

HK-39 – Is there a role for neutrophil-to-lymphocyte ratio and monocyte-to-lymphocyte ratio in diagnosing periprosthetic joint infections?

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Response/Recommendation:

Serum neutrophil-to-lymphocyte (NLR) and monocyte-to-lymphocyte ratio (MLR) are promising adjunctive diagnostic markers for PJI, but they should not be used as standalone tests.

Strength of recommendation: Moderate

Delegate Vote:

Rationale:

The neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) have been identified as valuable biomarkers for differentiating between bacterial and viral infections and predicting clinical outcomes[1]. The NLR, in particular, has garnered increasing attention as an inflammatory marker across various diseases due to its prognostic importance. It represents the balance between neutrophils, key mediators of innate immunity that amplify pro-inflammatory responses, and lymphocytes, which regulate adaptive immune responses. Elevated NLR values reflect a shift toward a pro-inflammatory state, which may contribute to unchecked systemic inflammation that could impact a vulnerable joint. The NLR has been used to predict prognosis in conditions such as cancer, sepsis, COVID-19, cardiovascular disease, diabetes, and increasingly in periprosthetic joint infection (PJI)[2,3]. The NLR and MLR are inexpensive, readily available from routine white blood cell count differentials, and can be seamlessly integrated into clinical workflows[4]. However, there is limited research specifically examining their relationship with PJI[5,6]. Jiang et al. investigated the role of NLR and MLR in detecting occult infections among septic arthritis patients undergoing total hip arthroplasty (THA) and concluded that these markers are unreliable in this context [7]. In contrast, Varady et al. concluded that serum NLR and SF-NLR have superior diagnostic and prognostic ability for septic arthritis, compared with current clinical standards[8]. Conversely, Zhao et al. observed elevated NLR and MLR values in patients who have early PJI in a preliminary study, suggesting their potential utility in identifying early postoperative infections[9]. Prior studies evaluating the diagnostic utility of NLR and MLR in PJI have yielded conflicting results. However, recent meta-analyses suggest that these markers can serve as a diagnostic marker for PJI following total hip or knee arthroplasty.

The systematic review identified 1,112 studies from three major databases (PubMed, Web of Science, and Scopus) and one additional study from other sources. After removing 401 duplicates, 711 studies were screened based on titles and abstracts, with 669 excluded for not meeting inclusion criteria. Following this, 42 full-text studies were assessed for eligibility, of which 13 were excluded due to insufficient data (n = 1), wrong study design (n = 5), wrong patient population (n = 1), wrong evaluated parameter (n = 1), or ineligible article types such as meta-analyses or reviews (n = 6). The final systematic review included 28 studies, with no studies categorized as ongoing or awaiting classification.

A total of 26 studies assessed the role of the serum NLR in the context of PJI [10–35]. The diagnostic criteria for PJI varied among these studies, with 13 using the MSIS criteria, five employing the EBJIS 2020 guidelines, one following the CDC/NHSN criteria, one following the IDSA criteria, and five adhering to the ICM 2018 consensus. Additionally, one study utilized culture results as the diagnostic reference, while two did not specify any diagnostic criteria. Across the pooled data, which included 2,238 PJI patients and 10,177 aseptic-loosening patients, NLR levels were consistently higher in PJI cases than in those with aseptic loosening. In the PJI group, the mean NLR values ranged from 2.16 ± 0.58 to 89.72 ± 92.46 , while in the aseptic loosening group, they ranged from 1.84 ± 0.59 to 13.80 ± 7.87 , reflecting a clear distinction between the two conditions. The analysis indicates that NLR has moderate diagnostic accuracy for distinguishing between PJI and aseptic loosening. The pooled sensitivity (68.4%) and specificity (69.8%) suggest that NLR can moderately identify PJI cases and rule out non-PJI cases. However, the diagnostic odds ratio (DOR = 0.995) indicates weak overall discrimination ability. Subgroup analyses revealed that NLR performs consistently across PJI and arthroplasty subtypes, with the highest SMD observed in TKA subgroups. Heterogeneity was generally low, further supporting the consistency of these findings. Publication bias analysis showed no significant bias based on Begg's test, but Egger's test detected potential asymmetry, suggesting a need for caution in interpreting the results. The funnel plot also indicated mild asymmetry.

Regarding serum MLR, 11 studies assessed the role of the MLR in diagnosing PJI [10–13,15,16,21,31,36–38]. The diagnostic criteria for PJI varied among these studies, with four using the MSIS criteria, two employing the EBJIS 2020 guidelines, two following the IDSA criteria, and two adhering to the ICM 2018 consensus. Additionally, one study utilized culture results as the diagnostic reference. Across the pooled data, which included a total of 1,159 PJI patients and 8,526 aseptic loosening patients, MLR levels were consistently higher in PJI cases compared to those with aseptic loosening. In the PJI group, the mean MLR values ranged from 0.25 to 0.71 ± 0.38 , while in the aseptic loosening group, they ranged from 0.2 ± 0.59 to 0.46 ± 0.27 , reflecting a distinction between the two conditions. The analysis indicates that MLR has moderate diagnostic accuracy for distinguishing between PJI and aseptic loosening. The pooled sensitivity (67.4%) and specificity (70.6%) suggest that MLR can moderately identify PJI cases and rule out non-PJI cases. However, the diagnostic odds ratio (DOR = 5.54) indicates only moderate overall discrimination ability. Subgroup analyses revealed that MLR performs similarly across PJI types and arthroplasty subtypes, with the highest SMD observed in acute PJI and THA subgroups. Heterogeneity was generally low to moderate, further supporting the consistency of these findings. Publication bias analysis showed no major bias based on Begg's test, but Egger's test detected potential asymmetry, suggesting a need for caution in interpreting the results. The funnel plot also indicated mild asymmetry.

There were two studies that evaluated the diagnostic performance of synovial NLR, reporting sensitivities of 74.1 and 52.4%, respectively, and specificities of 80.7 and 88.9%, respectively [33,35].

Conclusion:

In conclusion, while serum NLR and MLR are promising adjunctive diagnostic markers for PJI, they should not be used as standalone tests. Combining these serum markers with other

diagnostic criteria or biomarkers may enhance their clinical utility. Further high-quality studies are needed to validate these findings and address potential publication bias.

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