Reviewer's report

Title: Retrospective observational study of diagnostic accuracy of the Xpert(R) MTB/RIF assay on fiberoptic bronchoscopy sampling, for early diagnosis of smear-negative or sputum-scarce patients with suspected tuberculosis

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Reviewer: Cedric Gunaratnam

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Submitted manuscript

Retrospective observational study of diagnostic accuracy of the Xpert® MTB/RIF assay on fiberoptic bronchoscopy sampling, for early diagnosis of smear-negative or sputum-scarce patients with suspected tuberculosis

Is the question posed original, important and well defined?

The question posed in the study is a very important clinical question, and the results can change the way we practice clinically. The question itself isn’t novel, and as the authors themselves have alluded to, has been preceded by two similar studies/publications. However, this study is done in a country with a low TB burden (which differs from the two previous studies) which makes it novel and very relevant to anyone practicing in such countries.

Is the data sound and well controlled?

The data is sound. There isn’t a control group in the study. In the ideal world the study data would be more robust if there was a control group of individuals with no lung disease to control for false negatives and false positives of the assay being studied. However, individuals with normal lungs do not undergo bronchoscopy, and therefore in the real world it isn’t possible to have such a control group.

Is the interpretation (discussion and conclusion) well balanced and supported by the data?

The discussion and conclusion are balanced and supported both by the data and also by the two previous studies mentioned.

Are the methods appropriate and well described, and are sufficient details provided to allow others to evaluate and/or replicate the work?

This is a retrospective single centre study. The centre is a regional TB diagnosis, treatment and reference centre. They adopted the assay four years ago and this study looks retrospectively over their patient cohort for this time period. It would be interesting to know what overall numbers of patients they had who were diagnosed with TB (by all methods) over this time period, given that final number of patients diagnosed with TB in the study cohort (sputum smear negative, or sputum scarce) was only 30. The methods are described in an easy to follow
What are the strengths and weaknesses of the methods?

The sample size for a real life clinical study is reasonable (162 patients). The authors highlight 3 study limitations. I do not feel that any of these limitations are significant.

Firstly the authors pointed out that their study is retrospective. I do not think that this is a limitation given the clinical question being posed. Secondly the authors pointed out that they are a single centre study. Both two previous studies from South Korea and South Africa respectively, were also single centre studies.

Lastly the authors point out that they didn’t distinguish between BA and BAL samples tested. I personally don’t believe there is sufficient evidence to date that would make either sample more or less suitable for microbiological testing. There is arguably a difference between BA and BAL for immunologic/ cytokine testing, but I don’t believe this applies to microbiologic testing.

I don’t feel any of the limitations pointed out by the authors are significant limitations. These should not deter from the discussion and conclusions of the study which are very clear.

I had initially considered the number finally diagnosis with TB (n=30) to be fairly low. However, in retrospect I think this is would be clinically intuitive given that the cohort of 175 patients being looked at could be considered difficult diagnosis (given the negative sputum to start with and others being sputum scarce, in a population with a low incidence of TB to start with).

Can the writing, organization, tables and figures be improved?
The writing and organization is systematic and clear. Tables are well laid out without clutter of information.

When revisions are requested.
Suggest accept as is.

Are there any ethical or competing interests issues you would like to raise?
The authors have complied with local ethical guidelines and laws and don’t have any conflicts of interest.

Are the included additional files (supplementary materials) appropriate?
Yes

Summary
I think this is a useful study that isn’t overambitious and seeks to answer an important clinical question. The study itself isn’t novel but the importance is that it is done in a country with a low TB burden (in contrast to the two previous published studies done in). The publication of this study will change my clinical practice. I suggest the manuscript is accepted as it is.
I have two minor suggestions for the authors to consider. One of the benefits of this assay is that it does not pick up false positives for Non-tuberculous mycobacteria compared to smear testing (SM). Is it worth highlighting this? Secondly I wonder if the authors would formally convey their opinion (based of their study) as to whether the Xpert MTB/RIF assay should replace or compliment smear testing (SM) on FOB BA/BAL?

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**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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