HK 17: Is there a role for serum procalcitonin for diagnosis of periprosthetic joint infection (PJI).?

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Response/Recommendation: There is no role for the use of serum procalcitonin for diagnosis of periprosthetic joint infection (PJI).

Level of Evidence: Strong

Delegate Vote:

Rationale:

Procalcitonin (PCT) is a precursor of calcitonin. While serum PCT in healthy uninfected individuals is very low, increased serum levels have been noted in systemic bacterial infection [1, 2]. Procalcitonin has been proposed as an alternative biomarker for diagnosing periprosthetic joint infection (PJI), particularly in some cases where traditional serum and synovial biomarkers show lower accuracy. These include early postoperative infection, chronic, deep or low-grade infection which elicit a less pronounced systemic inflammatory response [3] as well as in some cases of non-infectious causes of CRP elevation as in inflammatory arthritis and obesity. [4] While many studies reported high diagnostic accuracy for PCT in systemic bacterial infection [5], the reported results for PCT in PJI have been highly variable.

The aim of this comprehensive systematic review and metanalysis was to evaluate the diagnostic accuracy of PCT in PJI. The systematic literature search was conducted by two independent reviewers using the PubMed/Medline, Web of Science and Cochrane databases based on selected MESH terms related to PJI and serum procalcitonin. We included clinical studies on PJI exploring diagnostic accuracy of serum procalcitonin as a biological marker. A standardized data extraction form was created and pilot-tested to collect study characteristics and outcomes. Risk of bias (ROB) of the included studies was assessed using the QUADAS-2 tool[6].

Fourteen studies were included in the final analysis, enrolling a total of 993 patients. Among them, 561 cases involved the hip, 465 the knee, and 7 the shoulder.
The optimal PCT cutoff varied across the studies. Three studies [7-9] identified 0.5 ng/mL as the optimal cutoff, while two studies [10, 11] reported 0.1 ng/mL. Additional cutoffs reported were 0.3 ng/mL [12], 0.35 ng/mL [13], 0.05 ng/mL [14], 0.081 ng/mL [15], 2.29 ng/mL[16] , and 46 ng/mL [17]. Two studies [18, 19] did not specify the optimal cutoff, and one study [20] identified 0.025 ng/mL as the optimal threshold for detecting low-grade infections. Eight studies [10, 11, 13-17, 20]used the MSIS criteria [21] for PJI diagnosis, one study [8] used ICM definition 2013 [22] , one study [7] used ICM definition 2018 [23], three studies [9, 12, 18] relied on culture and histological examination without using a specific definition, and one study [19] did not mention their criteria for PJI diagnosis.

The pooled sensitivity of PCT for diagnosing PJI was 0.47 (95% CI: 0.42–0.51) and the pooled specificity was 0.84 (95% CI: 0.80–0.87) (Figure;1,2). The pooled positive likelihood ratio (PLR) was 4.02 (95% CI: 2.11–7.66), suggesting that PCT is moderately useful for ruling in PJI. However, the pooled negative likelihood ratio (NLR) was 0.62 (95% CI: 0.50–0.77), reflecting limited ability to rule out PJI effectively. The pooled diagnostic

odds ratio (DOR) was 7.91 (95% CI: 4.18–14.98), and the area under SROC (the pooled AUC) was 0.7916) (Figure;3). This indicates that PCT has moderate diagnostic efficacy in distinguishing between septic and aseptic cases. This means that while PCT can provide some diagnostic value, its moderate accuracy limits its reliability, particularly in scenarios requiring high precision, such as detecting low-grade infections.

Bottner et al [12] reported a low sensitivity of 33 % for PCT. However, they claimed that PCT is highly specific for diagnosis of PJI (98%). They suggested that PCT could serve as a useful confirmatory tool in patients with positive CRP or elevated levels of interlukin-6. Similarly, Randau et al [17] reported a low sensitivity (12.9%) and high specificity (100 %) of PCT. Conversely, Glehr et al [13] reported that PCT is a sensitive but less specific marker for PJI. With a sensitivity of 90% and specificity of 67%, Glehr et al reported that PCT is a useful marker for PJI. Tahta et al [10] demonstrated that PCT, when combined with other markers, is useful biomarker for PJI, particularly in patients with inflammatory joint disease. Busch et al [7] reported that PCT is specific but less sensitive marker for PJI, however, they concluded that PCT is not a reliable marker to differentiate between PJI and aseptic loosening. They did not recommend single use of PCT to rule out PJI. Similarly, Worthington et al [18] reported that PCT could not differentiate septic and aseptic causes of THA loosening. All patients with aseptic loosening and 94 % with septic loosening had a PCT level < 0.5 ng /ml only one case of septic loosening had levels >2 ng/ml. Ettinger et al [20] concluded that PCT cannot be used to distinguish aseptic loosening from low grade infection. Sun et al [14] reported that PCT is not a reliable marker for PJI. They compared PCT with ESR, CRP, fibrinogen, and platelets. PCT had the lowest diagnostic accuracy. Adding PCT to other markers as CRP improved the diagnostic accuracy. Similarly, Yuan et al [9] demonstrated that PCT did not offer advantage over CRP for diagnosis of PJI.

