

## **Diagnostic Utility of a Novel Point-of-Care Test of Calprotectin for Periprosthetic Joint Infection in Total Knee Arthroplasty Patients**

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**Introduction:** Recently several synovial fluid biomarkers for diagnosis of periprosthetic joint infection (PJI) are being investigated. Point-of-care (POC) tests using these biomarkers are not widely available. Synovial calprotectin has been reported to effectively exclude diagnosis of PJI and a novel lateral flow POC test for synovial calprotectin has shown potential to be an effective PJI diagnostic tool. Thus, the objective of this study was to test the sensitivity, specificity, and positive and negative predicted values (PPV and NPV) of a calprotectin POC test for PJI in total knee arthroplasty (TKA) patients, using the Musculoskeletal Infection Society (MSIS) 2013 PJI diagnosis criteria as the gold standard.

**Methods:** Synovial fluid samples were prospectively collected from 73 patients who underwent revision TKA (rTKA) at two academic institutions from October 2018 to May 2019. The study was conducted under IRB approval. Patients followed the hospital standard for their diagnostic work-up. Data collection included demographic, clinical, and laboratory data in compliance with the MSIS 2013 PJI diagnosis criteria. Synovial fluid samples were analyzed by calprotectin POC tests for synovial fluid in accordance with manufacturer's instructions. Quantitative calprotectin read-outs were categorized into high risk (>50 mg/L), medium risk (14-50 mg/L) and low risk (<14 mg/L) for infection by the test reader system.

Patients were categorized as septic or aseptic using MSIS 2013 PJI diagnosis criteria by two independent reviewers blinded to the calprotectin results. Test performance characteristics including sensitivities, specificities, PPV, NPV, and areas under the curve (AUC) were calculated for 2 scenarios: 1) a threshold of >50 mg/L for infection, 2) a threshold of >14 mg/L for infection.

**Results:** Following MSIS criteria, 26 rTKAs were MSIS positive, while 47 rTKA were MSIS negative (Table 1). The corresponding calprotectin classifications were 28 high, 8 medium, and 37 low risk. Of the MSIS criteria positive cases, 25 were high risk and only 1 was medium risk, while all 37 low risk read-outs were infection negative. In the 1) >50 mg/mL threshold scenario, the POC performance showed a sensitivity, specificity, PPV, NPV and AUC, respectively, of 96.2%, 93.6%, 89.3%, 97.8%, and 0.95. In the 2) >14 mg/mL threshold scenario, there was a sensitivity, specificity, PPV, NPV and AUC, respectively, of 100.0%, 78.7%, 72.2%, 100.0%, and 0.89 (Table 2).

**Conclusion:** The calprotectin POC test has excellent diagnostic properties including high sensitivity and specificity for diagnosing PJI in rTKA. However, further investigations with larger cohorts are necessary to further validate these results.

Table 1: Demographics

Demographic and Index Surgery	MSIS Criteria	
	Negative (n=47)	Positive (n=26)
Age	65 ± 9	68 ± 10
Body Mass Index	33.4 ± 6.8	35.1 ± 10.4
Charlson Comorbidity Index	3.5 ± 2.1	4.1 ± 2.5
Female	28 (58.3%)	11 (42.3%)
Smoker	4 (8.5%)	4 (15.4%)
Type of Surgery		
Aseptic Revision	40 (85.1%)	0 (0.0%)
DAIR	1 (2.1%)	8 (30.8%)
Explant Spacer, Conversion to TKA	5 (12.5%)	2 (7.7%)
Explant TKA, Implant Spacer	1 (2.1%)	14 (53.8%)
Reimplant Spacer	0 (0.0%)	1 (3.8%)
Explant TKA, No Spacer	0 (0.0%)	1 (3.8%)
Calprotectin Point of Care Test		
High Risk (>50 mg/L)	3 (6.3%)	25 (96.2%)
Medium Risk (14-50 mg/L)	7 (14.9%)	1 (3.8%)
Low Risk (<14 mg/L)	37 (77.1%)	0 (0.0%)

DAIR – debridement, antibiotics, implant retention; TKA – total knee arthroplasty

Table 2: Sensitivities, Specificities, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Areas Under the Curve (AUCs) and of the Calprotectin point of care (POC) Test

1) &gt;50 mg/L Threshold for Infection

		MSIS Criteria		AUC
		Positive	Negative	
POC Test	Positive	25	3	0.949
	Negative	1	44	
Sensitivity	Specificity	PPV	NPV	
96.2%	93.6%	89.3%	97.8%	

2) &gt;14 mg/L Threshold for infection

		MSIS Criteria		AUC
		Positive	Negative	
POC Test	Positive	26	10	0.894
	Negative	0	37	
Sensitivity	Specificity	PPV	NPV	
100.0%	78.7%	72.2%	100.0%	