Utility of Serum Biomarkers in Diagnosing Fracture-Related Infections: A Pilot Study

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Purpose: Fracture related infections (FRIs) are a potential devastating outcome for patients and costly for society. "Classic" inflammatory markers (white blood cell count, erythrocyte sedimentation rate, and C-reactive protein [CRP]) are not sufficient for confirmatory diagnosis, and improved diagnostic biomarkers are needed. The purpose of this pilot study was to compare a large panel of serum-based inflammatory biomarkers in patients with confirmed FRI to patients without infection.

Methods: This is a single center, comparative diagnostic Level III study. The recently proposed FRI definition was used as the "gold standard" for assigning cases as infected. 13 patients meeting the confirmatory FRI criteria were matched to 13 controls based on age, time after surgery, and fracture region. Serum was assessed using the Milliplex human cytokine magnetic bead panel immunology 47-plex immunoassay, as well as hospital laboratory CRP measurements. Group differences were assessed by matched t tests, and receiver operating characteristic (ROC) curve analyses were used to determine optimum cut-points for each biomarker.

Results: CRP, interleukin (IL-6), platelet-derived growth factor (PDGF)-AB BB, and vascular endothelial growth factor (VEGF)-A levels were significantly different when comparing the FRI and matched control groups (all $P<0.05$). Cut-points optimizing the ROC curve analyses were 7.8, 10,443, and 77.5 pg/mL for IL-6, PDGF-AB BB, and VEGF-A, respectfully, and 2.8 mg/dL for CRP. Table 1 shows the sensitivity, specificity, and area under the ROC curve for these cut-points. Having all 4 of the biomarkers below the cut-point was 100% specific for FRI.

Conclusion: This pilot study demonstrates the feasibility of undertaking a larger study to look at the utility of serum biomarkers for establishing the diagnosis of FRI. The data suggest that having multiple biomarkers measuring below a threshold may reliably identify no infection. This should be further investigated in a cohort of patients who meet suggestive FRI criteria.

	Sensitivity	Specificity	AUC
Il-6	53.9	84.6	0.692
PDGF-AB BB	61.5	84.6	0.731
VEGF-A	38.5	92.3	0.654
CRP	46.2	92.3	0.692

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