The Infected Diabetic Foot: Can Serum Biomarkers Predict Re-Infection After Hospital Discharge For Diabetic Foot Infections?

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Introduction

- Diabetic foot infections (DFI) are one of the main underlying factors leading to hospitalization and amputation in people with diabetes.
- After treatment for DFIs, up to 48% of patients get re-infected and require re-hospitalization
- Aim: To evaluate biomarkers to identify osteomyelitis after initial treatment for diabetic foot infections (DFIs).

Methods

- Thirty-five patients enrolled
- Inclusion Criteria: ≥ 21 years of age, moderate – severe infection based on the Infectious Diseases Society of America classification with suspicion of underlying osteomyelitis (OM), suspicion of OM based on initial clinical presentation, probe to bone, radiographic and advanced imaging findings (x-ray, MRI)
- Exclusion Criteria: Other infectious diseases, previously diagnosed OM, immunosuppressive therapies, organ or hematological malignancy, ESRD on dialysis
- Received standard of care medical and surgical treatment
- Serum biomarkers drawn at baseline, three, and six weeks
    - Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-8 (IL-8), procalcitonin (PCT), and monocyte chemoattractant protein 1 (MCP-1)
- Bone samples obtained from all patients via percutaneous or intraoperative surgical cultures
- Statistical Analysis: Clinical characteristics and outcomes compared using χ^2 test and an α=0.10 given the exploratory nature of the study. Relationship between serum biomarkers and re-infection (osteomyelitis) assessed for collinearity using variation inflation factor (VIF) analysis. VIF of 5.0 (α=0.20) was used to denote significant collinearity.

Results

Table 1: Biomarkers and OM Re-Infection

Laboratory value	Re-Infection^	No Re-Infection^	P*
ESR (mm/h)	73.11 (41.92)	38.78 (22.87)	< 0.01
CRP (mg/dL)	1.44 (1.04)	0.73 (0.92)	0.08
IL-6 (pg/mL)	9.01(8.85)	4.22 (5.62)	0.08
IL-8 (pg/mL)	27.11(49.11)	9.59 (4.08)	0.08
MCP-1 (pg/mL)	44.78 (28.61)	75.26 (44.34)	0.08
PCT (ng/mL)	0.06 (0.05)	0.07 (0.05)	0.85

^Values are presented as mean (standard deviation)
*α=0.10

Table 2: Biomarker Cut-Points for OM Re-Infection

Laboratory value[b]	Sensitivity	Specificity	AUROC[a]	95% CI
ESR > 73.5 mm/h	0.45	1.00	0.66	(0.43-0.89)
CRP > 1.5 mg/dL	0.40	0.90	0.54	(0.30-0.79)
PCT > 0.034 ng/mL	0.56	0.79	0.63	(0.38-0.87)
IL-6 > 6.56 pg/mL	0.50	0.86	0.57	(0.31-0.82)
IL-8 > 13.3 pg/mL	0.50	0.86	0.72	(0.52-0.93)
MCP-1 > 42.5 pg/mL	0.60	0.82	0.60	(0.34-0.87)

[a]Area under the receiver operative characteristic curve
[b]Optimal cutoffs determined by ROC analysis

- Eleven patients were identified to have soft tissue infections (STI) and twenty-four patients were diagnosed with OM by bone culture and histology at study initiation.
- Nine patients were identified with osteomyelitis during follow up.
    - Five of these were in patients initially diagnosed with STI.
    - Six were diagnosed with OM prior to healing the index wound.

Results (Cont)

- Those who had re-infection with OM had respective :
    - Antibiotic course: 11.8 ± 4.7 vs 5.9 ± 3.7 weeks (p<0.01)
    - Amputation after admission: 55.6% ± 5 vs. 3.8% ± 1 (p<0.01)
    - Time to healing: 164.7 ± 80.4 vs. 91.2 ± 86.3 days (p=0.06)
    - Re-ulceration same foot: 44.4% ± 4 vs. 11.5% ± 3 (p=0.06)

Discussion

- Biomarkers can be inexpensive in comparison to repeated MRI or SPECT/CT
- Although these inflammatory markers are non-specific in nature, elevated ESR, CRP, IL-6, IL-8 and decreased MCP-1 can be associated with developing OM
- These can prompt earlier intervention such as biopsy, change in antibiotic coverage, or surgery earlier in the disease
- This study was prospective in design and operational definitions were consistent.
- Gold standard of osteomyelitis diagnosis was used (bone culture or bone histology)
- Limited by a small sample size (n=35)
- Budget was limited and unable to evaluate the biomarkers over a longer period of time such as 12 months

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