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### Reviewer A:

Comment 1: They should stress in their discussion that the treatment of infection is antibiotics and not surgery. Hence doing a MIS operation should be preferred to one that is more invasive.

Response 1: We agree that emphasis should be placed on the point that surgery is only a viable option for refractory cases. We added a paragraph to the discussion highlighting the importance of antibiotics as first line therapy for IS. Change in text: lines 149-158

Comment 2: A comparison between MIS and CT guided biopsy should also be mentioned. The former has a higher chance to relive pain and gets more tissue for diagnosis.

Response 2: for sake of completeness we agree that CT guided biopsy deserves mention for its role in helping to identify causal organisms. A paragraph was added to the discussion.

Change in text: Lines 139-148

### Reviewer B:

Comment 1: This study is not without merit, but several large important studies on surgically treated spondylodiscitis have been left out. It is not easy to conduct a feasible meta analysis using only case series with maximum of 60 patients-this might work for some rare disease entities, but there is a trunk of literature on spondylodiscitis which can be used for the review and analysis.

Response 1: We did go back and preform the literature search again for any additional articles that would meet inclusion criteria for the paper. Further, since receiving your review we extended our search for any new papers published through June of 2021. From this we believe that we have located all papers that are relevant and meet inclusion criteria to comment on pre and post-operative ESR/CRP/VAS. The study that you suggested specifically with first author Pola does not differentiate the outcomes between 3 groups. The 3 groups contain within them patients that were treated with both an open and MIS approach. For this reason we are not able to include it as the data for patients that underwent an MIS procedure cannot be separated from patient that underwent an open procedure. We agree that a larger sample size is preferable in most studies, however, after going through the literature search process again all relevant articles have been included. Further we believe that the current sample size is large enough to hold merit with its findings.

#### Change in text: Lines 51-57 (explanation of expanded search)

Comment 2: Several other important parameters should have been taken into analysis duration of hospital stay, neurological outcome, presence or absence of empyema (which leads to decision to perform open surgery instead of MIS); revision surgeries; concomitant infections if any. One important source of bias in this context is the fact that the patients with sepsis, empyema and neurological deficits are more likely to undergo open surgery than MIS; this was not discussed.

Response 2: We agree that it would be beneficial to specify which patients could benefit most from an MIS vs Open approach. We specified in the discussion situations where MIS techniques can provide the most benefit. In regards to including duration of hospital stay/neurologic outcomes/empyema in the analysis we are not able to due to too few of the included papers having that data available. The sample size for each of these factors would not be large enough for meaningful analysis and thus we chose not to include them.

Change in text: Lines 131-140

## Reviewer C:

Comment 1: 1. I do think the discussion is a bit short and more information is required. Response 1: We thought it would be beneficial to touch on primary management of IS with antibiotic therapy and the role for CT guided biopsy for identify causal organisms in the discussion. Additionally clarification was given for particular modifying factors that can help determine which patients would be best suited for a minimally invasive approach.

Change in text: Discussion section lines 139-158

Comment 2: The reasons to proceed with a MIS technique in an established spinal infection should be identified (related to the patient, comorbidities, poor surgical candidate etc)

Response 2: We agree that the benefits for MIS could be more clearly explained. More specifically we thought it was necessary to be more specific on which IS patient would benefit most from a minimally invasive technique. We clarified this in the discussion. Change in text: Lines 129-138

Comment 3/4: The outcome after the surgery should be presented(early discharge if present in MIS group, postoperative complications etc). The above can be part of the table of the results.

Response 3/4: The majority of papers included in this study did not provide data concerning length of hospital stay. Regarding post-operative complications multiple papers did not discuss post-op complications leaving the reader unsure if there were none or they weren't talked about. For these reasons we did not include the parameters in our analysis

Change in text: NA

Comment 5: The fact that the level of evidence is low should be emphasized better and perhaps better underlined in the abstract.

Response 5: It was clarified in the discussion that 13 of 14 of the included studies were level 4 evidence. The method that we used to ensure a low risk for bias for each paper was also explained.

Change in text: Lines 164-166