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QUESTION 7: Is there a role for synovial fluid alpha-defensin in the diagnosis of shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Synovial alpha-defensin may aid in the diagnosis of shoulder PJI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

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 PJI following hip and knee arthroplasty with a reported 98% sensitivity and 100% specificity [1–11]. However, there is limited evidence regarding the use of alpha defensin as a biomarker for infection in shoulder arthroplasty.

Thirteen studies in the past three years have demonstrated the efficacy of this test in the diagnosis of hip and knee PJI, and better prognostic results have been reported compared to leukocyte esterase [3,6,9,11–14]. However, the role of alpha-defensin in diagnosing shoulder PJI is less well known. The literature contains only one study that specifically evaluated alpha defensin in shoulder arthroplasty. In this study by Frangiamore et al, alpha-defensin levels were obtained in 33 patients at the time of revision shoulder arthroplasty [6]. Patients were classified as infected or not infected by a standard criteria based on clinical evaluation, laboratory studies, histology and culture results. The area under the curve, sensitivity, specificity and positive and negative likelihood ratios for alpha-defensin in the diagnosis of infection 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 [.21-4.74] versus .21 [.19-.23] p = .006). The authors concluded that alpha-defensin may be an appropriate test in the evaluation of infection in the painful shoulder arthroplasty.

A point of care device is now available for direct assessment of alpha-defensin in synovial fluid during surgical procedures (lateral flow immunoassay) [9,13]. Initial reports with this device report a 92% sensitivity and 100% specificity for the diagnosis of PJI in hip and knee arthroplasty [16]. However, some studies have concluded that the point of care lateral flow assay has a lower sensitivity and specificity when compared with the laboratory-based alpha-defensin test (sensitivity 77%, specificity 91%) [9,13,15]. This device has not been evaluated for the diagnosis of shoulder PJI.

Although the clinical presentation and diagnostic challenges are different in shoulder PJI than in hip and knee PJI, detection of high levels of alpha-defensin in synovial fluid in the shoulder could be a good predictor of infection. However, the cut-off values are not well defined, with authors reporting a range from 5.20-7.72 mg/L [16–18]. Further research and validation of alpha-defensin as a marker for PJI in shoulders is required.

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QUESTION 8: Is there a role for serum D-dimer in the evaluation of periprosthetic joint injection (PJI) following shoulder arthroplasty?

RECOMMENDATION: Unknown. There is currently only limited evidence related to the evaluation of hip and knee PJI and no study to date evaluating its use in shoulder PJI.

LEVEL OF EVIDENCE: No Evidence

DELEGATE VOTE: Agree: 96%, Disagree: 4%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

A literature review (Medline, PubMed) was performed to identify relevant studies on the role for serum D-dimer in shoulder arthroplasty infections. Terms used included "periprosthetic infection," shoulder infection," "D-dimer," "diagnosing PJI," "serum biomarkers PJI." D-dimer is a fibrin degradation product, a small protein present in the blood after a blood clot is degraded. The D-dimer test has been used for diagnosing thrombosis, pulmonary embolus and disseminated intravascular coagulation (DIC). Lippi et al. [1] found that in an urban population the most common reason for an elevated D-dimer was infection (15%).

There has been a growing interest in the use of serum biomarkers to diagnose periprosthetic joint infections, especially given the imperfect nature of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) tests. A literature search found no studies regarding D-dimer and shoulder arthroplasty. There are however, reports in the hip and knee arthroplasty literature. Lee et al. [2] studied the postoperative levels of D-dimer after elective total hip arthroplasty. Only one paper was found regarding D-dimer as a diagnostic test for periprosthetic infection. Shahi et al. [3] reported on a prospective study of 245 patients undergoing primary arthroplasty (23), revision for aseptic failure (86), revision of PJI (57), reimplantation (29) and infection in a site other than a joint (50) (urinary tract infection, pneumonia, upper respiratory infection). The study included only hip and knee arthroplasties. The median serum D-dimer was significantly higher for patients with PJI and the 850 ng/mL was determined as the optimal threshold value for serum D-dimer for the diagnosis of a PJI. The sensitivity (89%) and specificity (93%) for serum D-dimer was better than for ESR, CRP and ESR & CRP combined. An interesting finding was that D-dimer was elevated in cases of *C. acnes* infection, a common pathogen in the shoulder which typically does not cause elevation in serum ESR or CRP. The authors concluded that serum D-dimer is a promising marker for the diagnosis of PJI.

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