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authors reported that the optimal cutoff for diagnosing PJI in the early postoperative period should be higher than those that are traditionally used and recommended by the MSIS.

In conclusion, although serum ESR and CRP are the first line for screening PJI, a negative test result does not exclude the possibility of infection. Surgeons need to be cognizant of this fact and considering the huge burden of misdiagnosed PJIs, in presence of high clinical suspicion we recommend a comprehensive work up using combination of tests to refute or confirm the possibility of infection.

REFERENCES


QUESTION 3: What is the diagnostic accuracy and threshold of D-dimer in the diagnosis of periprosthetic joint infections (PJIs)?

RECOMMENDATION: Recent literature supports the use of D-dimer as a serological marker for the diagnosis of PJIs. D-dimer has been shown to best perform at a threshold of 850 ng/mL. However, this threshold was determined internally from a cohort in a single institution study. Further studies are needed in order to validate this threshold or establish a more rigorous threshold.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 74%, Disagree: 16%, Abstain: 10% (Super Majority, Strong Consensus)

RATIONALE

Serological markers are typically the first line investigations in patients suspected of having PJIs [1]. Current practice as dictated by the American Academy of Orthopaedic Surgeons (AAOS) Clinical Practice Guidelines recommends the collection of blood for the measurement of serum erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). These tests fall short on multiple accounts.

ESR and CRP may be falsely elevated in patients with a systemic inflammatory state or some other extra-articular infection [2,3]. Secondly, ESR and CRP may produce a false negative result in patients infected with low virulence organisms such as Cutibacterium acnes (C. acnes) [4]. Lastly, ESR and CRP may be physiologically elevated in the early postoperative period following the index arthroplasty procedure, making it difficult to interpret in the acute setting [5–7]. In light of these shortcomings, there is a clear need for alternative serological markers.

D-dimer, a fibrin degradation product, is a ubiquitous test that has been used as a screening test in patients with a suspected pulmonary embolism [8–10]. In a study by Shahi et al. [11], a consecutive series of 143 revision arthroplasties undergoing surgery for both septic and aseptic failure had blood drawn preoperatively and sent to the lab for serum measurements of D-dimer, ESR and CRP. Using the MusculoSkeletal Infection Society (MSIS) definition of PJI [12] as a gold standard and a D-dimer threshold of 890 ng/mL, D-dimer demonstrated a sensitivity and specificity of 89% and 93%. ESR and CRP demonstrated sensitivities of 73% and 79%, and specificities of 78% and 80%, respectively. In another study by Lee et al, serial blood draws were performed at baseline, postoperative days one, two, three and weeks two and six. Blood was sent for measurements of serum D-dimer, ESR and CRP [13]. Overall, ESR did not normalize until 6 weeks postoperatively while CRP remained elevated until 2 weeks after surgery. Serum D-dimer levels normalized by postoperative day 2. Thus the advantages of D-dimer are twofold: superior sensitivity and specificity, as well as a rapid decline to baseline levels following surgery, allowing for use in evaluation of a suspected acute PJI.

While it is clear that D-dimer outperformed both ESR and CRP at a threshold of 850 ng/mL, it is important to note that this threshold was calculated internally in order to maximize the
performance of D-dimer in this specific cohort. Larger cohorts are needed to not only further validate D-dimer as a serological marker of PJIs, but also to develop a D-dimer threshold that can be used universally. Given its superior diagnostic performance and universal availability in hospitals, we recommend the routine use of D-dimer as part of the battery of serological markers used in evaluating a patient with suspected PJI.

REFERENCES


QUESTION 4: How does the level of leukocyte count and neutrophil percentage in the synovial fluid change with time following total joint arthroplasty?

RECOMMENDATION: The levels of leukocyte count and neutrophil percentage in the synovial fluid drop as one moves further away from the index arthroplasty. The latter is the rationale behind using different thresholds for these parameters in the diagnosis of acute versus chronic periprosthetic joint infections (PJIs).

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 90%, Disagree: 4%, Abstain: 6% (Super Majority, Strong Consensus)

RATIONALE

We have recognized that the synovial composition changes as postoperative time increases, which is the reason for separate optimal cut-off values in the diagnosis of acute and chronic PJIs. During the last consensus meeting, the recommended cut-off value for the diagnosis of acute PJ Is (< 6 weeks from surgery) for synovial white blood cell (WBC) count was > 10,000 cells/μL and > 90% polymorphonuclear cells (PMNs) [1]. Likewise, the synovial fluid cut-off values for a chronic PJI were a WBC count > 3,000 cells/μL and > 80% PMNs [1]. When the optimal cut-off values are adjusted for the span of time after a procedure to differentiate an acute and chronic PJIs, synovial analysis remains a highly reliable diagnostic tool with similar diagnostic accuracy between acute and chronic PJIs.

Although adjustments in the WBC count and percentage of PMNs have improved the diagnostic accuracy for acute and chronic PJIs, we have a limited understanding of the change in reliability of synovial analysis on a week-by-week basis. For instance, we do not have a strong understanding whether application of the same threshold two-weeks and six-weeks postoperatively has the same diagnostic reliability. Because we do not have literature to compare the proposed situation specifically, we must qualitatively compare two studies utilizing similar threshold cut-off values at different times postoperatively.

Kim et al. and Bedair et al. each investigated the diagnostic accuracy with similar optimal cut-off values from synovial analysis in the early postoperative period following primary total knee arthroplasty (TKA); however, each utilized differing patient inclusion criteria of three- and six-weeks, respectively [4, 6]. Applying a WBC count threshold of >11,200 cells/μL, Kim et al. had a sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 100, 98.3, 65.4, and 100%, respectively [6]. Similarly, a percentage PMN threshold of >88% had a sensitivity, specificity, PPV, and NPV of 100, 65.6, 5.7, and 100%, respectively [6].

When compared to the diagnostic characteristics published by Bedair et al. (Table 1), the two studies demonstrate similar diagnostic accuracy for synovial WBC count and percentage PMNs. Therefore, increasing postoperative timespans appears to have limited influence on the diagnostic accuracy between three- and six-weeks from surgery. However, the same might not hold true for the diagnosis of chronic PJI.

Christensen et al. investigated the effect of increasing time intervals on synovial analysis in TKA patients who underwent aspiration as part of an evaluation for PJI and ultimately were determined not to have a PJI [7]. The authors investigated synovial analysis at 545 days, 45 to 90 days, 3 months to 1 year, and 1 to 2 years after surgery. Their data demonstrated synovial WBC count and percentage PMNs normalized between three months and one year after surgery [7]. As a result, it is possible increasing postoperative time intervals could alter the interpretation of synovial analysis in the setting of diagnosing a chronic PJI.

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