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The Mail
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Washington DC 20049

Dear Editors:

As a Medical Laboratory Scientist, I read with much interest the article by Dr. Nancy Snyderman in the August/September 2013 issue of AARP The magazine, "Fighting a Killer Infection". I must update both her and your readers about a statement made in that article, saying that "We don't have a diagnostic test for sepsis". In fact, there is a very good, FDA-approved diagnostic test for patients at risk for sepsis called **procalcitonin**.

In 2006, a systematic review and meta-analysis was reported from researchers from France, who used 33 published studies in multiple clinical sites and with a large range of patient types to determine procalcitonin's accuracy as a diagnostic test for sepsis and septic shock. They concluded that "Procalcitonin should be used in diagnostic guidelines for sepsis and in clinical practice in intensive care units".

Crit Care Med. 2006 Jul;34(7):1996-2003.

Procalcitonin as a diagnostic test for sepsis in critically ill adults and after surgery or trauma: a systematic review and meta-analysis.

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Abstract

OBJECTIVE: To quantify the accuracy of serum procalcitonin as a diagnostic test for sepsis, severe sepsis, or septic shock in adults in intensive care units or after surgery or trauma, alone and compared with C-reactive protein. To draw and compare the summary receiver operating characteristics curves for procalcitonin and C-reactive protein from the literature.

DATA SOURCE: MEDLINE (keywords: procalcitonin, intensive care, sepsis, postoperative sepsis, trauma); screening of the literature.

STUDY SELECTION: Meta-analysis of all 49 published studies in medical, surgical, or polyvalent intensive care units or postoperative wards. Children, medical patients, and immunocompromised patients were excluded.

DATA EXTRACTION: Thirty-three studies fulfilled inclusion criteria (3,943 patients, 1,828 males, 922 females; mean age: 56.1 yrs; 1,825 patients with sepsis, severe sepsis, or septic shock; 1,545 with only systemic inflammatory response syndrome); eight studies could not be analyzed statistically. Global mortality rate was 29.3%.

DATA SYNTHESIS: Global odds ratios for diagnosis of infection complicated by systemic inflammation were 15.7 for the 25 studies (2,966 patients) using procalcitonin (95% confidence interval, 9.1-27.1) and 5.4 for the 15 studies (1,322 patients) using C-reactive protein (95% confidence interval, 3.2-9.2). The summary receiver operating characteristics curve for procalcitonin was better than for C-reactive protein. In the 15 studies using both markers, the Q* value (intersection of summary receiver operating characteristics curve with the diagonal line where sensitivity equals specificity) was significantly higher for procalcitonin than for C-reactive protein (0.78 vs. 0.71, p = .02), the former test showing better accuracy.

CONCLUSIONS: Procalcitonin represents a good biological diagnostic marker for sepsis, severe sepsis, or septic shock, difficult diagnoses in critically ill patients. Procalcitonin is superior to C-reactive protein. Procalcitonin should be included in diagnostic guidelines for sepsis and in clinical practice in intensive care units.

A second systematic review of the research literature in 2013 provided the conclusion that "Procalcitonin is a helpful biomarker for early diagnosis of sepsis in critically ill patients. Nevertheless, the results of the test must be interpreted carefully in the context of medical history, physical examination, and microbiological assessment".

Lancet Infect Dis. 2013 May;13(5):426-35. doi: 10.1016/S1473-3099(12)70323-7. Epub 2013 Feb 1.

Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis.

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Abstract

BACKGROUND: Procalcitonin is a promising marker for identification of bacterial infections. We assessed the accuracy and clinical value of procalcitonin for diagnosis of sepsis in critically ill patients.

METHODS: We searched Medline, Embase, ISI Web of Knowledge, the Cochrane Library, Scopus, BioMed Central, and Science Direct, from inception to Feb 21, 2012, and reference lists of identified primary studies. We included articles written in English, German, or French that investigated procalcitonin for differentiation of septic patients--those with sepsis, severe sepsis, or septic shock--from those with a systemic inflammatory response syndrome of non-infectious origin. Studies of healthy people, patients without probable infection, and children younger than 28 days were excluded. Two independent investigators extracted patient and study characteristics; discrepancies were resolved by consensus. We calculated individual and pooled sensitivities and specificities. We used I(2) to test heterogeneity and investigated the source of heterogeneity by metaregression.

FINDINGS: Our search returned 3487 reports, of which 30 fulfilled the inclusion criteria, accounting for 3244 patients. Bivariate analysis yielded a mean sensitivity of 0 · 77 (95% CI 0 · 72-0 · 81) and specificity of 0 · 79 (95% CI 0 · 74-0 · 84). The area under the receiver operating characteristic curve was 0 · 85 (95% CI 0 · 81-0 · 88). The studies had substantial heterogeneity (I(2)=96%, 95% CI 94-99). None of the subgroups investigated--population, admission category, assay used, severity of disease, and description and masking of the reference standard--could account for the heterogeneity.

INTERPRETATION: Procalcitonin is a helpful biomarker for early diagnosis of sepsis in critically ill patients. Nevertheless, the results of the test must be interpreted carefully in the context of medical history, physical examination, and microbiological assessment.

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The Mayo Clinic in Minnesota includes this in its testing menu, found at http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/83169. They report that "ProCT becomes detectable within 2 to 4 hours after a triggering event and peaks by 12 to 24 hours. ProCT secretion parallels closely the severity of the inflammatory insult, with higher levels associated with more severe disease and declining levels with resolution of illness… In the appropriate clinical setting, a ProCT of >2.0 ng/mL predicts sepsis and a level of >10 ng/mL indicates likely septic shock. Reported sensitivity and specificity for the diagnosis of sepsis range from 60% to 100%, depending on underlying and coexisting diseases and the patient populations studied. The higher the ProCT level the worse the prognosis".

So there definitely is a test for sepsis currently in use in the United States. I hope you can include a part of this in a Letter to the Editor so that the AARP members can have this important information. Additional information can be found at our consumer website, Lab Tests Online, http://labtestsonline.org/understanding/analytes/procalcitonin/tab/test.

Sincerely,

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