Critical Review Form
Diagnostic Test

Bacterial or Crystal-associated Arthritis? Discriminating Ability of Serum Inflammatory Markers, *Scand J Infect Dis* 1998; 30: 591-596

Objective: "**To evaluate the diagnostic information obtained by measuring the concentrations of various acute phase reactants in serum samples from patients with bacterial arthritis compared to patients with a non-infectious acute inflammatory joint condition, crystal-associated arthritis.**" (p. 591)

Methods: A retrospective review of all patients with culture verified bacterial arthritis or crystal associated arthritis at Örebro Medical Centre (Sweden) from 1993 – 1995. All subjects had cultures and polarized light direct microscopy, but additional synovial fluid testing was only available for 61% (33/54) bacterial arthritis and 91% (31/34) crystal-associated arthritis patients. In addition 87% (47/54) septic arthritis and 88% (30/34) crystal arthritis patients had serum available to test for TNF_α, IL-8, IL-6, G-CSF, lactoferrin, CRP, and procalcitonin.

	Guide	Comments
I.	**Are the results valid?**	
A.	**Did clinicians face diagnostic uncertainty?**	Not clear. These patients were referred to the Infectious Disease Division, so somebody must have suspected septic arthritis. Possible *spectrum bias* limiting external valid.
B.	**Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?** **(Confirmation Bias)**	Yes, all patients had synovial fluid culture and polarized microscopy.
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard?** **(Ascertainment Bias)**	Doubtful, since many of the serum tests were performed at a later date from frozen serum (p 592)
II.	**What are the results?**	

A.	**What likelihood ratios were associated with the range of possible test results?**	- Septic arthritis patients were younger (median 72 vs. 78 years) with more rheumatoid arthritis (20% vs. 3%) than crystalloid arthritis. 15 septic arthritis cases involved prosthetic joints and arthroscopic surgery and three followed intra-articular injections. 36% of septic arthritis cases had positive blood cultures with the same organism. - The predominant organisms were Staphylococcus aureus (48%), β-hemolytic streptococci (20%), and coag-negative staph (11%) - Gram staining revealed bacteria in only 42% of septic arthritis cases. 11% of bacterial arthritis cases died (vs. none of crystal arthritis). - Half of crystal arthritis cases received antibiotics for mean of 2-days (versus mean 10-day antibiotic course for septic arthritis).

Synovial WBC >100,000	Septic arthritis +	-	Sen = 30% Spec = 94%
+	10	2	LR+ = 4.7
-	23	29	LR- = 0.75

Synovial WBC >50,000	Septic arthritis +	-	Sen = 58% Spec =7 4%
+	19	8	LR+ = 2.2
-	14	23	LR- = 0.57
			Prevalence = 51.6%

- Medium jWBC in septic arthritis was 70,000 (range 4400-246,500) compared with crystal-associated arthritis 20,000 (range 140-104,000) which was significantly different (p = 0.009).
- A reduction in synovial glucose was seen in 64% septic arthritis vs. 15% crystal arthritis.
- ESR (81 vs. 54) and CRP (182 vs. 101) were both significantly higher inn septic arthritis as were TNF_α (4.9 vs. 4.3), IL-8 (19.5 vs. 13.5), G-CSF (35 vs. 20), but significant overlap existed between each of these and optimal cut-points were not determined.

		• WBC and lactoferrin, IL-6, and procalcitonin levels did not differ between septic and crystalloid arthritis.

III.	**How can I apply the results to patient care?**	
A.	**Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?**	For serum WBC, ESR, and CRP likely yes. Since cytokines, lactoferrin procalcitonin are not readily available, perhaps not.
B.	**Are the results applicable to the patients in my practice?**	Probably not since these were a highly select group already referred to ID, not undifferentiated ED patients.
C.	**Will the results change my management strategy?**	Probably not, since dissimilar patients are reported upon using a host of tests not readily available in 2007 and authors failing to report acceptable diagnostic performance measures such as ROC curve, AUC, optimal cut-points and likelihood ratios.
D.	**Will patients be better off as a result of the test?**	Cannot deduce this from current paper.

Limitations

1. Selection bias – recruited only subjects referred to ID with either positive crystals or bacterial growth on synovial fluid. These are different from ED patients with lower a prevalence of septic and crystal arthritis and therefore different diagnostic test characteristics.
2. Incomplete Gold standard. Given the limited sensitivity of culture, a composite Gold standard of positive culture or positive Gram stain or prevalent joint aspirate/operative drainage would have been superior.
3. Incomplete data reporting lacking ROC curve, AUC, optimal cut-points and LR's. Additionally, failed to stratify data by co-morbidity (immunocompromised, rheumatoid arthritis, etc.)
4. Limited demographic reporting making assessment of external validity impossible.

Bottom Line

In a Swedish single center methodologically challenged retrospective review, patients referred to ID with septic arthritis or crystalloid arthritis might be distinguished by synovial WBC > 100,000 (LR^+ = 4.70, 95% CI 1.1-20) (LR^- = 0.75, 95% CI 0.58-0.95) or synovial WBC > 50,000 (LR^+ = 2.2, 95% CI 1.2-4.3) (LR^- = 0.57, 95% CI 0.37-0.90). ESR, CRF, TNF_α, and G-CSF might be useful to distinguish the two arthropathies, but substantial overlap between septic and crystalloid arthritis exists for all of these. WBC, PCT, IL-6, and lactoferrin are clinically useless for this indication. Synovial fluid gram stain was only positive in 42% of septic arthritis cases and 11% of bacterial arthritis cases died.