Reviewer’s report

Title: Validation of the Pneumocystis pneumonia score in haematology patients with acute respiratory failure

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Reviewer's report:

Thank you for the opportunity to peer review. Indeed, identifying patients most (and least) at risk of PJP is an important goal as it can help reduce health care utilization, costs, and morbidity. In this manuscript the authors attempt to validate a previously derived clinical prediction rule (PCP Score) in their cohort of 140 hematology patients who were admitted to intensive care in South Korea with acute respiratory failure. While the overall cohort size was reasonable at 140, there were only 13 patients with PJP in this retrospective cohort. It should be stated that this meets the authors' prespecified power criteria (and post-hoc calculated power). Unfortunately, they are unable to validate the clinical score in their population. The explore why this may be (and this can be further revised).

Notably, one limitation is that they rely on pathological stains only and not fluorescent antibody or PCR which could be more sensitive. I wonder if the authors could easily add patients who had "presumptive PJP" - e.g. people who were treated as PJP anyways despite having negative BAL results. Adding those patients may find that the score works better. It isn't essential to do this, but I think it would really add punch to the story here if the score didn't even predict those with "presumptive disease". Likewise, if B-d-glucan or radiology (CT) findings could salvage the score this would represent not only a validation paper but also an extension paper and would have greater scientific value. That said, external validation is important for any clinical prediction and the authors are commended for actually doing it!

There are some grammatical points which will need copy-editing but which I have, for the most part, not touched.

Specific comments follow:

Background:
Line 23 - indolent vs. insidious?" More frequently" present with abrupt onset…
Line 28 - Rephrase? Delays in anti-PCP treatment are associated with poor outcomes
Line 30 - Why would it be extremely challenging? Because of the need for invasive sampling? Because you risk intubation with bronchoscopy? Because you can't perform transbronchial biopsy on bronchoscopy safely with positive pressure ventilation?

I might make it even MORE explicit why we care. We want to avoid undertreating PJP but we also don't want to subject 100+ patients who don't have PJP to potentially toxic doses of TMP-SMX empirically (risk of AKI, K+, other adverse drug reaction, delay in getting real diagnosis).

Methods:
Line 33 - "those who received BAL" – even if they didn't have ARF? Or weren't in the ICU? What is the difference between this population and all ARF?
Line 35 - what do you mean PJP "smear"? Do you do PJP PCR? Do you do direct fluorescent antibody testing? Will you include cases which were PJP smear negative but got treated as PJP anyways (as possible or presumptive cases?)
Line 50+ – can you add to the summary how many patients they looked at total and with PJP and how PJP was confirmed in Azoulay? Will be important to make sure they are using similar microbiological methods to you.
Page 7 - line 4 - you mean in the derivation study?

Results:
Page 9 - Line 32 - "in our haematology patients"
Line 55 - please rephrase "no significant meaning"

Discussion:
I think that you can move some of the discussion of Azoulay's work to the background and methods sections of your paper and then spend more of the discussion focusing on your results and why they don't validate Azoulay's prediction rule. Some discussion on the limitations of your diagnostic testing and what could have been gained with other methods? Some specific comparison to the diagnostic methods used by Azoulay is important.
What about beta-d-glucan? What about combining the score with B-D-G and radiologic findings?
Is there anything you can salvage from the Azoulay score in your population if you add some of these things? Or is it completely hopeless?
Page 12 line 21 - this is why you may want to look at a sensitivity analysis for "presumptive PJP" - people who ended up being treated for PJP despite negative BAL results.

Table 1 - Cumulative dose of steroid over what period? Over the duration?
Table 2 - Absolute lymphocyte count would be nice to include.
Table 4 - (and methods) was there a reasonable "rule out" score even if you sacrifice specificity? Or was it completely useless in your population? For example, is there a post-test probability below 5% at any of these score thresholds? Is this worth you adding to the manuscript? Avoiding unnecessary empiric TMP-SMX in even 15-20% of the patients could still be helpful.
Can you add the # and % of patients who would have had these scores to give context of how common they would be?
Table 5 - I get different p-value for no prophylaxis. Is this because you use fisher's method here? If so, perhaps indicate in the legend which p-values are from chi-sq vs. which fisher.

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Yes

Are the methods sufficiently described to allow the study to be repeated?

Yes

Is the use of statistics and treatment of uncertainties appropriate?

Yes

Is the presentation of the work clear?

Yes

Are the images in this manuscript (including electrophoretic gels and blots) free from apparent manipulation?

Yes