

Article information: <https://dx.doi.org/10.21037/aoj-22-45>

Reviewer comments

Dear authors, thank you for the opportunity to read and review your manuscript. This is indeed an interesting topic that needs attention in scientific literature. There are several publications describing results from MoM hip arthroplasty revision surgery, but the detailed information of the surgical revision procedure is of value. While the retrospective design of this study limits the power of the results, the authors acknowledge this limitation. However, more concise and rigorous reporting on study procedures, variables and LTFU is needed before publication can be considered. Please refer to the remarks below which need to be addressed before publication is an option.

Abstract session

1. In line 30-31 is written that the purpose of the study is to analyze revision outcome of revisions due to pseudotumor. This is confusing with line 38 that 3 patients underwent revision surgery due to sepsis. In the main text it becomes clear that this sepsis is a perioperative finding. This should be better explained or described in the methods section of the abstract.

**R: Results revised: more than the methods, the results were unclear and the abstract was confusing.
Line 38: Three patients (14.2%) with pseudotumor underwent a resection arthroplasty due to infection (perioperative finding) and could not be reimplanted due to septic relapses.**

2. Line 31-32: please add an indication of a timeframe to the purpose of this study to make it more specific (i.e. mid term outcomes or something similar)

**R: Provided
Line 31: 3-year outcomes of MOM arthroplasty revisions**

3. Line: 33-34: “A consecutive, retrospective series of 21 patients (8 males / 13 females) with pseudotumor due 34 to MOM hip arthroplasty and surgically treated at a single tertiary center was selected.” This sentence should read “A consecutive, retrospective series of 21 patients (8 males / 13 females) with pseudotumor due 34 to MOM hip arthroplasty and surgically treated at a single tertiary center.”

**R: rewritten
Line 33: Consecutive, retrospective series of 21 patients (8 males / 13 females) with pseudotumor due to MOM hip arthroplasty was surgically treated at a single tertiary center.**

4. Line 41: A clinical improvement at a mean post-revision follow-up 3.3 ± 2.2 . To me it is clear that ± 2.2 is the standard deviation but this is not explained in the text.

**R: rewritten:
Line 41: A clinical improvement at a mean post-revision follow-up 3.3 years (standard deviation: ± 2.2) was observed, from 50.3 (standard deviation: ± 4.6) to 88.3 (standard deviation: ± 9.2) HHS points ($p < 0.001$).**

5. Line 43: now the three cases with infections are presented as complications. Are these infections which became apparent after the revision surgery

R These are three revisions which had an infection (not the three infections mentioned above)

Line 42: Among revisions, there were 5 complications (23.8%): one dislocation, one psoas impingement and 3 infections (14.2%).

6. Line 45-46: These lines state: “After MOM arthroplasty revisions, patients with Cr and Co blood ions beyond the threshold decreased from 61.5% to 0%.” However, the number of metal ion concentration samples is quite limited with a large LTFU. Presenting this data in this manner with percentages only is too optimistic, this should be rephrased with more detailed context in place.

R Rewritten

Line 45: At the final follow-up, Cr and Co blood ions beyond the threshold decreased from 85.7% cases to 0% in the seven patients that could be evaluated.

7. Line 47-48 states “A complete eradication of a pseudotumor should be performed every possible time: revisions with non-MOM couplings seems effective, even with a one-stage strategy. However, complications are frequent (23%), mostly sepsis and dislocations. Recurrences are not rare (14%)”. Although I agree complete eradication is the goal, this conclusion can not be derived in such strong words from a retrospective study without a control group. This should be rephrased. Furthermore there was only one dislocation in this series, not multiple. And although recurrences are not rare, re-revisions for recurrence were not necessary, this is worth mentioning.

R: rewritten

Line 46: The one-stage strategy of radical excision and revision with non-MOM couplings in pseudotumors due to MOM hip arthroplasty achieved good 3 year outcomes. However, complications were frequent (23%). Recurrences were not rare (14%), but did not require implant re-revision

8. In the key findings box: “revision hips may carry a high risk of complications and the optimal surgical strategy is still unknown”. In my opinion the word “may” is obsolete.

R: removed

Line 64: Pseudotumors after MOM hip arthroplasty are challenging: revision hips carry a high risk of complications and the optimal surgical strategy is still unknown.

9. Line 64-70 (1.2 rationale and knowledge gap): Not only is the surgical strategy debated, the threshold for revision surgery is also worth mentioning, with a mix of relevant factors (symptoms, metal ion levels, soft tissue damage) coming into play. Please add this debate to this section.

R: added

Line 81: There are no unanimous indications for failed MOM hip arthroplasty revisions: the decision to revise a failed implants is usually made considering the metal ion level (whose

thresholds are still debated), symptoms (which can be very subtle) and soft tissue damages (1,2,5)..

10. Line 71-76 (objective): please be more specific in what you are trying to define, especially provide context on the time frame (short term, long term etc)

R: added

Line 91: We aimed to define: 1) the clinical and radiographic outcomes; 2) complications and re-revision rates; 3) metal ion concentrations in the serum, at a mean follow-up of 3 years.

