

One Combination is Better than the Others: Comparing Single, Double and Triple Combination Serum Markers to Diagnose Periprosthetic Joint Infection

Jonathan S Yu, Troy Bornes¹, Mark Youssef², Kathleen W Tam², Allina A Nocon², Peter Keyes Sculco, Alberto V Carli
¹Hospital for Special Surgery, ²Hospital For Special Surgery

INTRODUCTION:

Establishing the diagnosis of periprosthetic joint infection (PJI) remains challenging due to factors influencing host status, pathogen virulence and chronicity. Without a ‘gold standard’ test, recent PJI literature has explored the utility of combining serological results, with promising findings. However, previous studies evaluate fewer than two hundred patients and often studied only 1-2 test combinations. The purpose of this study was to accumulate the largest single institution cohort of revision total joint arthroplasty (rTJA) patients to date to determine the diagnostic utility of combination serum biomarkers to identify PJI.

METHODS: A single institution longitudinal database was assessed to identify all patients that underwent rTJA from 2016-2020. PJI was diagnosed post-rTJA utilizing 2011 MSIS criteria. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), D-dimer, and interleukin 6 (IL-6) were systematically collected for all patients. Diagnostic performance through and receiver-operator-curves and Youden’s index were calculated for individual serum biomarkers and their combinations.

RESULTS: 1,363 rTJA patients including 273 PJI cases (20%) were analyzed. When assessed individually, CRP exhibited the highest AUC (0.899±0.023) compared to ESR (0.878±0.035), WBC (0.739±0.036), IL-6 (0.553±0.023) and D-Dimer (0.549±0.036). When combined, CRP + ESR performance yielded a notably higher Youden’s index (0.58) compared to single tests alone (0.478 and 0.47 respectively). Although combining CRP + D-dimer, CRP + IL-6 and even CRP + ESR + D-dimer all produced higher Youden indexes versus each single test alone, none were higher than the index of CRP or ESR alone.

DISCUSSION AND CONCLUSION: Combining two or even three serum tests improve their performance for diagnosing PJI. In our cohort, interpreting the combination of CRP and ESR results yielded the most diagnostically useful information for establishing or ruling out PJI. Furthermore, no non-CRP/ESR combination outperformed CRP and ESR alone, reaffirming the utility of these established markers as first-line tests.

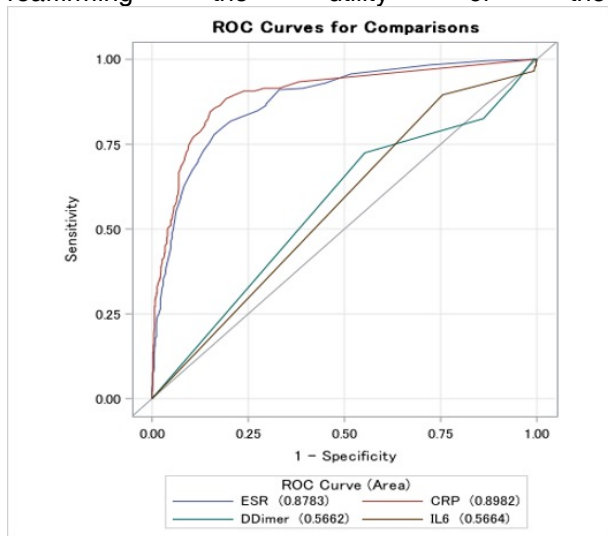


Table 1. Diagnostic Values of Biomarkers.

Biomarkers		Youden Index	Sensitivity	Specificity	PPV	NPV	DOIs	p-value
Two Marker Combinations	CRP	0.48	51.4%	96.7%	90.7%	76.2%		
	ESR	0.47	54.4%	95.2%	78.7%	81.0%		
	D-dimer	0.17	25.3%	91.0%	62.5%	68.0%		
	IL-6		7.8%	50.0%	67.9%	3.9%		
Two Marker Combinations	CRP + ESR	0.58	65.3%	92.8%	75.2%	88.8%	24.10	<0.001
	CRP + D-dimer	0.47	53.9%	95.9%	59.2%	91.3%	15.25	<0.001
	ESR + D-dimer	0.47	55.7%	91.3%	47.9%	93.5%	13.14	<0.001
Three Marker Combinations	CRP + ESR + D-dimer	0.47	55.7%	91.3%	47.9%	93.5%	23.40	<0.001