

and proximal femur resulted in significantly increased positive culture rates when compared to aspiration of synovial fluid alone [11]. However, it is difficult to extrapolate these findings to assume that obtaining a bone sample in a patient with PJI is likely to increase the yield of culture. In the absence of adequate data, we have refrained from recommending that bone samples for culture should be taken routinely in patients with PJIs.

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QUESTION 4: Is there a role for obtaining cultures before, and at the time of, insertion of prosthesis during second stage (reimplantation) of a two-stage exchange arthroplasty?

RECOMMENDATION: Preoperative aspiration of a joint should be determined based on the index of suspicion for persistent infection. During reimplantation, however, multiple fluid and tissue samples should be sent for culture. There is a direct correlation between the outcome of two-stage exchange arthroplasty and culture results during reimplantation.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 95%, Disagree: 4%, Abstain: 1% (Unanimous, Strongest Consensus)

RATIONALE

Two-stage exchange arthroplasty consists of removal of the infected prosthesis in the first stage, usually replacing it by an antibiotic-loaded cement spacer and treatment with systemic antibiotics. Once the infection is thought to be under control, the second-stage of reimplantation is performed. The metrics that determine the optimal timing of reimplantation are not known. However, many surgeons rely on a combination of metrics that may include aspiration of the joint prior to reimplantation. The exact role of preoperative joint aspiration prior to reimplantation remains undefined. Furthermore, there is also no specific test to determine if the infection has or has not been controlled.

Although aspiration of a joint is critical for the diagnosis of periprosthetic joint infections (PJIs) [1], it is not obvious if culture of synovial fluid with a polymethyl methacrylate (PMMA) spacer in place before reimplantation is helpful for the diagnosis of persistent infection [2]. In fact, it has been demonstrated that aspiration for microbial culture before the second stage has a low sensitivity for predicting infection [3–6]. Lonner et al. investigated the role of knee aspiration for detection of persistent infection before reimplantation and after cessation of a four- to eight- week course of antibiotics. They found that knee aspiration performed after resection arthroplasty had a sensitivity of zero, a positive predictive value (PPV) of

zero, a negative predictive value (NPV) of 75% and a specificity of 92% [6]. Janz et al. studied the diagnostic performance of synovial aspiration in resected hips without a PMMA spacer, for detection of infection persistence prior to total hip arthroplasty (THA) reimplantation. They found a sensitivity of only 13% and specificity of 98% and concluded that aspiration of a resected hip neither reliably confirmed nor excluded the persistence of infection [5]. Hoell et al. investigated 115 patients with two-stage hip or knee arthroplasty and found that the sensitivity of the aspiration culture before reimplantation was 5% (95% confidence interval (CI), 0.13–24.87) and the specificity was 99% (95% CI, 94.27–99.97). The NPV was 83% and the PPV was 50% [4]. Preininger et al. investigated the diagnostic validity of synovial PMMA spacer aspiration after two weeks of antibiotic holiday for detection of persistent infection. They included 73 patients who underwent two-stage revision for infection and found only 21% sensitivity for synovial PMMA space aspiration. They concluded that synovial PMMA aspiration cannot be recommended for exclusion of persistent infection [7].

There are some potential explanations for this finding. First of all, it is possible for bacteria to be in a biofilm and remain adherent to cement spacer, which in turn leads to uncertain predictability of culture from aspirations before reimplantation [8–10]. Secondly, the

elution of antibiotics from PMMA into the joint may interfere with isolation of the infecting organism from the joint aspirate. Although major elution of antibiotics from PMMA cement spacer occurs early, there is usually adequate elution of antibiotics at later dates that can interfere with isolation of the infective organism [11,12].

Another controversial aspect of two-stage revision for infection is the role of reimplantation microbiology [13,14]. Hart et al. reviewed 48 patients underwent two-stage revision for infected total knee arthroplasty (TKA). They found 11 (22.9%) positive cultures at the time of reimplantation; seven of them were different from the primary infecting microorganisms. They could not find any relation between the positive reimplantation culture and the outcome [15]. Bejoen et al. review 152 patients with PJI who underwent two-stage revision over a 4-year period. Patients were managed with antibiotic free interval before reimplantation. They found that reimplantation microbiology was positive in 21 cases (14%) but did not correlate with eventual outcome. The same organism, determined by comparing species and antibiotic susceptibility patterns, was isolated at both excision and reimplantation in four cases (3%). In 10 cases (6%) a different organism was isolated and in 7 cases (5%) reimplantation cultures were positive following negative cultures at the first stage. They could not find any association between positive culture and outcome; however, patients with positive culture at the time of reimplantation received prolonged antibiotics. Overall, 57% of patients with positive reimplantation microbiology received very prolonged (>1 year) antibiotics [14]. Puhto et al. reviewed 107 patients treated with two-stage revision and found 5.2% positive reimplantation microbiology. Most of the reimplantation cultures were unrelated to organisms cultured at the first stage, which is similar to the results of earlier studies. They treated all patients with positive reimplantation culture as an acute postoperative PJI. The success rate of two-stage revision was not significantly different in patients with positive versus negative microbiology at reimplantation. However, the only case with positive reimplantation culture who failed had the same organisms in both excision and reimplantation [13].

Tan et al. reviewed 267 PJIs (186 knees and 81 hips) treated with two-stage exchange arthroplasty. Here, 33 patients (12.4%) had >= 1 positive culture result at the time of reimplantation. The isolated microorganism at reimplantation was the same as the initial infecting organism in six (18.2%) of the 33 cases. They found that positive intraoperative culture at the time of reimplantation, regardless of the number of positive samples, was independently associated with > 2 times the risk of subsequent treatment failure and earlier reinfection [2]. Akgun et al. reviewed 63 two-stage revision arthroplasties involving 84 THAs and 79 TKAs. They found >= 1 positive culture at the time of reimplantation in 27 patients (16.6%), which was the same initially infection organism in 9 (33%) of them. The risk of the failure of treatment was significantly higher in patients with a positive culture [16].

It seems that the result of culture at the time of reimplantation is related to the outcome of treatment of two-stage exchange arthroplasty. There are several limitations for those studies that implicate reimplantation microbiology do not affect the outcome of two-stage revision for PJI. Firstly, in some studies they found higher rates of failure in patients with positive reimplantation culture, but this

finding did not reach statistical significance due to lack of power from the small cohorts available for analysis [13,15]. Secondly, they considered even one positive culture at the time of reimplantation as acute postoperative infection and put the patients on long term antibiotics sometimes longer than a year which makes the success of treatment doubtful [14].

Based on the current evidence, routine cultures during reimplantation should be obtained and relied on. At least four specimens (tissue and fluid) should be taken at second stage surgical reimplantation, using different sterile unused instruments for each sample for subsequent culture. Even single-positive cultures increase the risk of reinfection and failure of treatment and therefore should not be considered as contamination. Patients with positive reimplantation microbiology should receive further antibiotic after reimplantation [2]. Positive culture during reimplantation with the same initial infecting organism or new organisms is independently associated with higher rate of subsequent failure and earlier reinfection [2,16].

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