Author’s response to reviews

Title: Secondary purulent infections of the elbow joint: a retrospective, single-center study.

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Author’s response to reviews:

Reviewer #1:

Remark 1.:
Would you be able to comment on why you feel so many surgeries were required with these patients who developed septic arthritis of the elbow (mean was around 5, but some had up to 25 surgeries)

Response:
Thank you for this remark. Patients suffering a chronic infection were revised multiple times to treat the infection. The patient that was operated 25 times was ultimately treated with a resection arthroplasty and a chronic fistula. We added a sentence regarding this issue.

Changes:

Line 166: “Three patients needed &gt;10 procedures, since the infection recurred after the initial treatment, in one patient this led to a resection arthroplasty and chronic fistula with 25 procedures in total.” was added to the manuscript.
Remark 2.: 

For your culture negative joint infections, how long were cultures held before being confirmed negative?

Response:

Thank you for this remark. All cultures were held for 14 days before being confirmed negative. We added this to the manuscript.

Changes:

Line 120: “All microbial cultures are held for 14 days including stains for fungus and acid fast bacteria before being confirmed negative.” was added to the manuscript.

Remark 3.: 

Also, were additional stains/cx for fungus and AFB done with your culture negative isolates?

Response:

Thank you for this remark. Additional cultures for fungus are routinely done but remained negative in all cases. However, we routinely tested for tuberculosis in the microbial cultures. We added this for clarification to the manuscript.

Changes:

Line 120: “All microbial cultures are held for 14 days including stains for fungus and acid fast bacteria before being confirmed negative.” was added to the manuscript.

Remark 4.: 

I may have missed this, but it would be worth seeing what the average joint aspirate cell count and differential numbers were with your cohort of patients, to see if there truly is variability or if some pattern was noted.

Response:

Thank you for this remark. Unfortunately, we did not test the WBC and differential numbers from the joint aspirate throughout our patients, especially in the beginning of the investigated period. We therefore did not add this information to the manuscript. Kindly indicate in case you nonetheless wish us to include this incomplete data set.
Changes:

No changes.

Remark 5.:
Make sure all infectious organism names are italicized.

Response:
Thank you for this remark. All infectious organisms are italicized.

Changes:
No additions.

Remark 6.:
Line 39- Place 'seven patients were female, 23 were male' in Results section--this statement should not be in the methods section

Response:
Thank you for this remark. The statement was moved to the results section.

Changes:
Line 39: “Seven patients (23.3 %) were female, 23 (76.7 %) male.” was moved to the results section of the abstract in Line 41.

Remark 7.:
Line 48- Please add a comma after the word 'courses'

Response:
Thank you for this remark. The change was made accordingly.

Changes:
Line 49: A comma was added behind “courses”.

Remark 8.:
Line 49- Add the word 'and' after the word 'treatment', and change the word 'as' to 'was'
Response:
Thank you for this remark. The changes were made accordingly.

Changes:
Line 50: “and” was added, “as” was changed to “was”.

Remark 9.:
Line 62- Add the word ''The' before 'Most important...'
Response:
Thank you for this remark. The changes were made accordingly.

Changes:
Line 63: “Most important” was changed to “The most important”.

Remark 10.:
Line 66- Change 'could be' to 'has been'
Response:
Thank you for this remark. The changes were made accordingly.

Changes:
Line 67: “could be” was changed to “has been”.

Remark 11.:
Line 74- Eliminate the word 'especially'

Response:

Thank you for this remark. The change was made accordingly.

Changes:

Line 76: “Especially” was removed from the sentence.

Remark 12.:  
Line 75- Remove comma, and change the word 'part' to 'proportion'

Response:

Thank you for this remark. The changes were made accordingly.

Changes:

Line 77: The comma was removed, “part” was changed to “proportion”.

Remark 13.:  
Line 78-Change 'out' to 'our'

Response:

Thank you for this remark. The change was made accordingly.

Changes:

Line 80: “out” was changed to “our”.

