Reviewer’s report

Title: Biomarkers for diagnosing serious bacterial infections in older outpatients: A systematic review

Version: 0 Date: 30 Apr 2019

Reviewer: Anum Fasih

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Biomarkers for diagnosing serious bacterial infections in older outpatients: A systematic review

General Comments

A total of eleven studies were analyzed by the authors of this manuscript. The extremely small number of studies which were included in this systematic review limit its clinical utility. Furthermore, when divided into sub-categories (bacteremia, UTI, intra-abdominal infection and bacterial infection), the number of studies allotted to each category falls to a minimum of 1 (intra-abdominal infections) and a maximum of 4 (UTI and bacteremia).

Answers to specific questions regarding the value of this study:

Will the article add enough to existing knowledge?

- No. It is a well-established fact that biomarkers do not serve as good stand-alone measures of clinical assessment and decision making. The results of this study, albeit statistically significant, have little clinical relevance or application in real world clinical settings.

Will this article help readers make better decisions?

- No (see above)

Specific Comments

Salivary biomarkers

It is stated in the abstract and background that the diagnostic accuracy of salivary biomarkers for the diagnosis bacterial infections in older adults has been studied by the authors of this
systematic review. However, there is no mention of salivary biomarkers in the preceding sections comprising the main text of the article.

Which salivary biomarkers were the authors referring to?

Exclusion criteria

While reasons behind some of the exclusion criteria are easily understood, others are more difficult to elucidate. For instance, the article states that in studies in which patients' co-morbidities were used to select participants have been excluded. This statement requires further elaboration.

Studies conducted in developing countries have been excluded from this systematic review.

What is the scientifically relevant justification for this?

Figure 1 lists 'wrong study design' as one of the exclusion criteria. Please elaborate on what the 'wrong study design' is defined as.

Setting

The objective of this study was to determine the value of biomarkers for diagnosing serious bacterial infections in older adults in ambulatory care settings. However, 7 of the 11 studies in this review article were based in the emergency department, which caters to the full spectrum of clinical illness; from stable patients to acutely ill patients requiring Intensive Care. Given this fact, the stated objective of the study is inaccurate and perhaps misleading.

Bacteremia

It is important to keep in mind that procalcitonin values may be influenced by preexisting comorbid conditions such as chronic kidney disease and congestive heart failure, which have been shown in studies to be associated with higher PCT values at baseline [1,2]. In the population being studied, there is a high prevalence of these comorbid conditions.


Therefore, it was prudent to include these confounding factors in this analysis. The studies included in this systematic review did little to address comorbid conditions and baseline procalcitonin levels. Examples are as follows:

1. Caterino et al (reference 17): Patients with antibiotic use within the preceding 48 hours were excluded as antibiotics decrease PCT levels.

2. Dwolatzky et al (reference 21): The baseline medical diagnoses of the study populations were similar, and there was no difference between the groups with regard to medical therapy

3. Lai et al (reference 24): Exclusion criteria were missing data or loss of follow-up and preexisting thyroid disease, because of its possible effect on PCT evaluation

Urinary tract infection

Line 187 - 188: One study effect size was large and the confidence interval was wide [+ve LR 188 54.90 (95% CI 3.5 to 861.29)]. A confidence interval of 3.5 - 861 provides no clinically significant data on which to base future practice. The results stated in this section are weak at best, and do not add anything of value to pre-existing clinical knowledge.

Intra-abdominal infection

Major shortcoming: Only one study which assessed a correlation between the WBC count and intra-abdominal infection was included in this systematic review. Furthermore, this study was published 20 years ago, in 1999. Data for this study was collected from November 1992 to September 1995.

The retrospective observational study of diagnostic accuracy by Potts et al used a surgical diagnosis to identify patients with intra-abdominal infection. However, it is uncertain whether these patients were had evidence of bacteremia as seen on blood cultures. This clinical consideration can exert a large effect on WBC count and other biomarkers. It is not clear whether
this systematic review took this consideration into account, since a study of biomarkers for the diagnosis of bacteremia is one of the objectives of this study.

Bacterial infection

How did the authors distinguish between 'bacteremia' and 'bacterial infection'? Both these conditions can and do co-exist within the same patient. An explanation of the criteria upon which this distinction was based is missing.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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