Establishment and Validation of a Synovial Fluid C-Reactive Protein Clinical Decision Limit for Periprosthetic Joint Infection

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INTRODUCTION:
C-reactive protein (CRP) has long served as a prototypical biomarker for periprosthetic joint infection (PJI). Recently, synovial fluid CRP (SF-CRP) has garnered interest as a diagnostic tool. Although previous studies have identified diagnostic cutoffs for SF-CRP, they have been limited in scope and employed various CRP assays without formal validation for PJI diagnosis. This study aimed to conduct a formal single clinical laboratory validation to determine the optimal cutoff of SF-CRP for the diagnosis of PJI.
METHODS:
A retrospective analysis of prospectively collected data was performed using Receiver Operating Characteristic (ROC) and Area Under the Curve (AUC) analyses. Over 2,600 institutions submitted hip and knee synovial fluid samples to a single clinical laboratory for diagnostic testing between 2017 and 2022. Samples meeting specimen integrity requirements and possessing a full biomarker dataset were included. A total of 108,948 samples were classified as Infected, Not Infected, or Inconclusive based on the synovial fluid category of the 2018 International Consensus Meeting (ICM) criteria. Data were divided into training (n=67,242) and validation (n=28,819) sets, which only included samples classified as Infected or Not Infected. The Youden Index was employed to optimize the decision threshold.
RESULTS:
The SF-CRP clinical decision limit for PJI diagnosis was established at 4.45 mg/L, with a sensitivity of 86.3% (95% CI: 85.6%-87.0%) and specificity of 87.2% (95% CI: 87.0%-87.4%). Applying this cutoff to the validation dataset yielded a sensitivity of 86.1% (95% CI: 85.0%-87.1%) and specificity of 87.1% (95% CI: 86.7%-87.5%). No statistically significant deviation in diagnostic performance was observed between the validation and training sets.
DISCUSSION AND CONCLUSION: This study represents the largest single clinical laboratory evaluation of a SF-CRP assay for PJI diagnosis. The optimal CRP cutoff (4.45 mg/L) is 36% lower than the generally recommended value (6.9 mg/L), underscoring the importance of validating individual SF-CRP assays for PJI diagnosis.