Reviewer's report

Title: Leukocytes as a Prognostic Factor for Patients with Pulmonary Embolism

Version: 1 Date: 27 May 2013

Reviewer: Michael Lu

Reviewer's report:

This is an interesting and novel investigation that has the potential to make a contribution to the field. The authors found that SIRS and leukocytosis are significant predictors of 30-day mortality after acute pulmonary embolism.

Major suggestions for revision:

1) A major limitation of this study is that it does not differentiate between leukocytosis/SIRS due to a known source (e.g. sepsis, recent major surgery, pancreatitis, etc...) vs. an unknown source (presumably PE). As a result it is not possible to assess whether leukocytosis/SIRS is a predictor of outcome independent of one these coincident events. The authors could address this by including these factors in the multivariate analysis or by repeating the analysis for the subgroup of patients in whom PE is the only or most likely source for an elevated WBC/SIRS.

2) There is an inadequate discussion of limitations. Only ~ ½ of pts had NT pro-BNP. Was this test was ordered only in patients for whom there was a specific clinical indication and does this bias the results? For the other clinical and laboratory values, was your data complete? How was 30-day mortality assessed, and were any patients lost to follow up?

3) Shock is generally accepted as the strongest predictor of outcome after pulmonary embolism. In this study, 5.3% of patients met the author’s definition of shock, and these patients had a high (25%) 30 day mortality rate. It is then curious that shock was not a significant predictor in the multivariate analysis. What were the p-values of shock and the other non-significant variables in the multivariate analysis? In the Discussion the authors correctly state that their findings are at odds with most published reports, but should discuss possible reasons why.

4) In general the quality of the written English is acceptable. However several sentences are ambiguous or potentially misleading. For example, Page 8, second paragraph, first sentence. Do you mean the patients were reclassified according to the original and final model? On page 9, first paragraph of the Discussion, second sentence. Do you mean that the models based on WBC count and SIRS satisfying peripheral WBC count were significantly associated with mortality? On page 8, last subheading. The phrase “Leukocytes for 30-day mortality of PE” suggests that you are assessing PE-related mortality, while the authors actually assess all-cause mortality. I would suggest changing to
“Leukocytes for 30-day mortality after PE.”

5) Was the “final model” any more accurate than “PESI+WBC”? Both had an AUC of 0.76 yet I could not find a direct comparison. Which model do the authors recommend for clinical practice?

Minor points:

1. Last paragraph, page 11. This data should be included in the results before the discussion.

2. Page 9, first two sentences of the discussion. The authors state that the RV/LV ratio and SIRS satisfying WBC criteria were the two significant independent predictors of 30 day mortality. However, in table 3 the authors state that altered mental status was also a significant predictor. Why is AMS not included?

3. There are several typos where the reference is placed after the trailing period, for example for reference 21 on page 5.

4. Page 5, third paragraph, second sentence. “The ratio of right ventricular diameter to the left ventricular diameter (RV/LV ratio) was calculated using CT scan images showing the interventricular mediastinum and myocardium from the longitudinal axis of the heart [19-20].” Do you mean “interventricular septum” rather than “interventricular mediastinum”? Please clarify how the RV/LV measurement was made. Were the measurements made on a single axial image, and how was this image chosen? What type of CT scanners (e.g. 4 – 64 detector row helical CT) and what slice thickness was employed? Who made the measurements?

5. On page 9, 4th sentence you state that the p value comparing the AUC of PESI and PESI+WBC is < 0.001, but in the abstract you state a p value of < 0.01. Which is correct?

6) Regarding the references, a pubmed search for “pulmonary embolism leukocytosis” yielded this article by Huang CM et al Clin Biochem 2011, which has similar findings about leukocytosis in assessing prognosis after PE. The authors should include a paragraph in the Discussion contrasting their results to published work.

6. Page 5, second to last sentence of the “Study Methods”. Insert “retrospectively” between the words “We” and the remainder of the sentence “collected all of the clinical and laboratory data at the time of diagnosis of PE.” Also, please clarify what “all of the clinical and laboratory data” includes here in the Methods.

7. The title suggests a focus on leukocytes as a prognostic factor after pulmonary embolism. In fact the other SIRS criteria are also a major focus. Perhaps the title could be reworded to reflect this?

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.