Critical Review Form

Diagnostic Test

The clinical presentation and impact of diagnostic delays on emergency department patients with spinal epidural abscess,
J Emerg Med 2004; 26:285-291

Objectives: **To investigate "the early presentation and impact of diagnostic delays on SEA (spinal epidural abscess) and explore the use of risk factors assessment as a screening strategy in a population of Emergency Department (ED) patients presenting with spine pain." (p. 286)**

Methods: **Single center (University of California in San Diego) case-control study which identified all SEA patients via ICD-9 discharge codes (intra-spinal abscess 324.1) for the period April 1992 through March 2002. Although vertebral osteomyelitis or discitis patients were also screened for concurrent SEA, the investigators do not describe how vertebral osteomyelitis or discitis patients were identified. Exclusion criteria included ED evaluations for symptoms unrelated to SEA, in addition to fungal or tuberculoses spinal infections.**

Each SEA case was hand-matched to two controls matched on age and gender who presented to the ED with back or neck pain. Four investigators abstracted data from medical records onto a standard form. Discrepancies were referred to the principle investigator "to maintain consistency". (p. 286) Elements extracted included demographics, presenting complaint and duration, prior ED or medical evaluations, PMI emphasizing *a priori* risk factors, and lab results (CBC, ESR, blood work and wound culture). A priori risk factors for SEA included DM, IVDA, liver disease, renal failure, indwelling catheter, immunocompromised status, recent invasive spinal procedures, vertebral fracture, and distant site of infection. Attending EP notes were used if documentation discrepancies were noted. Diagnostic delay, defined as multiple ED visits without SEA diagnosed or hospital admission without SAE mentioned or <24º to diagnostic study. Signs of symptoms of SEA during the ED evaluation were required for patients to be included in the diagnostic delay group. SEA patients were analyzed in the group (with our without diagnostic delay) into which they fell.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did clinicians face diagnostic uncertainty?**	Yes – back pain patients of various etiologies with differential diagnosis including rare SEA.
B.	**Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?** **(Confirmation Bias)**	No. "The final diagnosis of SEA was confirmed by operative reports or final MRI or CT interpretations." However, not every SEA had MRI, CT or operative pathologic diagnosis. And most non-SEA back pain patients did not have MRI or surgery. Therefore, how do we know that SEA had an epidural abscess (i.e. were true-positives) and that non-SEA did not (i.e. were true-negatives)?
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard?** **(Ascertainment Bias)**	No single test (i.e. WBC) is being assessed for the diagnosis of SEA. However, the constellation of symptoms (i.e., the classic triad) and signs undoubtedly influenced clinicians' decisions to obtain or not obtain MRI, CT or neurosurgical consultations. Furthermore, data abstractors were aware of the study hypothesis and could have looked more intensely for any documentation of signs, symptoms, labs, etc. in SEA patients. Therefore, there is great potential for *ascertainment bias* on two levels.
II.	**What are the results?**	

A. **What likelihood ratios were associated with the range of possible test results?**

What the authors believe:

	SEA^+	SEA^-		
Classic Triad Present	5	1	Sen	= 5/63 = 7.9%
			Spec	= 125/126 = 99.2%
			LR^+	= sen/1-spec = 10
Classic Triad Absent	58	125	LR^-	= 1-sen/spec = 0.93

	SEA^+	SEA^-		
Classic Triad Present	5	10	Sen	7.9%
			Spec	99.8%
			LR^+	35.7
Classic Triad Absent	58	4490	LR^-	0.925

	SEA^+	SEA^-		
Classic Triad Present	5	346	Sen	7.9%
			Spec	92.3%
			LR^+	1
Classic Triad Absent	58	4154	LR^-	1

This is interesting. The authors report sensitivity, specificity, positive predictive value, negative predictive value, LR^+, and LR^- in Table 1. (p. 287). <u>This is completely inaccurate in a case-control study</u> where the controls have been artificially selected because the prevalence of disease-negative patients is completely unknown so specificity, LR^+, LR^-, PPU, and NPV cannot be determined by this study design. Why? Look at the 2x2 table at the left to understand.

However, during the 10-year interval of this study there were many more patients in whom SEA would have been considered in the differential diagnosis, but who ultimately did not have SEA. The authors stated that they have 45000 ED visits/year. If back pain represented 1% of those visits then UCSD would have seen (45000)*(10-years)*(0.01) ≈ 4500 back pain patients during this time most of whom did not have SEA. Try using these figures to recalculate a more accurate 2x2 table (at left).

