Reviewer's report

Title: Clinical and Inflammatory Response to Bloodstream Infections in Octogenarians

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Reviewer: Jacek M. Witkowski

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The manuscript by Green et al. aims at characterizing the responses (clinical and inflammatory) to blood infection (confirmed culture-positive sepsis) in the cohort of octogenarians by comparing them to younger cohort, paying special attention to mortality with regard to comorbidities. The main conclusion and novelty of the work seems to be that the Charlson Index of Comorbidities (applied in the study) is the strongest predictive factor for older patients' mortality, better than hypotension and advanced age itself. The topic of this work seems to be adequate and possibly interesting to the readers of BMC Geriatrics.

However, in its current form, it leaves some loose ends which require clarifications and revision before the paper can be accepted.

Major compulsory revisions:

These concern their study groups, and exclusion – inclusion criteria: Although their initial number of patient episodes is high, the number of those included (167 out of 1367) seems barely adequate. These patients were divided into the older cohort (80+ years of age) and the younger one, consisting of people aged 18 – 80 (!) years. Although understandable in the light of relatively small study groups, inclusion of subjects commonly defined as young, middle-aged and old in a single “younger” cohort seems a mistake, as numerous reports show that they grossly differ in their immunological and inflammatory responses. It would be desirable if the authors split their ‘younger’ cohort into young, middle-aged and old sub-cohorts or, alternatively, removed their youngest subjects in order to define their ‘younger’ cohort as elderly. The authors do not discuss this possibility, and its inclusion in the analysis could affect the predictive role of age of the subjects. Especially, when the Index of Comorbidities (IoC) comes into the picture – one would expect that young (18+ years old) and possibly middle-aged subjects would not have any co-morbidities at all or just single ones; thus, one would expect that IoC will show correlations with age, and possibly later with mortality; however, it would be more interesting to see if people of similar age with different IoC experiencing bacteriemia/sepsis are at similar or different mortality levels?

Also, the authors never mention the ethnicity of their subjects, and it is a factor that might affect the results; were their cohorts ethnically uniform, or at least balanced?
The paper describes a single hospital study – could it affect the result (by preferential types of nosocomial infections in a single hospital)? Would not a multi-hospital approach be better, as averaging the types of infections present in the study cohorts as well as increasing the numbers of those finally included in the study?

Finally, the authors mention that “Patients were excluded from the study if their blood culture specimen contained likely contaminants, or if they were undergoing chemotherapy.” However, they give no explanation of these ‘likely contaminants’ and their meaning other than saying “contaminants were determined on a case by case basis by file review by an infectious diseases physician”. It is unclear what the authors mean by the statement “Chemotherapy patients were excluded as they are immunosuppressed and often do not grow organisms despite high fevers.” What kind of chemotherapy they have in mind? Anti-microorganism? Anti-tumor? Once again the text is imprecise and thus hard to perceive.

In the Discussion, the authors use the term “bacteremic patients”. Do they consider it synonymous to “patients developing sepsis”? Bacteremia may not lead to septic complications!

Later on the same p.11, the authors summarize that “… older patients do not mount a poorer immune response than younger patients. In fact, on average these patients had higher C-reactive protein, white cell count and neutrophil count.” Apparently, the authors are not familiar with the concept of inflamm-aging, describing increased pro-inflammatory factors in a subgroup of an elderly cohort as putting them at high mortality risk.

The abstract concludes that their “older patients are more likely to have an undifferentiated presentation”; however, the term is not explained and vague, especially in the light of next sentence “However, importantly, there is no significant difference in the likelihood of fever or inflammatory markers.”. What do authors have in mind? In the Introduction (p.5) they mention that older patients are more likely to react to infections in a nonspecific way, but never use the term ‘undifferentiated’. It would be desirable if they were more precise.

In the Data Analysis section of M&M, the authors mention the reference model, but under that name they list the name and version of the SPSS statistical package. Only from the legend of Table 2 the reader can understand that they applied one of the SPSS Regression Models, but it remains a mystery which one. Also, they never reference any source for the major tool they applied in their study, i.e. the Charlson Index of Comorbidities. Did they apply the original, or any of its variants and if the latter, which one? Especially, that on p. 12 they mention factors that were not examined in their study, including possibly kidney and liver ailments, which clearly are included in the original Charlson Index!

There are inconsistencies in their numbers. For instance, they mention 167 subjects included (in the Abstract), but then only 155 (117 ‘younger’ and 38 ‘older’) in the text, which agrees with the data in tables. Where this inconsistency
comes from?

However, data presentation in the tables also leaves plenty to wish for. The tables' row descriptions do not include any units, so they are hard to read. Also, the listed totals in the table 4 never (!) equal the sum of the columns.

Description of the results is also imprecise and doubtful. For instance, on p. 11 the authors say “The difference in neutrophil count was on average three x109/L higher in older patients…” which is hard to understand. Was the difference in neutrophil count higher? Or, more likely, the neutrophil count itself?

The most important results of the study are illustrated in the Table 2. However, the factors included in the analyses are imprecise again. What is “lower systolic blood pressure”? “Lower oxygen saturation”? “Greater respiratory rate”? What are the numerical delimiters for “lower” and “greater” in each case? In fact, table 3 should precede table 2, as it lists the vital parameters of the subjects, while table 2 is the result of their analysis.

On p. 11, they mention “This study also demonstrated a similar total number of gram positive and gram negative organisms…”; certainly, they did not mean the actual numbers of bacteria per person, as might be interpreted from that statement.

Minor revisions:

The authors refer to Tables and Appendices, yet there are no Appendices included in the file nor available online. Please explain and/or correct.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests