HK13: Is there a role for joint-specific (hip versus knee) cut-offs for serological tests in the diagnosis of periprosthetic joint infection (PJI)?

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Response/Recommendation: There is no strong justification for establishing separate cut-off thresholds for serological tests, like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), in diagnosing periprosthetic joint infection (PJI) between the hip and knee.

Level of Evidence: Limited

Delegate Vote:

Rationale:

Diagnosing Periprosthetic Joint Infection (PJI) based on serologic markers is challenging due to the retrospective nature of most studies, which often combine data from hip and knee PJI, complicating joint-specific conclusions. Serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) have been routinely used as part of the diagnostic workup for PJI with the thresholds of 10 mg/liter (L) (1 mg/dL) for CRP and 30 mm/hour (mm/hour) for ESR, as recommended by the Musculoskeletal Infection Society (MSIS) [1] and the International Consensus Meeting (ICM) [2]. However, some studies suggested that these thresholds were too high, leading to false negatives, and proposed lower cut-offs [3, 4]. Notably, the 2021 European Bone and Joint Infection Society (EBJIS) PJI definition [5] removed ESR from the diagnostic criteria. It is important to note that these thresholds were set arbitrarily, and their clinical utility should always be considered alongside other clinical and laboratory findings for an accurate diagnosis.

The 2010 meta-analysis by Berbari et al. [6] found that CRP had higher diagnostic accuracy than ESR for identifying hip and knee PJI, but neither marker was sufficient alone, recommending a combination of tests with clinical evaluation. In 2017, a meta-analysis by Huerfano et al. [7] further evaluated the diagnostic accuracy of CRP and ESR using the thresholds recommended by MSIS/ICM in hip PJI. The study found that CRP had 87% sensitivity and 79% specificity, while ESR had 86% sensitivity and 72% specificity, indicating moderate diagnostic accuracy for both tests. A prospective study in 2024 by Tarabichi et al. [8] evaluated the same thresholds for hip and knee PJI and found that CRP had 90% sensitivity and 70% specificity, while ESR had 74% sensitivity and 85% specificity. Additionally, a meta-analysis in 2022 by Tang H et al. [9] , which included 216 studies, found that the optimal CRP thresholds for chronic hip and knee PJI were 13.5 mg/L (sensitivity 84%, specificity 83%), slightly higher than MSIS/ICM recommendations, while the ESR threshold of 30 mm/hour remained optimal (sensitivity 79%, specificity 78%).

The accuracy and optimal thresholds of ESR and CRP in diagnosing PJI vary across studies due to factors such as pathogen virulence [10-12], chronicity [12, 13], time since surgery [14], type of arthroplasty (e.g., hemiarthroplasty) [15], inflammatory conditions [16], obesity [17], age [18], and sex [19]. For instance, ESR was found to increase with age, particularly in women and African Americans, while CRP showed a slightly positive trend with age [18]. Alijanipour et al. [14] found that for early postoperative hip and knee PJI (within four weeks of arthroplasty), the optimal thresholds were 23.5 mg/L for CRP and 54.5 mm/hour for ESR. Salimy et al. [15] identified different thresholds for hip hemiarthroplasty, with 40 mg/L for CRP and 52 mm/hour for ESR. In

inflammatory arthritis with chronic PJI, Cipriano et al. [16] recommended a CRP threshold of 17 mg/L and an ESR threshold of 30 mm/hour Additionally, obesity, which is associated with a pro-inflammatory state, can lead to elevated baseline CRP. Liu et al. [17] found that a higher CRP threshold of 36 mg/L was more accurate in diagnosing knee PJI in obese patients. These variations highlight how patient demographics and comorbidities impact the accuracy of CRP and ESR in diagnosing PJI.

We reviewed the evidence on whether joint type (hip versus knee) is another factor that influences the CRP and ESR thresholds in PJI diagnosis. The data evaluating separate cut-off thresholds of other serologic markers (such as interleukin-6 and D-dimer) for hip versus knee PJI are much less established. While only three studies have specifically addressed separate thresholds of ESR and CRP for hip versus knee PJIs, other studies have focused on either hip or knee PJIs individually.

The 2010 retrospective study by Piper et al. [20] investigated the diagnostic value of CRP and ESR in infections of hip, knee, and shoulder arthroplasties, as well as spine implants. The study reported the CRP thresholds of 10.3 mg/L for hip and 14.5 mg/L for knee PJI. The optimal ESR thresholds for hip and knee PJI were 13 and 19 mm/hour, respectively. A large retrospective study by Alijanipour et al. in 2013 [14] analyzed 1,962 patients and found that, for chronic PJI, the optimal CRP thresholds were 13.5 mg/L for hips and 23.5 mg/L for knees, with ESR thresholds of 48.5 mm/hour for hips and 46.5 mm/hour for knees. In 2019, a retrospective study by Unter Ecker et al. [11] found that the optimal CRP threshold was 8.9 mg/L for hip and 9.9 mg/L for knee PJI. This study did not evaluate the diagnostic performance of ESR.

When comparing the findings from Piper et al. [20], Alijanipour et al. [14], and Unter Ecker et al. [11], several differences and similarities emerge in the optimal thresholds for CRP and ESR in diagnosing chronic PJI. For CRP, the thresholds for knee PJI tend to be higher than for hip PJI across the studies. Specifically, Piper et al. (14.5 mg/L) and Alijanipour et al. (23.5 mg/L) reported higher thresholds than Unter Ecker et al. (9.9 mg/L). For hip PJI, the CRP thresholds vary less: Piper et al. 10.3 mg/L, Alijanipour et al. 13.5 mg/L, and Unter Ecker et al. 8.9 mg/L. In terms of ESR, there is substantial variation. Piper et al. reported ESR thresholds of 13 mm/hour for hip and 19 mm/hour for knee PJ, while Alijanipour et al. found much higher thresholds, with 48.5 mm/hour for hips and 46.5 mm/hour for knees. Interestingly, unlike CRP, the ESR trend is not consistent across the studies.

In 2009, Ghanem et al. [21] published a retrospective study focusing on hip PJI and found a CRP threshold of 20.5 mg/L and an ESR threshold of 30 mm/hour For chronic knee PJI, a prospective study by Greidanus et al. [22] in 2007 identified optimal thresholds of 13.5 mg/L for CRP and 22.5 mm/hour for ESR. In a 2017 retrospective study, Kim et al. [23] found that a CRP threshold of 34.9 mg/L had the best diagnostic performance for acute knee PJI (within three weeks of arthroplasty). However, none of these studies addressed the cut-offs for knee versus hip PJI within the same analysis.

In summary, common diagnostic methods for PJI include clinical evaluation, microbiological culture, imaging, and serological tests. While CRP and ESR are well-established markers, the need for joint-specific cut-off thresholds (hip versus knee) remains under investigation. Some studies suggest higher thresholds for the knee compared to hip PJI, but the current literature is scarce and inconclusive, and findings can vary depending on study design, sample size, and population.

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