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QUESTION 16: How should divergent results between intraoperative tissue cultures (TCs) and sonication of the prosthesis be managed?

RECOMMENDATION: Evidence on how to address contradictory results between intraoperative TCs and sonication of the prosthesis is still lacking. Current research shows that sonication yields superior sensitivity and specificity over intraoperative TC for the pathogen identification of prosthetic joint infection. There is statistical support for ≥ 5 colony forming units (CFUs) as optimal threshold defining a positive sonicate fluid culture (SFC), however, clinical outcomes and validation are lacking. We recommend that the data be evaluated in light of clinical picture presented.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 86%, Disagree: 6%, Abstain: 8% (Super Majority, Strong Consensus)

SEARCH METHODOLOGY: The literature search was performed utilizing the OVID Medline search database. Search terms included "prosthetic joint infection," "sonication" and "total joint sonication." A total of 134 articles were returned. Abstracts were reviewed and the articles read when necessary to determine inclusion. Exclusion criteria included non-English language, review articles, case reports, non-orthopaedic, non-clinical studies or did not include tissue culture. Thirty-two articles were available for inclusion. These articles were reviewed in entirety, including their bibliography for other potential sources. Eleven of these manuscripts compared SFC to TC and reported on dis-coordinate culture results [1–11].

RATIONALE

A major challenge in the diagnosis and management of periprosthetic joint infections (PJIs) is the accurate identification of the causative organism [12]. Traditional culture methods of synovial fluid, and intraoperative tissue cultures have an unacceptably low sensitivity (0.65) [1,5,12–15]. Most organisms found in PJI reside in a biofilm wherein they are less metabolically active and are surrounded by a protective glycocalyx that shields them from antibiotics and the host immune system [16]. Sonication is a process by which the biofilm is dislodged from the removed prosthesis using ultrasound, permitting these bacteria to be accessible for cultures [1].

SFC has shown consistently superior sensitivity over intraoperative TC in the diagnosis of PJI [1–5,7,9,10]. Trampuz et al. from the Mayo Clinic published one of the earliest and most notable prospective case series utilizing sonication for the diagnosis of PJI [1]. They reported on 331 patients, both aseptic (n = 253) and septic (n = 79) failures and compared synovial fluid, tissue and sonicate fluid culture. The sensitivity and specificity of SFC was 78.5% and 98.8% respectively and was significantly greater than that of synovial fluid (56.3% and 99.2%) and tissue (60.8% and 98.1%). Recently Rothenberg et al. published a study on 503 sonicate cultures and found a sensitivity of 97.0% and specificity of 90.0% while TC was 70.0% and 97.0% [9]. Two meta-analyses have been published regarding sonication and the diagnosis of PJI [17,18]. Zhai published the first in 2013 and reported a pooled sensitivity of 80% and specificity of 95% [17]. Liu, in 2017, corroborated these results, and with additional studies included, reported a sensitivity of 79% and specificity of 95% [18]. In addition SFCs increase the isolation of pathogens when antibiotic therapy is stopped within two weeks from surgery [1].

As with any microbiological process, sonication has the potential for contamination producing false-positive culture results [5,13,19]. Therefore, an essential designation when analyzing SFC results is defining what qualifies as a positive culture. Sonicate cultures are often quantified using CFUs. Trampuz recommends ≥ 5 CFU as a cutoff for positivity to optimize specificity and limit false positive results [1]. Rothenberg et al. analyzed their results of 503 sonicated prostheses and independently determined ≥ 5 CFU is the optimal threshold for diagnosing infection with a sensitivity of 0.97 and specificity of 0.90 [9]. Other published studies have reported cutoff values of 1, 3, 5, 20 and 50 CFU but omit the statistical method by which the cutoff was determined [2,10,14,20–22]. In the meta-analysis published by Zhai, the authors reported the optimal cutoff is ≥ 5 CFU [17].

Trampuz identified 14 of 79 (18%) patients with PJIs that had positive SFC but negative TC [1]. Holika et al. found that the bacteria species cultured differed between SFC and TC in six cases [2]. Portillo reported that SFC detected significantly more pathogens than TC (62 vs. 45, $p < 0.001$) as well as more cases of PJI than TC (56 vs. 41, $p < 0.01$) [6]. Other studies have reported greater bacterial isolation in SFC as compared to TC [3,7,8,10,11]. There was no clinical intervention or follow-up reported in any of these studies. A recent study published by Rothenberg et al. reported results of 503 revision procedures with two-year follow-up [9]. Three hundred twenty-five of these patients were presumed aseptic at the time of surgery based on Musculoskeletal Infection Society (MSIS) criteria (53 of 325 had positive SFC and negative tissue culture postoperatively, and 24 had ≥ 5 CFUs/plate). Ultimately 18 of 53 (34%) were treated with antibiotics as the discretion of the treating surgeon and infectious disease team. At the average follow-up of 22 months, only 4 of 53 patients (7%) required surgical intervention. Only 3 of 24 patients (13%) with ≥ 5 CFU required reoperation. Further study is needed to clinically validate the recommendation of ≥ 5 CFU as a true infection.

Although several studies exist that support sonication as a superior method for microbiological diagnosis over tissue culture there are several limitations. First, studies prior to publication of the Musculoskeletal Infection Society definition of infection used a

more abbreviated system that may have misdiagnosed patients as not infected [23]. Additionally, the number of tissue samples collected varied widely between studies from two to nine per case [2,3,10]. Lastly, in regard to sonication, studies differed in reporting CFU cutoff for positive culture results and lack of clinical correlation. These inconsistencies influence the reported sensitivity and specificity within this report and limit the strength of recommendation. Further studies with clinical outcomes and validity are warranted.

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