

Reviewer 2 v.1

Comments to the Author

In this metanalysis, Li et al. pooled data from 10 available prospective cohort studies incorporating 3,723 patients with ARDS. They found that higher circulating Ang-2 (which is a molecular mediator of ARDS in animal studies) is associated with higher mortality in patients with ARDS. This is the first systematic review and meta-analysis exploring the prognostic value of Ang-2 in ARDS patients. Although the topic is of interest to the broad readership of the Journal, there are several major questions that need to be addressed:

Please check primary data! I just went through some of the (less familiar) studies and found different ORs than shown in Figure 1. For example, the study by Susan Margulies (first author is Yehya N), the unadjusted OR for mortality in the cohort was 1.12 (CI 95% 1.03. to 1.22), but in Figure 2 this association with mortality appears to be non-significant?! Further, the study by Matthay (first author is Calfee CS), the OR for mortality at 90 days for every 1-log increase in Ang-2 was 1.53 (95% confidence interval [CI] 1.27–1.83; $p < .001$). Again, in Figure 2 it appears non-significant. Please comment, amend.

Please check references – e.g. ref #13 (Calfee C et al. – see above) is cited as a proof for -and two sentences later against (!?) - an association between Ang-2 and mortality in the introduction. In the results and discussion section, #13 is then accused of not showing mortality data at all – which is not true (1.53 (95% confidence interval [CI] 1.27–1.83; $p < .001$).

Figure legends are quite short. For example, what “(highest versus lowest category)” in the legends #2 mean? The ORs display continuous Ang-2 increases (usually 1ng/ml steps), correct? Or do the authors want to show low vs high quartiles (but this information is not available in most of the original papers)? Please amend.

Only few readers are familiar with funnel plots. Please explain Figure 3 and 4 in more detail or move them to the supp data.

Table 1: please indicate the ARDS/ALI definitions used (and percentages of ARDS/ALI respectively).

Studies included in the final analysis should be clearly labeled by citing the first author’s name – not by the group leader, the senior author or the Journal’s abbreviation. Please revise. Please also indicate the reference numbers for example in Table 1.