11. Line 86. I understand that you only include one stage revisions. But it is unclear if there were cases indicated for two-stage revision but that were not selected for this analysis? As mentioned the STROBE guideline was followed, it would be useful to include a detailed study flow diagram in the manuscript, including an overview of excluded MoM revisions (if any) with reasons.

R: added

Table 1: flowchart of the study

12. Line 107. Pseudotumors were stratified according to the Anderson grading system. This does not come back anywhere else in the manuscript other than line 186. What classifications were the pseudotumors which reoccurred after the revision surgery for example? And were the cases with incomplete eradication only C3 type pseudotumors?

R: added

Line 210-211: We reported 3 (14.2%) recurrences of pseudotumor: all the patients complained of local symptomatology, without evidence of metal ion level beyond the threshold. One pseudotumor recurrence was due to an incomplete excision of the mass due to the large intrapelvic extension (Anderson grading system: C3). The other two recurrences were observed in explanted patients (Anderson grading system: C2). One recurrence was surgically treated, one treated with selective arterial embolization and one followed with close follow up.

13. Line 119: different surgical approaches were used. On what decision or preference was the surgical approach chosen?

R: added

Line 141: . The approach was chosen according to the surgeon experience and the pseudotumor location.

14. Line 156 and further on: the follow up adherence is unclear. In line 87 an annual follow up is described (- adherence to post-revision clinical and radiological follow-ups (annual) but a Strobe flow chart should provide more detail on this. Also it is striking (line 196) that only a limited number of metal ion samples were collected preoperatively (13 samples) and 1 year (only 7) after revision surgery. Was this not a standard procedure? Can the authors explain this in more detail? In line 203 only percentages are presented to describe improvement in metal ion concentrations but this is misleading since only a minor number of patients has been analyzed for change in metal ion concentrations. This is an issue that needs correction throughout the manuscript. Another question on this topic: were the 7 postop metal ion samples all from patients who were also measured preoperatively. Or are these (in part) not overlapping?

R: for a technical problem, some data were lost. The 3.3 paragraph was revised because percentages

were erroneous

Line 218: Samples of 13 patients preoperatively (61.9%) and 7 (33.3%) correspondent samples 1 year after surgery were available. No patient has been exposed to any other known metal ion source. The mean post-revision Co ion value in serum was $2.7 \pm 3.1 \mu\text{g} / \text{l}$ (range 0.2- 6.7 $\mu\text{g} / \text{l}$), with a pre-revision Co ion level of $18.8 \pm 27.2 \mu\text{g} / \text{l}$ (range 0.1–102). In the 7 cases that could be evaluated, patients with Co ions in serum over the threshold decreased from 85.7% to 0%.

The level of Cr ions in serum was $14.3 \pm 27 \mu\text{g} / \text{l}$ (range 0.6-103 $\mu\text{g} / \text{l}$) in the pre-revision sampling and reached an average postoperative value of $2.8 \pm 2.8 \mu\text{g} / \text{l}$ (range 0.5-6.4 $\mu\text{g} / \text{l}$). In the 7 cases that could be evaluated, patients with Cr ions in serum over the threshold decreased from 85.7% to 0%.

15. Line 213 and further on: the quite considerable LTFU on several items should be reported in the limitations section

Added

Line 239: The study provided a sound surgical revision strategy for a sizeable case series of large pseudotumors in failed MOM arthroplasty. However, the retrospective design, the lack of control group, the mean 3-year follow-up after revision were the main limitations of the study. Only a small part of the cohort underwent metal ion level analysis. Moreover, the presence of many confounding factors (demographics and intraoperative) was another notable drawback: the unique features of patients, implants and pseudotumors, depicting different specific revision scenarios, preclude standard surgical treatment algorithm in adverse local tissue reactions and require tailored revision surgeries.

16. Line 223: there is mentioning that in this case series predicting onset of pseudotumor formation is not possible. This was not the aim of this study or part of the presented analysis. This sentence should be rephrased or removed.

Removed

17. Line 244: again on the infections: are these infections complications of the revisions surgery (meaning not present at time of the revision surgery but induced by the revision surgery) or not? This is again not clear.

These are complication of the revision, not the three aforementioned infections.

Line 204: There were 3 (14.3%) wound infections in the first month after revision

18. Line 251, 3 cases of pseudotumor recurrence. What grade (C1/2/3?) with symptoms and high metal ion levels?

R: added

Line 210-211: We reported 3 (14.2%) recurrences of pseudotumor: all the patients complained of local symptomatology, without evidence of metal ion level beyond the threshold. One pseudotumor recurrence was due to an incomplete excision of the mass due to the large intrapelvic extension (Anderson grading system: C3). The other two recurrences were observed in explanted patients (Anderson grading system: C2). One recurrence was surgically treated, one treated with selective arterial embolization and one followed with close follow up.

19. Line 272: please add that revision surgery studies with a control group are not presented in

literature and also unlikely to be conducted due to ethical considerations. In general, it is understandable that case series such as the present study are probably the highest achievable study design for this matter, but that also results in studies which need to be careful in stating firm conclusions. This should be reflected in the wording in this manuscript in a more concise manner.

Added in 4.5

Line 301 Any definitive conclusion cannot be drawn due to the many limits of the current study (the retrospective design, the modest cohort, the lack of control group), however the technical and ethical difficulties in the conduction of comparative trails hinder obtaining higher quality findings.