Several metanalyses confirmed the inferior performance of PCT as a marker for PJI. Sun et al [24], in a recent metanalysis, confirmed the poor diagnostic accuracy of PCT recommending against its use for ruling in/out PJI. Yoon et al [25], in their metanalysis, did not recommend the use of PCT to rule out PJI. Moreover, Xie et al [26] reported a low sensitivity for PCT which limits the clinical application of PCT.

There are many explanations for such inferior diagnostic performance of PCT. PCT is released in response to bacteremia which is not essentially present in PJI [27]. Infection with slow growing organisms does not elicit much of physiological response and release of PCT [7]. Transient bacteremia, even in healthy individuals, can induce PCT release [28]. Moreover, renal disease can cause PCT retention resulting in higher PCT levels than in normal individuals [29, 30].

Conclusions: The evaluation of available litearure revelaed that serum procalcitonin has little to no role in diagnosis of PJI.

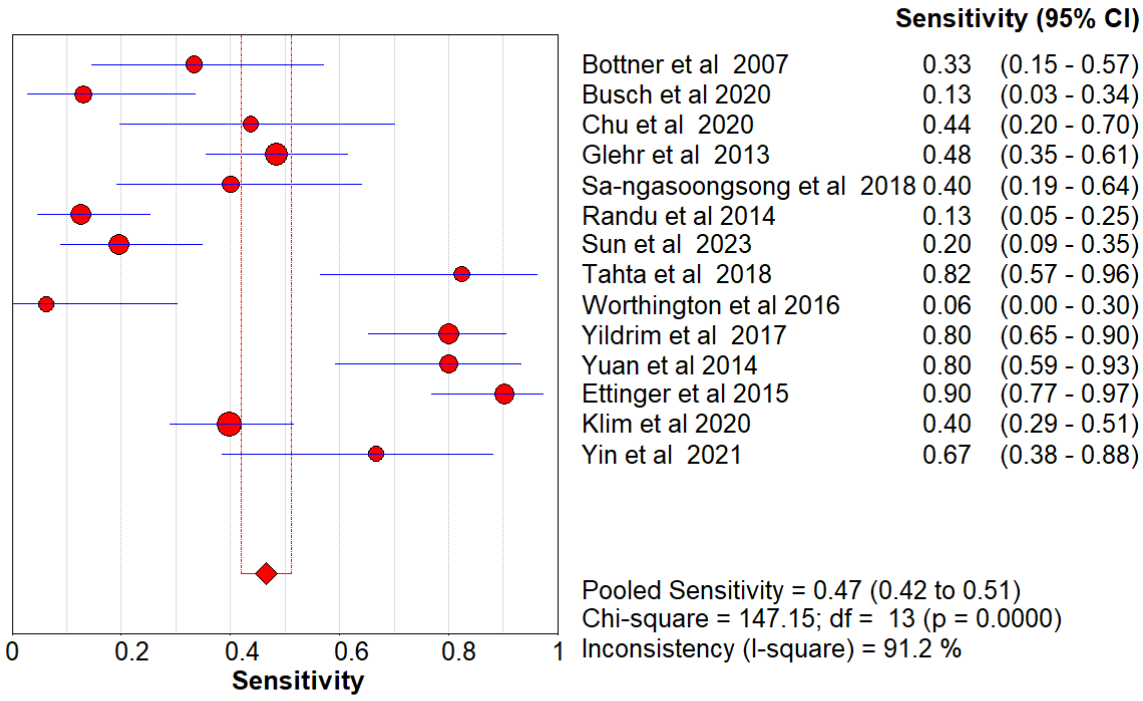

Figure (1); pooled Sensitivity.

