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QUESTION 6: Is there a role for procalcitonin (PCT) blood test in the diagnosis of surgical site infection/periprosthetic joint infection (SSI/PJI) in orthopaedic patients?

RECOMMENDATION: No. The literature demonstrates the existence of biomarkers with superior diagnostic value compared to a serum PCT blood test in determining the presence of infection in orthopaedic patients.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 92%, Disagree: 3%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

PJI remains one of the most challenging complications that can result from total joint arthroplasty (TJA). Because the symptoms of PJI are often non-specific and there is no gold standard threshold or criteria for the currently-available laboratory tests, PJI is difficult to diagnose with precision [1,2]. Therefore, it remains imperative in determining the most valuable markers for use in diagnosing PJI in order to expedite treatment for this patient population. For example, serum biomarkers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cell (WBC) count are not sufficiently specific to diagnose PJI on their own [3]. Numerous studies focusing on the diagnostic accuracy of novel biomarkers have suggested that the PCT serum blood test may be a useful biomarker because of its rapid assessment and high specificity [4–6].

A meta-analysis by Shen et al. in 2013 determined that serum PCT had some benefit for use, but only as a diagnostic tool for determining patients with septic arthritis and/or osteomyelitis [7]. Additionally, Bottner et al. and Worthington et al. also suggested that serum PCT was only an accurate marker for systemic bacterial infections and Bottner et al. additionally endorsed it as a diagnostic tool because of its heightened specificity. Bottner et al. recommended that PCT had limited usefulness as only being a confirmatory test for systemic infection and not PJI and only after screening with IL-6 and CRP simultaneously because of its high specificity (.98) and low sensitivity (.33) [8]. A small prospective study by Yuan et al. was conducted examining 74 total hip arthroplasty (THA) revision cases and compared preoperative values of PCT with WBC counts and CRP in order to determine which test was the most valuable diagnostic marker [9]. Respectively, the areas under the curve (AUCs) for serum PCT, CRP and WBC count were 0.851 (95% confidence interval (CI) 0.773 to 0.929), 0.830 (95% CI 0.751 to 0.910), and 0.633 (95% CI 0.518 to 0.747) showing that PCT and CRP were significantly greater in diagnostic accuracy than WBC count ($p < 0.05$). The population size of this study was relatively small and there was no significant difference ($p = 0.0367$) in the diagnostic value of PCT and CRP.

In contrast, Worthington et al. examined predictors of infection in revision TJA and determined that PCT was not valuable in differentiating patients with aseptic loosening from those with septic loosening and they showed the greater diagnostic ability of CRP ($p = 0.0001$), ESR ($p = 0.0001$) and WBC ($p = 0.003$) signals as they were all significantly higher in patients undergoing revision for septic loosening [10]. The higher quality in combining IL-6 with CRP as a diagnostic marker in comparison to PCT was also demonstrated by Ettinger et al. as they inspected revision patients and scrutinized them for either having a low-grade joint infection or aseptic joint failure [11].

Similarly, Sousa et al. also showed that PCT synovial fluid tests showed no difference in patients with PJI and those without PJI [12]. These studies confirmed that the usefulness of PCT testing lies with serum testing and not in synovial fluid analysis for patients.

Additionally, Drago et al. showed that the levels of serum PCT did not differ between patients with PJI and those without PJI and determined that only IL-6 was an accurate diagnostic marker of PJI [13]. Equally, a recent meta-analysis by Yoon et al. in 2018 compared PCT with IL-6 in its ability to diagnose PJI [14]. They also demonstrated that IL-6 was far superior in its diagnostic ability compared to serum PCT. They further recommended that PCT was not useful as a rule-out diagnostic tool owing to its high negative likelihood ratio and that IL-6 had a greater diagnostic value in comparison to PCT because of its higher AUC of 0.93 (95% CI 0.91 to 0.95) vs. an AUC of 0.83 (95% CI 0.79 to 0.86) for PCT.

In 2017, a meta-analysis performed by Xie et al. compared the PJI diagnosing utility of α-defensin with PCT and found that α-defensin was also ,superior to serum PCT with regard to specificity (.95 vs. .92)positive likelihood ratio (19.6 vs. 6.8) and AUC (.99 vs. .76) [15]. This showed that α-.defensin was a superior biomarker in the diagnosis of PJI by comparison to serum PCT

The majority of the aforementioned studies provide irrefutable evidence that serum PCT does not have utility in its diagnostic ability in detecting PJI in arthroplasty patients. However, the same literature provides evidence that there are far superior tests in providing a diagnosis of PJI in the same setting. In summary, considering the insufficient support in the literature for the use of PCT in the diagnosis of PJI, we recommend that other diagnostic tests that have superior value be used in its place.

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