

SH41. Is synovial alpha defensin positive important for diagnosis of PJI? Should it still be included in the minor criteria? If so, what weighted score should it be given in the diagnostic criteria?

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Methodology: A comprehensive literature review was performed to identify all studies evaluating the use of synovial alpha defensin in the diagnosis of PJI of the shoulder. Searches for the terms “alpha defensin”, “synovial alpha defensin”, “shoulder”, “shoulder arthroplasty” and “shoulder replacement” were performed using the search engines PubMed and Google Scholar which were searched through December 2024. Inclusion criteria for the systematic review were all English studies (Level I-IV evidence) that reported on use of synovial alpha defensin in the diagnosis of PJI of the shoulder. Exclusion criteria were non-English language articles, nonhuman studies, retracted papers, case reports, studies with less than <10 patients in the sample size, studies without clinical follow-up, and technique papers without patient data. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria were followed. Three articles met inclusion and exclusion criteria and were reviewed.

Recommendation: Synovial alpha defensin may aid in the diagnosis of shoulder PJI and should still be included in the ICM minor criteria. The weighted score should remain as 2 points.

Strength of Recommendation: **Limited** (Evidence is insufficient and does not allow a definitive recommendation for or against use)

Rationale:

Alpha defensin is an antimicrobial peptide that is released by neutrophils in response to bacterial or fungal pathogens. The presence of alpha defensin in synovial fluid has been thoroughly investigated as a biomarker for hip and knee PJI, with a reported 98% sensitivity and 100% specificity across studies.¹⁻¹⁴ Despite limited evidence on its use as a biomarker for shoulder PJI,^{8,9} the promising results with regards to its diagnostic performance led to the incorporation of synovial alpha defensin as a minor criteria in the weighed diagnostic scoring system for PJI of the shoulder developed at the 2nd International Consensus Meeting (ICM) on Orthopedic Infections. An elevated synovial alpha defensin level was given a weighted score of 2 points.¹⁰

However, there remains limited evidence on the role of synovial alpha defensin in diagnosis of shoulder PJI. Only one study specifically evaluated alpha defensin in shoulder arthroplasty prior to the development of the ICM minor criteria. Frangiamore et al⁸ obtained synovial alpha defensin levels in 33 patients at the time of revision shoulder arthroplasty. Patients were classified as infected or not infected by standard criteria. The AUC, sensitivity, specificity, and positive and negative likelihood ratios for alpha defensin in the diagnosis of shoulder PJI were 0.78, 63%, 95%, 12.1, and 0.38, respectively. There was a significant difference in the median alpha defensin level between the infection and no infection groups (3.2 [0.21-4.74] vs. 0.21 [0.19-0.23]; p=0.006), and synovial alpha defensin was also elevated in the presence of a culture positive for *C. acnes* (median, 1.33 S/CO; p=0.03). One subsequent study since the introduction of the ICM minor criteria has shown even better diagnostic performance of synovial alpha defensin in the shoulder in a larger cohort of patients. Unter Ecker et al¹⁵ evaluated synovial alpha defensin levels in 105 revision shoulder arthroplasty cases and reported an AUC, accuracy, sensitivity,

specificity, and positive and negative predictive value for alpha defensin in the diagnosis of shoulder PJI of 0.91, 91%, 75%, 96%, 86%, and 93%, respectively. In both the Unter Ecker et al and Frangiamore et al studies, the threshold for a positive synovial alpha defensin test was determined based on receiver operating characteristic (ROC) analysis, with different thresholds used in each study (0.9 versus 0.48, respectively).

A point-of-care test is also available for the assessment of alpha defensin in synovial fluid during surgical procedures (lateral flow immunoassay). Overall, this lateral flow assay has also shown high sensitivity and specificity for the diagnosis of hip and knee PJI, but some studies have found that the point-of-care test has lower sensitivity and specificity compared with the laboratory-based synovial alpha defensin test.¹⁶⁻²² Only one study has specifically evaluated the point-of-care lateral flow assay for synovial alpha defensin in shoulder arthroplasty. Weigelt et al obtained synovial alpha defensin levels in 29 revision shoulder arthroplasty cases, with patients classified as infected or not infected by MSIS criteria. They reported an accuracy, sensitivity, specificity, and positive and negative predictive value for alpha defensin in the diagnosis of shoulder PJI of 79%, 60%, 83%, 43%, and 91%, respectively.

Although there remains limited data on its use in the shoulder, the synovial alpha defensin test appears to be a promising and helpful marker for diagnosis of PJI of the shoulder. The diagnostic test should remain a part of the ICM minor criteria for shoulder PJI with a weighted score of 2 points. Further research and validation of synovial alpha defensin as a marker for PJI of the shoulder is needed, including determining the optimal cut-off level of a positive test.

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