Reviewer's report

Title: Is Albumin Gradient Or Fluid To Serum Albumin Ratio Better Than The Established Criteria In The Diagnostic Separation Pleural Effusion? An Analysis Of Data From 200 Patients.

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Reviewer: Dr Elmer Villanueva

Level of interest: A paper of limited interest

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

This report constitutes a statistical review of the paper.

1. Materials and methods
   a. "Final response rate...": inappropriate terminology and uncertain significance. I am unclear as to the importance of this proportion. It should be enough to state that samples from 200 patients with pleural effusion of known aetiology were included. Unless the authors are prepared to speculate about how the 12 exclusions might be different from the 200 inclusions, the proportion is meaningless.

2. Statistical analysis:
   a. "selecting the points of test values...": this is unclear and misleading. Sensitivity and specificity are inversely related to each other. As one increases, the other decreases. To claim that a cut-point was chosen on the basis of maximising both values at the same time is an impossibility. Given that the choice of cut-point is central to the discussion, the authors must elaborate on this point.
   b. Use of standard errors of the mean: It is more acceptable to use the standard deviation as a measure of spread in samples since one would first want to show how the individual measures are variable. Using the standard error also artificially deflates the variability as the typical reader interprets these measures in the standard deviation sense. I would refer the authors to Martin Bland's or Doug Altman's books on basic stats on the use of standard errors versus standard deviations.
   c. Addition: I would suggest that the authors include a statement saying that all results are presented as mean +/- SD. It is out of place in the Results section.

3. Results:
   a. "One hundred fifty six effusions were...": Sentence to read "One hundred fifty six (78%) effusions". The complement can be worked out in one's head.
   b. I question the use of means and SDs as summary measures given the use of a non-parametric test. The use of a non-parametric test is (among other things) due to the deviation of the distribution from the normal, bell-shaped curve. If this were so, it would be more appropriate to use medians and interquartile
ranges as summary measures of centrality both in the text and in the tables.
c. "FLDH was the best...": this statement is open to mis-interpretation. To claim that the FLDH test is "the best" is far-reaching because only one aspect of test methodology was examined. It is more accurate to state "FLDH showed the highest AUC among the three tests".
d. "...FLDH were 0.81 (0.75 to 0.87),...": what do the numbers in parentheses represent?
e. "...FLDH was significantly more than...": this is confusing given that, if the numbers in parentheses are 95% confidence intervals, the AUC results for SEAG and FLDH overlap while those for ALBR and FLDH don't. The statement is better made with the FLDH-ALBR comparison. Even then, an exact p-value wouldn't hurt.
f. Multiple comparisons. The authors make three implicit comparisons when trawling through AURs: SEAG vs ALBR ("...the AUC for SEAG and ALBR were of similar magnitude."), FLDH vs SEAG ("...the AUC for FLDH was significantly more than the AUC for SEAG."), and FLDH vs ALBR (by not mentioning the presence of a result). I would suggest giving p-values correcting for these multiple comparisons.
g. "...correctly classified 132 (85%)": suggest sticking confidence intervals on these results.
h. "There was a significant negative correlation...": I am unclear why this was done. Reading on, the authors make a claim that a negative correlation implies similarity of mechanism. This is hard to swallow given that (i) Pearson's rho is only a test for LINEAR correlation and (ii) association certainly does not imply causation. I have yet to see a mechanism of action proven through the use of Pearson's rho. I suggest eliminating this statement and result, or offering extra-clinical evidence.
i. Additions: The authors must describe the characteristics of their population in more detail. Readers will want to know how their own patients compare to this sample. All that is provided them are the aetiologies of the pleural effusion and the genders. What other characteristics may be included?

4. Discussion:
a. Would the authors speculate about the study's implications for further research and for future clinical practice? For instance, if the SEAG and ALBR are less accurate than the FLDH, what about against TPR or LDHR? Should clinicians still consider using SEAGs and ALBRs? Is there a place for these in clinical practice?

5. Conclusion:
a. There isn't one.

6. Figure legends:
a. They don't refer to the appropriate graphs.
b. "A significant negative...": leave descriptive. As it stands, the legend may be read in the results and discussion section. Would suggest changing to "Association between ALBR and SEAG in pleural effusion". As noted previously, leave out any mention of causation given the limited value of Pearson's rho. Also, the r value, apart from it being off by a factor of 0.1, is a duplication of what appears in the graph.

7. Table 1:
a. Use medians and interquartile ranges. Better yet, present a boxplot.

8. Figure 2:
a. The legends overlap. I suggest re-drawing the figure.
b. Include the line of identity to allow the eye to focus on a "baseline" instead of white space.
c. Units of measurement are missing for SEAG.

9. Copyediting:
a. Put references in BioMed Central format.
b. Check capitalisation and grammar.
c. Heading levels should be made more distinctive.
d. Abbreviations should be defined on first use.

10. Conflicts of interest:
a. No statement included.

**Competing interests:**

No known competing interests as it relates to this paper. However, I am an employee of CSL Ltd, a pharmaceutical company.