The last 2x2 table to the left simply assumes the classic triad is as prevalent in SEA patients as in non-SEA patients. Bottom Line: **Since consecutive patients were not enrolled and since disease-negative subjects did not have the same criterion standard applied we cannot comment on specificity or LR's.**

Here's what this case-control study does tell us:

- Over the 10-year period 63 patients were evaluated in the ED and had SEA with a mean symptom duration of 5-days at the first ED visit and 9-days at admission.
- The median number of ED visits for SEA patients was 2.
- The median age of SEA patients was 46 years and 59% were male and 98% had at least one risk factor (DM, IVDA, liver disease, renal failure, indwelling catheter, immunocompromised, recent invasive spinal procedure, vertebral fracture or distant site of infection).

		<table><tr><th>Finding</th><th>Sensitivity for SEA (1%)</th></tr><tr><td>Classic Triad</td><td>7.9%</td></tr><tr><td>IVDA</td><td>60</td></tr><tr><td>Immunocompromised</td><td>21</td></tr><tr><td>ETOH abuse</td><td>19</td></tr><tr><td>Recent spine procedure</td><td>16</td></tr><tr><td>Distant site of infection</td><td>14</td></tr><tr><td>DM</td><td>13</td></tr><tr><td>Indwelling catheter</td><td>11</td></tr><tr><td>Recent spine fracture</td><td>3</td></tr><tr><td>Chronic renal failure</td><td>3</td></tr><tr><td>Cancer</td><td>3</td></tr><tr><td>Temperature > 38°C During ED visit</td><td>32</td></tr><tr><td>Focal spine tenderness</td><td>52</td></tr><tr><td>Diffuse spine tenderness</td><td>65</td></tr><tr><td>Positive straight leg raise</td><td>13</td></tr><tr><td>Loss of sensation</td><td>17</td></tr><tr><td>Weakness</td><td>29</td></tr><tr><td>Abnormal rectal tone</td><td>5</td></tr><tr><td>Saddle anesthesia</td><td>2</td></tr><tr><td>WBC > 1000 cells/mm^3</td><td>60</td></tr><tr><td>ESR > 20 mm/hr</td><td>98</td></tr><tr><td>Blood culture</td><td>57</td></tr><tr><td>Osteo on x-ray</td><td>24</td></tr></table> • Diagnostic delays were noted in 75% of SEA patients; with a diagnostic delay 45% had a residual weakness at discharge versus 13% of those without a diagnostic delay (p=0.037). • 71% of SEA had operative management.
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?**	Uncertain. Would need to assess the reliability and accuracy of clinicians defining and identifying these findings prospectively faced with many more non-SEA patients than SEA patients. With that consideration the specificity remains undefined and all the above sensitivities are likely overly optimistic (see Newman TB, Kohn MA; Evidence-Based Diagnosis, Cambridge University Press 2009, p 100).

B.	**Are the results applicable to the patients in my practice?**	Yes, although how to efficiently identify these patients remains largely undefined. "Only one out of every 50 patients with a risk factor would be expected to have SEA and performing MRI on each patient with a risk factor for SEA would not be practical." (p. 290)
C.	**Will the results change my management strategy?**	Yes by recognizing the low sensitivity for history, physical exam and labs for SEA. The fact that specificity/LR's are completely unknown is another diagnostic consideration. Therefore, the test-treatment threshold cannot be determined. Therefore, the only way to rule-in or rule-out SEA is via criterion standard testing which cannot be confidently deferred based upon clinical findings.
D.	**Will patients be better off as a result of the test?**	Yes, if clinicians recognize the inaccuracy of history, physical exam and labs to diagnose or risk-stratify for SEA. Unfortunately, the purity of data, rarity of SEA, and devastating sequel of diagnostic delays will translate into increasing utilization of MRI unless subsequent trials identify accurate and reliable diagnostic alternatives or risk-stratification instruments.

Limitations

1) **Case-control design without the capability to report SEA incidence or specificity, likelihood ratios, positive or negative predictive values.**

2) **Failure to adjust for prognostic confounders with propensity score.**

3) **No 95% CI's for sensitivity.**

4) **Single center design with limited external validity and likely underestimated incidence of SEA.**

5) **Retrospective design with erroneous assumption that lack of documentation equates to absence of a finding. May have been present but not tested or present and tested, but not documented.**

6) **Some risk factors are poorly described. Example "recent invasive spinal procedure" what is "recent"? Does an LP or acupuncture count as "invasive" ro do investigators mean operative interventions only?**

Bottom Line

The classic triad of spine pain, fever, and neurologic abnormality has a sensitivity of 7.9% for spinal epidural abscess in ED patients. If emergency physicians were to evaluate every patient with at least one risk factor for SEA, 50 MRI's would be performed for every one SEA patient identified. Prospective consecutive sample studies are needed to better understand the sensitivity, specificity and LR's of traditional spinal epidural abscess risk factors.