Remark 14.:  
Line 82- Phrase 'without turbid fluid'--do you mean patients who did not have purulence of the joint were excluded, or simply had no turbidity of their joint fluid? I imagine you meant patients with no active purulence of the joint were excluded, but wasn't sure--would be precise with what word is used
Response:

Thank you for this remark. Patients without active purulence were excluded. We changed the wording accordingly.

Changes:

Line 86: “turbid fluid” was changed to “active purulence”.

Remark 15:

Line 111- Clarify Cefazolin (3 x 2g)--does this mean 2g three times a day? Every 8 hours? 3 doses?

Response:

Thank you for this remark. This means 2g Cefazolin every 8 hours. We changed this for clarification in the manuscript.

Changes:

Line 116: “i.e. Cefazolin 3 x 2g” was changed to “for example. Cefazolin 2g every 8 hours”

Remark 16:

Line 117- Change the word 'destructed' to either 'damaged' or 'destroyed'

Response:

Thank you for this remark. We changed the wording accordingly.

Changes:

Line 124: “destructed” was changed to “destroyed”.

Remark 17:

Line 118- Change the word 'infect' to infected joint

Response:
Thank you for this remark. We changed the wording accordingly.

Changes:

Line 125: “infect” was changed to “infected joint”.

Remark 18.:
Line 120- Remove the word ‘an’
Response: Thank you for this remark. The change was made accordingly.

Changes:

Line 127: “an” was removed from the manuscript.

Remark 19.:
Line 131- Change ‘made an’ to ‘resulted in’
Response: Thank you for this remark. We changed the wording accordingly

Changes:

Line 142 “made an” was changed to “resulted in”.

Remark 20.:
Line 168- Change sentence to "...a tennis elbow or chronic bursitis, for example."
Response: Thank you for this remark. We changed the wording accordingly

Changes:
Line 185: “for example a tennis elbow […]” was changed to “[…], for example”.

Remark 21.:
Line 169- Change 'of' to 'by'
Response:
Thank you for this remark. We changed the wording accordingly

Changes:
Line 186: “of” was changed to “by”.

Remark 22.:
Line 171- Remove the word 'particularly'
Response:
Thank you for this remark. However, the study by Mehta et al. is the only study specifically reporting on septic arthritis of the elbow joint, although other studies reporting on septic arthritis in general include results of septic arthritis of the elbow. We therefore changed “particularly” to “specifically”.

Changes:
Line 188: “particularly” was changed to “specifically”.

Remark 23.:
Line 181- Change gram to Gram
Response:
Thank you for this remark. The change was made accordingly.

Changes:
Line 199: “gram” was changed to “Gram”.
Reviewer #2:

Remark 1.:

The first question is the definition of the elbow: which interventions have you taken into account? (elbow prosthesis, supra-condyle fractures, olecranon fracture...)

Response:

Thank you for this remark. We included all septic arthritis of the elbow joint regardless of the prior therapy. This included intra- and supracondylar fractures as well as olecranon fractures that resulted in an infected elbow joint. We did however not include periprosthetic infections following total elbow arthroplasty or radial head arthroplasty.

Changes:

Line 55: “All patients with a trauma to the elbow or prior elective operative procedures to the elbow joint except total elbow arthroplasty or radial head arthroplasty were included.” was added to the manuscript.

Remark 2.:

There is a major lack in your publication: the analysis of the implanted material. Indeed, there is a difference between an infection after a double humeral plate for supra-condylar joint fracture, screwing of a diacondylar fracture, broaching.....

All this is extremely important because we know that the material generates the development of a biofilm that precludes the action of antibiotics. I did not find in the results or in the method any paragraph concerning the delay of occurrence of infections since the first intervention. An early infection, with a simple wash, is not the same as a later infection.

Similarly, we know that fractures still consolidate in a large number of cases, despite a treated infection. There are sometimes several interventions for successive washings before a "final" intervention, aimed at removing the material when the fracture is solid and to finally cure the infection.

