methods

After the institutional review board approval, we performed a retrospective review of 229 consecutive preoperative knee or hip synovial fluid aspirations performed between August 2014 and September 2016 by 2 board-certified adult reconstructive orthopedic surgeons in a single institution. Out of the 229 aspirations, 132 were excluded because they were performed either on a native joint (n = 10), on patients aspirated as part of a painful total joint workup and who did not undergo surgery (n = 112), before synovectomy (n = 1), on cases with coexistent metallosis (high false-positive rates reported [11,15]) (n = 2), or before irrigation and debridement with poly exchange (n = 5), or the results were indeterminate testing (n = 2).

The irrigation and modular part exchange cases were excluded because they were all performed in the early postoperative period; timing which has not been validated for α-defensin. As a result, 97 synovial fluid aspirations performed before revision arthroplasty due to septic or aseptic failures (n = 70) or before second-stage arthroplasty (ie, reimplant; n = 27) were analyzed (Fig. 1).

Prerevision workup involved multiple criteria in the MSIS including complete blood cell count, erythrocyte sedimentation rate, C-reactive protein, and joint aspiration. Synovial fluid was analyzed for cell count with differential, cultures, and α-defensin (Synovasure, CD Diagnostics, Inc., Wynnewood, Pennsylvania). Alpha-defensin was tested per standard laboratory techniques after being transported in sterile containers to Citrano Medical Laboratories, Inc which is a subsidiary of CD Diagnostics. The α-defensin diagnostic test uses enzyme-linked immunosorbent assay and defines 5.2 mg/L as a positive result.

Before surgery, revisions were categorized as either aseptic or septic based on the modified MSIS criteria [16]. Those cases that did not meet the MSIS criteria were revised and deemed to be aseptic while those that met the criteria were deemed septic and underwent firs-stage revision (ie, explant). During surgery, 4 samples for cultures were obtained including synovial fluid, synovial tissue, and implant-bone interface from the femur and tibia. Routine histological analyses of frozen sections were not obtained.

To evaluate MSIS criteria and α-defensin as predictors of successful reimplantation (second-stage) at 1 year after surgery, we reviewed reimplantation cases (second-stage) making use of our electronic medical records (EPIC). Failure was defined as the need for reoperation due to infection within 1 year after surgery.

Statistical Analysis

To test the accuracy of α-defensin and combined α-defensin-aspiration cultures in diagnosing PJI before revision total knee and hip arthroplasty, we compared α-defensin/preoperative cultures against MSIS criteria in the know that the latter is not an ideal or perfect "gold standard." However, the "gold standard" can be either the most used or the most accepted method. The use of α-defensin or the combination of α-defensin and preoperative synovial fluid cultures to predict infection status was presented using sensitivities, specificities, positive and negative predicted values. Categorical variables were described using numbers and percentages (frequencies) while continuous variables were described using means.

Results

The mean age of the entire total hip arthroplasty/total knee arthroplasty cohort (n = 97) was 66 years. Fifty percent (35/70) of

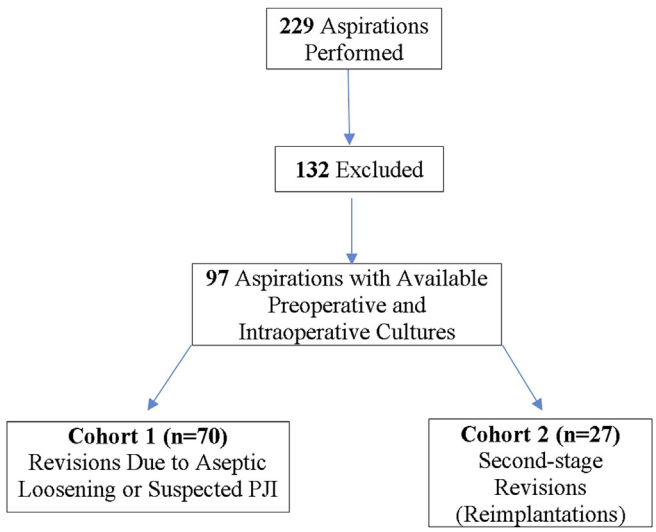

Fig. 1. Patient selection flowchart.