Diagnostic Utility and Thresholds for Commonly Obtained Serum and Synovial Markers prior to Reimplantation in Periprosthetic Joint Infection

Abhijit Seetharam, Julian Dilley[1], R Michael Meneghini[2], Michael Maher Kheir
[1]Indiana University Health, [2]Indiana Univ Hlth Phys

INTRODUCTION:
Diagnosis of persistent periprosthetic joint infection (PJI) during two-stage exchange is critical for determining appropriate timing for reimplantation. However, the diagnostic accuracy and threshold values of routine serum and synovial markers prior to reimplantation remains unclear. The purpose of this study was to evaluate the diagnostic performance of several commonly obtained serum and synovial markers, including newly studied neutrophil-to-lymphocyte ratio (NLR) and absolute neutrophil count (ANC), and to define thresholds for PJI diagnosis to better guide reimplantation. An additional purpose was to study the diagnostic utility of trends in serum markers such as erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) in PJI diagnosis prior to reimplantation.
METHODS:
This was a retrospective review of 249 patients who underwent two-stage exchange with antibiotic spacers for PJI. Charts were reviewed for most recent synovial and serum aspiration data obtained when patients had spacers but prior to planned reimplantation. Synovial makers included white blood cell count (WBC), polymorphonuclear percentage (PMN%), neutrophil-to-lymphocyte ratio (NLR), and absolute neutrophil count (ANC). Serum markers included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), WBC, PMN%, NLR, and ANC. Serum ESR and CRP were trended from initial infection diagnosis to prior to reimplantation. The collected markers had their utility in diagnosing PJI examined by area under the curve analysis (AUC). Pairwise comparisons of AUCs were performed for serum and synovial markers.
RESULTS: Serum CRP had the highest AUC of all studied markers (0.863). The threshold for serum CRP was 3.1 mg/dL, which provided a sensitivity of 65.3% and specificity of 78.9%. Serum ESR had an “acceptable” AUC of 0.749, however all other serum markers qualified as “poor” tests. The percentage change in serum CRP and ESR had poor diagnostic value compared to the respective absolute values (AUCs of 0.614 and 0.654 respectively). Synovial ANC had the highest AUC of all synovial makers (0.772), with a cutoff of 3,802 cells/uL, but it did not significantly outperform other synovial markers, which all had acceptable AUCs.
DISCUSSION AND CONCLUSION: The results show serum CRP to have excellent diagnostic utility for diagnosis of persistent PJI in revision total joint arthroplasty with antibiotic spacers. Absolute values of serum ESR and CRP have better diagnostic value than trends of these serum markers for guiding reimplantation timing. The study also defines diagnostic thresholds for many commonly obtained synovial and serum markers in spacer arthroplasty. There is no marker that can currently be used alone to diagnose PJI in these patients, but rather a combination of these markers along with the overall clinical picture should be reconciled together to make the final diagnosis.

Diagnostic Values and Thresholds for Serum Markers prior to Reimplantation

Test	AUC (95% CI)	Optimal Cutoff Value	Sensitivity	Specificity	Positive Likelihood Ratio	Negative Likelihood Ratio
ESR	0.749 (0.652 – 0.831)	81 mm/hr	45.83%	89.37%	4.31	0.61
CRP	0.863 (0.779 – 0.924)	3.1 mg/dL	65.31%	78.88%	3.09	0.44
WBC	0.683 (0.582 – 0.773)	9,900 cells/uL	57.14%	73.68%	2.17	0.58
PMN%	0.641 (0.539 – 0.735)	60%	89.66%	37.04%	1.42	0.28
NLR	0.686 (0.585 – 0.776)	3.88	68.97%	61.25%	1.78	0.51
ANC	0.695 (0.595 – 0.784)	4,590 cells/uL	82.76%	46.25%	1.54	0.37
ESR (% Change)	0.614 (0.530 – 0.693)	56.5%	54.05%	70.00%		
CRP (% Change)	0.654 (0.570 – 0.732)	75.4%	73.68%	61.90%		

ESR = erythrocyte sedimentation rate, CRP = C-reactive protein, WBC = white blood cell count, PMN% = polymorphonuclear percentage, NLR = neutrophil-to-lymphocyte ratio, ANC = absolute neutrophil count

Diagnostic Values and Thresholds for Synovial Markers prior to Reimplantation

Test	AUC (95% CI)	Optimal Cutoff Value	Sensitivity	Specificity	Positive Likelihood Ratio	Negative Likelihood Ratio
WBC	0.758 (0.699 – 0.809)	3,800 cells/uL	52.63%	92.19%	6.74	0.51
PMN%	0.758 (0.700 – 0.810)	86%	54.39%	85.42%	3.73	0.53
NLR	0.756 (0.698 – 0.808)	13.33	63.16%	83.33%	3.79	0.44
ANC	0.772 (0.715 – 0.822)	2,952 cells/uL	52.63%	92.71%	7.22	0.51

WBC = white blood cell count, PMN% = polymorphonuclear percentage, NLR = neutrophil-to-lymphocyte ratio, ANC = absolute neutrophil count