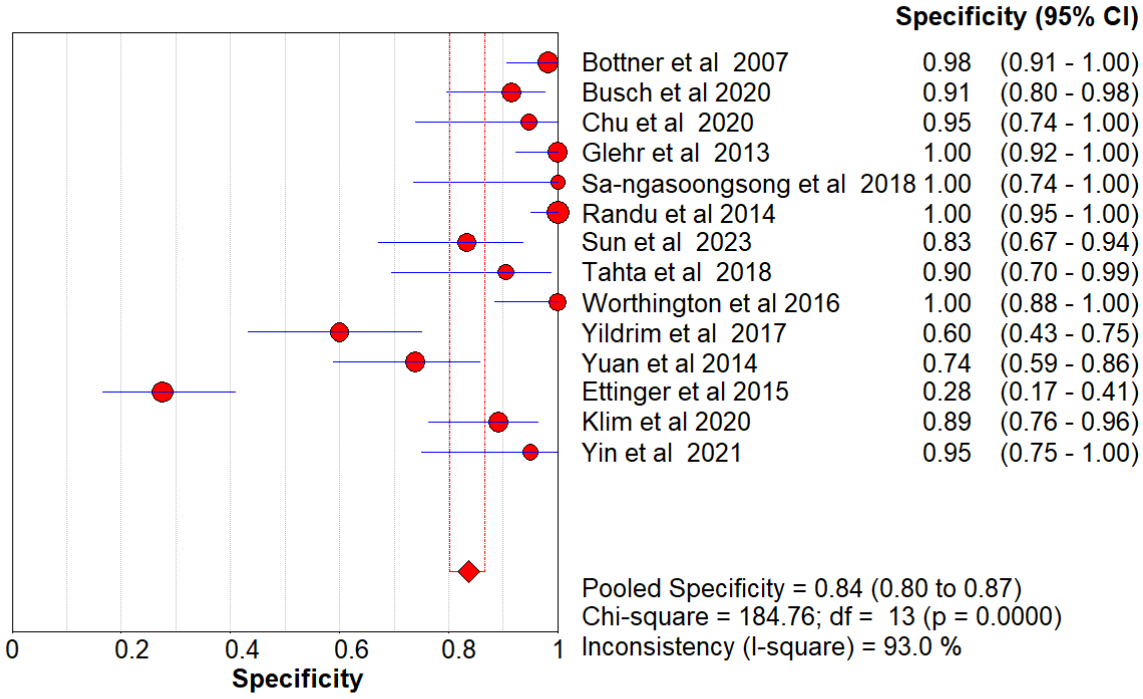

Figure (2); pooled Specificity.

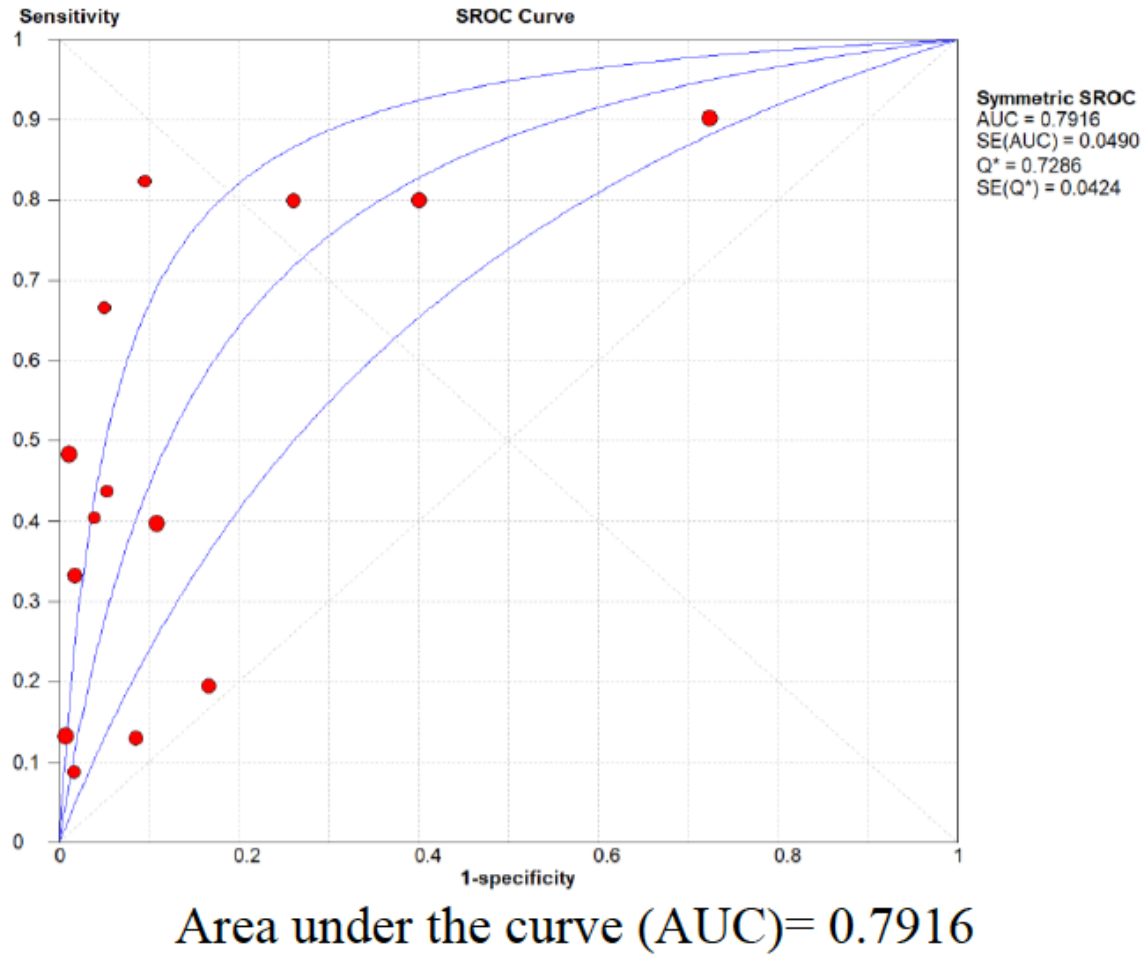

Figure (3); pooled AUC.

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