

The Synovial Fluid Alpha-Defensin, Cell Count, Polymorphonuclear Neutrophils Percentage, and C-Reactive Protein are Non-Redundant Biomarkers

Krista O'Shaughnessey Toler, Pearl Ravindra Paranjape¹, Van Thai-Paquette, Gregory K Deirmengian, Alexander C McLaren, Carl A Deirmengian²

¹Zimmer Biomet, ²Lankenau Hospital

INTRODUCTION:

Periprosthetic joint infection (PJI) has various formal definitions involving multiple synovial fluid (SF) biomarkers. The 2018 International Consensus Meeting placed the alpha-defensin (SF-AD) test and the SF white blood cell (SF-WBC) count in the same category, assuming a strong correlation. However a strong correlation has never been demonstrated. This study examined the correlation between SF biomarkers for PJI and their performance in the context of culture-positive rate.

METHODS:

A total of 143,168 synovial fluid samples from hip and knee arthroplasties were submitted by 2,974 institutions to a single clinical laboratory for a diagnostic PJI evaluation. Samples met integrity requirements and included SF-CRP, SF-AD, SF-WBC, and SF-PMN% results. Spearman correlations were calculated for each biomarker pair after scaling by percentile rank. Logistical regression and eigensystem analysis evaluated biomarker collinearity. The relative contribution of biomarker combinations to positive culture likelihood was assessed.

RESULTS:

No strong correlations were found between biomarker pairs, with all $[r] < 0.7$. Correlations between SF-AD, SF-WBC, and SF-PMN% ranged from 0.65-0.67, while all SF-CRP correlations ranged from 0.44-0.55. Multiple logistic regression showed all variance inflation factors < 2.5 , and eigensystem analysis yielded a condition number = 8.5, both indicating low biomarker collinearity.

SF culture-positive rates increased incrementally with each additional positive biomarker (0.4%, 1.9%, 8.3%, 37.1%, and 70.2% ; all $p < 0.001$). Each biomarker was evaluated for its ability to enhance culture-positivity stratification based on all possible combinations of the other three biomarkers' results. SF-AD had the greatest impact on culture-positivity stratification (9.4-fold), followed by SF-PMN% (4.5-fold), SF-WBCs (2.4-fold), and SF-CRP (1.7-fold).

DISCUSSION AND CONCLUSION:

This study, the largest to date assessing redundancy between SF biomarkers for PJI, found no strong correlations or collinearity between SF-CRP, SF-AD, SF-WBCs, or SF-PMN%. The AD/WBC pair did not demonstrate excess redundancy when compared to other biomarker pairs and yielded quite different impacts on the prediction of culture-positivity. These data agree with the only other study assessing collinearity between SF-AD and SF-WBC. Future formal systems defining PJI should consider assessments of collinearity before grouping biomarkers.