Author's response to reviews

Title: Systemic Inflammatory Response Syndrome in Adult Patients with Nosocomial Bloodstream Infections due to Enterococci

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Author's response to reviews: see over
To: The Editors

Thank you for the reviews. Listed below is an itemized description of the critiques and my response to them. Also, ethical approval was obtained through our institutional review board.

Review from Gregson:

1. Since laboratories vary in their methods of speciating enterococci, the actual method used in the laboratory should be stated.
   a. We added to the Methods section: After identifying to Enterococcus, a Strep API 20 kit was used to determine species.
2. The number of primary and secondary bacteremias (with the source) should be identified.
   a. We added to the Results section a description of the number of primary and secondary BSI, as well as the sources of the secondary BSI.
3. The number of central venous catheter infections that were present and the method of determining this should be stated.
   a. To the Methods/Definitions section, we added our method for determining catheter-related infections. The number of catheter-related BSI were added to the end of the Results section.

Review from Trick:

1. Information is lost in converting the APACHE II score from a continuous to a dichotomous outcome. The decision to use a cut-point and the reason from the value chosen should be used.
   a. Added to the Methods/Definitions section, we discuss that this methodology was used to remain consistent with our previous studies in this area.
2. Were all the BSIs primary or were secondary infections included? As the authors are aware, this distinction is important in assessing patient outcomes.
   a. We added to the Results section a breakdown of primary and secondary BSI.
3. The culture day should be defined. In some situations the date the culture was obtained is most relevant (eg…), while for others (eg…) the date of the culture result may be most relevant. In this paper, what was day 0.
   a. We added to the Methods/Definitions section that the day the culture was obtained was counted as Day 0 of the BSI
4. Did the authors evaluate in-hospital mortality? If so, were patient discharges within 7 days censored from the analysis of 7-day mortality?
   a. We addressed in both the Methods/Definitions section and the Results/Study Populations and Patient Characteristics, that we assessed only in-hospital mortality. If the patient was discharged in less than seven days from the positive blood culture, we assumed they were alive at 7 days. Of our 50 patients, 5 were discharged before day 7.
5. Abstract—The Method section describes the focus of the paper as defining the SIRS. However, tables 1 and 2 compare VRE to VSE and table 3 looks at predictors of
mortality. Also, the results describe a spectrum of illness that includes septic shock and death in addition to SIRS. Perhaps the analyses could focus on the progression of SIRS among patients or the methods could reflect the range of outcomes assessed. The last sentence should define the dependent variable for the multivariable analysis.

a. In the Methods section of the abstract, we reworded the intention of the study to: evaluating the associated systemic inflammatory response syndrome and mortality
b. added to the Methods section is that the dependent variable was mortality.

In the results, APACHE II cut point of 20 is reported…
c. This was changed to 18.

6. Background—the last sentence should be reworded. Currently, as worded the relationship being assessed is unclear to me.

a. This sentence changed to: This study was conducted to evaluate the inflammatory response, clinical course, and outcomes of nosocomial enterococcal bacteremia, as well as the affect of vancomycin resistance.

7. Methods, Definitions: third sentence. SIRS is defined as two or more clinical criteria, which is consistent with definitions used by other investigators; however this outcome does not appear to be used in the analyses. Figure 1 displays all possible SIRS scores. It would help the reader for the authors to state in the methods how the SIRS scores were to be used in the presentation of data. Also, sepsis is defined but does not appear to be used in the analyses. In summary, the clinical states relevant to the results presented should be used.

a. We added further explanation in the Methods/Definitions portion, as recommended below, that clinical conditions SIRS 0-4, severe sepsis, and septic shock are mutually exclusive categorie. We, then, define each state SIRS 0-4.

8. Methods, Statistical analysis—please clarify the outcome assessed for your model.

a. Our outcome was mortality, either 7-day or total in-hospital.

9. Methods, Study Design—I recommend that the clinical conditions SIRS 0-septic shock be explicitly stated as mutually exclusive categories and that SIRS 1 through 4 represents the sum of the clinical criteria used to score SIRS.

a. This was added.

10. The last sentence may more clearly state the study objective.

a. noted

Sincerely,

Katharine Bar