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QUESTION 4: What is the role for periprosthetic frozen section and permanent histology in evaluation of a shoulder arthroplasty for periprosthetic joint infection (PJI)?

RECOMMENDATION: Frozen sections or histology, reviewed by an experienced pathologist, may be useful in revision shoulder arthroplasty to evaluate for periprosthetic joint infection. The detection of infection with less virulent organisms, which make up a significant percentage of shoulder PJI, may be less reliable.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 95%, Disagree: 5%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Histologic analysis is well-established as a valuable tool for diagnosing lower extremity PJI [1–4]. Multiple studies of lower extremity revision arthroplasty have shown that frozen section has an accuracy in establishing PJI equivalent to that of permanent histologic analysis [2,5]. This led to the inclusion of frozen section in the American Academy of Orthopedic Surgeons (AAOS) clinical guidelines for the diagnosis of PJI [6], the Musculoskeletal Infection Society (MSIS) definition of PJI [7], and the first International Consensus Meeting on Periprosthetic Joint Infection definition of PJI in 2013 [8].

Intraoperative assessment of periprosthetic inflammation can serve as a quickly available tool in the evaluation for PJI. Despite the extensive evidence supporting its utility in the evaluation of lower extremity arthroplasty, the literature on histologic analysis in shoulder arthroplasty is very limited. Because *Cutibacterium acnes*, a less virulent pathogen, is the predominant cause of shoulder PJI a reassessment of standard markers for PJI is necessary [9–12]. For this purpose, a systematic review of histologic analysis for shoulder PJI was undertaken on Scopos [13] with the query, “(shoulder OR ‘upper extremity’) AND (arthroplasty OR replacement) AND (infection OR infected) AND (‘frozen section’ OR histology OR histologic).”

This query identified two articles directly evaluating the use of frozen section in revision shoulder arthroplasty [14,15]. First, Topolski et al. [15] evaluated the utility of frozen section histopathology in patients with unexpected positive cultures (UPC) during revision shoulder arthroplasty. In 75 patients undergoing revision shoulder arthroplasty who had occult infection defined as positive intraoperative cultures, 92% (67/73) had a negative result on frozen section—with a positive result defined as at least five neutrophils on any high-powered field. In this study, there was a single case with a discrepancy between frozen section (negative) and permanent histology (positive). This study demonstrated that most patients with unexpected positive cultures did not have a strong periprosthetic inflammatory response. They concluded that frozen section analysis was not helpful in cases of UPC when using the criteria of Mirra et al. [16].

The second study, Grosso et al., evaluated the results of frozen section in forty-five revision total shoulder arthroplasties [14]. Based upon their definition for infection, the cohort was divided into non-infected (n = 15), infected (n = 12), and *C. acnes* infection (n = 18). Using the threshold from Morawetz et al. [17], 23 neutrophils over five high-powered fields, frozen section had sensitivity and specificity of 67% and 100% for the infected group and 56% and 100%, respectively, for the *C. acnes* group. Re-evaluating the threshold for positive frozen section with a receiver operating characteristic (ROC) curve found that five high powered fields with a sum of at least ten neutrophils improved the overall sensitivity to 73% without sacrificing speci-

ficity. At that institution, with the aid of an experienced pathologist, these authors were able to demonstrate that a lowered threshold for these less-virulent infections can improve the accuracy and utility of frozen section analysis for diagnosing PJI during revision shoulder arthroplasty.

While these two studies are the only shoulder-specific analyses of frozen section for shoulder PJI, their developed thresholds have not been widely adopted by clinical pathologists. In fact, one of the two institutions noted above has since abandoned the clinical use of their published criteria. Therefore, utilization of the standard thresholds from the lower extremity arthroplasty community may be the most prudent currently.

Multiple studies of histologic analysis during lower extremity revision arthroplasty have demonstrated that the concordance between frozen section and permanent histology is very high. Thus, it is expected that the same difficulties with detection of infection by less virulent organisms in shoulder PJI would apply to both permanent, as well as frozen section, histology [2,5,18].

Histologic analysis is also used to evaluate for persistent infection during reimplantation of a hip or knee undergoing two-stage exchange [19–21]. These analyses found poor sensitivity but high specificity in identifying persistent PJI. Such analysis has not been completed in the shoulder and further work is required in this regard.

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QUESTION 5: What are the diagnostic criteria of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: See International Consensus Meeting (ICM) definition of shoulder PJI below.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 88%, Disagree: 12%, Abstain: 0% (Super Majority, Strong Consensus)

INTERNATIONAL CONSENSUS MEETING (ICM) FOR PERIPROSTHETIC JOINT INFECTION: DEFINITION, CATEGORIZATION AND SCORING SYSTEM FOR SHOULDER PJI

Definite PJI

Meeting one of the following criteria is diagnostic of **definite** periprosthetic shoulder infection:

- A sinus tract communicating with the prosthesis is present
- Gross intra-articular pus
- Two positive cultures with phenotypically-identical virulent organisms

Evaluation Scoring

Weighted values for all positive tests performed as part of the diagnostic evaluation of a failed shoulder arthroplasty are summed (Table 1).

- Six or greater with identified organism = **probable PJI**
- Six or greater *without* identified organism = **possible PJI**
- Six or less
 - single positive culture virulent organism = **possible PJI**
 - two positive cultures low-virulence organism = **possible PJI**
 - negative cultures or only single positive culture for low virulent organism = **PJI unlikely**

RATIONALE

The need for a consensus definition of shoulder PJI cannot be understated. A clear definition serves two purposes: (1) to aid in clinical decision making and (2) to provide a framework for consistent future research reporting. Furthermore, acceptance of a definition is a necessary first step in providing a well-tested diagnostic algorithm. As Hsu et al. demonstrated [1], the shoulder research community has used disparate definitions of PJI—likely leading to variable and inconsistent conclusions about the diagnosis and management. Adoption of a uniform definition of PJI for the lower extremity quickly led to hundreds of publications evaluating prevention, diagnosis and treatment of PJI based upon the same consistent diagnostic criteria [2,3]. This task is even more urgent in regard to shoulder arthroplasty due to the unique microbiologic and the ambiguity presented by high rates of positive intraoperative cultures in revision cases that otherwise appear aseptic [4-9]. In order to discuss diagnosis and evaluation of shoulder PJI, it is imperative that the shoulder community begin with a standardized and accepted definition of shoulder PJI.