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CORR Insights®: Is Synovial C-reactive Protein a Useful Marker for Periprosthetic Joint Infection?

Nathan W. Cummins MD

Where Are We Now?

Periprosthetic joint infections (PJIs) are expensive, difficult to treat, and devastating to patients. Despite the presence of consensus guidelines on the diagnosis of PJI [1, 2, 8], preoperative differentiation between PJI and aseptic failure remains a challenge, mainly because of the relatively low negative predictive value of routinely available clinical tests for patients deemed at risk. Those tests include synovial fluid cell count and C-reactive protein (CRP) analysis.

Because preoperative exclusion of PJI substantially alters surgical planning, we need to produce better preoperative diagnostic tests for PJI. Among the novel molecular and immunologic tests undergoing evaluation, synovial fluid CRP has shown promise in diagnosing PJI in previous preliminary studies [3, 4, 6, 7]. C-reactive protein is a nonspecific acute phase reactant synthesized by the liver, and should be present in synovial fluid in response to PJI secondary to translocation from blood through inflamed and leaky capillaries.

Where Do We Need To Go?

Previous studies [3, 4, 6, 7] on synovial fluid CRP for the diagnosis of PJI have been limited in size and have reported varying sensitivities based on the different immunoassays used. Building off of those studies, Tetreault and colleagues conducted a prospective, observational study of 119 patients undergoing revision total knee or hip arthroplasties for all causes. They compared the performance of serum and synovial CRP, using the same clinical assay and instrumentation for diagnosing PJI and a modified version of the Musculoskeletal Infection Society guidelines (removing serum CRP as a criterion) as the gold standard [5]. Importantly, they reported a significant correlation between serum and synovial fluid CRP, which would necessarily limit the clinical specificity in the setting of other potential causes of systemic inflammation, including other acute and chronic inflammatory arthritides. Additionally, while the two tests revealed identical area under the curves, the serum CRP outperformed

This CORR Insights® is a commentary on the article "Is Synovial C-reactive Protein a Useful Marker for Periprosthetic Joint Infection?" by Tetreault and colleagues available at: DOI: [10.1007/s11999-014-3828-y](https://doi.org/10.1007/s11999-014-3828-y).

The author certifies that he, or any member of his immediate family, has no funding or commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

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members are on file with the publication and can be viewed on request.

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This *CORR Insights®* comment refers to the article available at DOI: [10.1007/s11999-014-3828-y](https://doi.org/10.1007/s11999-014-3828-y).

N. W. Cummins MD (✉)
Division of Infectious Diseases,
Mayo Clinic, 200 1st Street SW,
Rochester, MN 55905,
USA
e-mail: cummins.nathan@mayo.edu

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the synovial fluid CRP in terms of negative predictive value (99% versus 95%), although this difference was not statistically significant. Additionally, nearly 15% of synovial fluid samples could not be assessed for CRP level due to excess viscosity or hemolysis. The results reported by Tetreault et al. may serve as the definitive study on the use of synovial fluid CRP for the diagnosis of PJI. The use of synovial fluid CRP seems limited in successful application and offers no additional diagnostic information beyond serum CRP, which is already widely clinically available. Additional research is needed to identify more sensitive and specific markers for PJI.

How Do We Get There?

Solving this problem will likely require application of the rapidly advancing “-omics” technologies (eg, genomics, transcriptomics, proteomics, metabolomics, etc ...) moving beyond repurposing of traditional biomarkers in novel settings, to biological discovery through unbiased approaches. This could come through increasingly sensitive molecular detection of host and pathogen gene expression with

advanced next generation sequencing technologies, or measurement of abnormal local production of novel biomarkers of the inflammatory response against infection through proteomic and/or metabolomics technologies. A secondary benefit of such an approach may be the discovery of novel biologic insights and identification of new therapeutic targets, beyond just developing a better diagnostic test.

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