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QUESTION 2: What is the preferred type of sample (tissue, fluid, etc.) for molecular analysis in the diagnosis of orthopaedic infections?

RECOMMENDATION: Several molecular methods have been developed in an effort to provide a viable culture-independent alternative for diagnosis of orthopaedic infections. However, due to the variation between studies with respect to the techniques and variety of samples collected, it remains difficult to recommend collection of one specimen type over another. While we cannot recommend a single molecular diagnostic test, careful assessment of the individual technique (location, volume, medium, temperature and transport) utilized is needed for appropriate collection and yield from the corresponding samples.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 87%, Disagree: 2%, Abstain: 11% (Super Majority, Strong Consensus)

RATIONALE

Identification of the infecting organism is imperative in the management of periprosthetic joint infection (PJI) [1,2]. Unfortunately, current methods, namely culture, have failed to perform at a level where the infecting organism is routinely identified, with up to half of PJIs yielding no known pathogen on microbiological culture [3–7]. Several molecular techniques have been examined to address this issue, however, no single technique has established itself to be superior to others. Furthermore, the optimal specimen type for maximizing the sensitivity and specificity of such technologies is an even greater dilemma.

Conventional cultures typically rely on synovial fluid from aspiration, when available, as well as multiple tissue samples obtained intraoperatively. Swabs have largely fallen out of favor with evidence demonstrating their lack of sensitivity and specificity [8]. Culture of sonicate fluid has shown some promise, however conflicting results and the need for specialized equipment preclude its routine use [9].

Synovial Fluid

Synovial fluid has been studied extensively as a source material for identifying the infective organism in PJI. When successfully obtained in the preoperative setting, it may provide the surgeon with crucial information to help guide further operative management of a patient with PJI. Various studies have reported on the performance of synovial fluid based molecular diagnostics in isolation or in parallel with other specimen types. In a study by Huan et al., samples of periprosthetic tissue, sonication fluid and synovial fluid were collected for both culture and 16S broad-range polymerase chain reaction (PCR). The authors concluded that PCR of sonication fluid and synovial fluid were significantly more sensitive than PCR of periprosthetic tissue alone, with no difference in specificity [10]. Multiple studies have shown superiority of synovial fluid PCR to conventional culture, however, these studies simply assessed synovial fluid with no direct comparison to other specimen types [4,11–13]. In contrast, a study comparing the combined sensitivity and specificity of joint fluid culture and serum C-reactive protein levels versus synovial fluid PCR demonstrated inferior results.

Periprosthetic Tissue

Periprosthetic tissue is a useful specimen due to its abundance, as opposed to synovial fluid which may only be present in limited quantities, if at all. A meta-analysis by Qu et al. comparing tissue, synovial fluid and sonication fluid concluded that tissue samples conferred the maximal sensitivity, while sonication fluid helped optimize specificity [14]. Other reports have claimed that tissue PCR is inferior to culture, however these studies focused on a comparison between sonicate fluid culture/PCR and tissue [15,16].

Swab

Swabs have been used in a limited fashion for molecular analysis. Omar et al. compared swabs sampled for 16S rRNA PCR with those sent for tissue culture, and showed a higher sensitivity in favor of swab PCR compared to culture. This is the only report assessing the utility of swabs for molecular diagnosis of PJI. However, no direct comparison was made to other specimen types in this study [17].

While 16S rRNA PCR forms the bulk of studies assessing the different specimen types, there are emerging reports of newer techniques such as next-generation sequencing that will also need to be further explored in order to delineate the optimal specimen type [18–20]. Emerging evidence suggests that the use of gauze or larger swabs that are able to potentially sample a greater intraoperative surface area may confer a better sequencing yield.

In conclusion, the optimal specimen type for molecular analysis of PJI remains unknown. There is significant heterogeneity between studies with regard to the techniques assessed as well as the samples analyzed. Careful assessment of specific techniques are advised when using these technologies as part of the diagnostic workup.

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