It is therefore necessary to completely review the description of patients and integrate the notion of delays +/- consolidation or pseudoarthrosis.

Response:

Thank you for this remark. We agree that the timing (early or late) of the infection and the type of the used osteosynthetic material is important for the infected elbow joint. We therefore added a more detailed description regarding the timing of the injury in relation to the initial injury.
(early or late) and whether a removal of the osteosynthetic material was performed. However, since this is a retrospective case study without an adequate comparison group for the respective injuries, we see no benefit in the detailed analysis of the osteosynthetic material used. Moreover, a detailed description of the delays in consolidation due to the infection is also not possible due to the retrospective design of the study.

Changes:

Line 133: “Of the patients with a history of trauma, four had an infected non-union. Ten patients suffered an early infection after a trauma or fracture of their elbow. In these cases, an early removal of the osteosynthesis was performed in five cases. Eight patients suffered an infection &gt;4 weeks after their initial surgery. In five patients, besides debridement and lavage of the joint, osteosynthetic material was removed.” was added to the manuscript.

Remark 3.: in methods, there is a contradiction: line 83/84: "Patients suffering from immunodeficiency (acquired or due to an underlying disease such as rheumatoid arthritis or HIV) were excluded" whereas line 112 and 113 states: "In patients with an immunodeficiency, we consider a broader antibiotic treatment aiming against methicillin-resistant Staphylococcus aureus (MRSA) or gram-negative bacteria".

Did you or did you not exclude immuno-compromised patients?
if so, for what reason?
if so, can you give us a flow chart?

Response:

Thank you for this remark. The statement in line 113 is misleading and was therefore revised. The statement was meant as a more general treatment algorithm for these patients. For the presented study, we excluded patients with immunodeficiency. Besides the presented collective, we generally consider a broader antibiotic treatment in cases with a larger risk for gram-negative bacteria or immunodeficiency.

Changes:

Line 115: “[…] generally […]” was added to the sentence.

Line 117: “In patients with an immunodeficiency” was changed to “In general, if patients show signs of an immunodeficiency, […]”
Remark 4.:

the analysis is not clear. It is not clear what the two subgroups "seropositive" and "seronegative" mean. Your Mann-Whitney test is also strange and has no clinical interest in my opinion; what is the point of knowing if the age is different according to the seropositive dans seronegative groups? Not to much in practice.

On the other hand, the number of interventions/ procedures (meaning the number of interventions before healing) IS THE parameter to be analyzed because it is the one that has a real clinical impact.

Response:

Thank you for this remark. For the clarification of the terms “seropositive” and “seronegative” we refer to our Methods-section. In our manuscript and throughout the literature, joint infections without microbial findings in bacterial cultures are termed “seronegative” whereas those with microbial findings in bacterial cultures are termed “seropositive” (Line 65). We find the comparison between these groups helpful, as this emphasizes that patients with a high clinical suspicion but without microbial finding should be treated like those with a microbial finding.

We used the Mann-Whitney-test to test for significant differences between ordinal scaled date. Differences were tested for the number of surgical procedures, age, outcome and laboratory parameters between the seropositive and seronegative group. We refer to our Results section (Line 124 and Figure 2). Please state if another statistical test for the comparison of these groups is seen as more appropriate.

Changes:

No changes

Remark 5.: practical questions: have you used the Masquelet technique?

Have you immobilized the patients? if so, with extended casts?

Response:

Thank you for this remark. In our practice, the Masquelet-technique on the upper extremity is only used in segmental defects of the diaphyseal bone if prior techniques (structural or non-structural allograft) have failed. However, only one infected non-union was treated using nonstructural grafting after debridement and temporary implantation of a spacer. Immobilization was tailored to each patient. Those without external fixation are generally immobilized with a long arm cast. We added this information to the manuscript.
Changes:

Line 114: “In patients without external fixation, immobilization is generally performed using a long arm cast.” was added to the manuscript.

Remark 6.: on the form, I don’t personally like « (ie ...) ». Because often when you used it, there were some informations that seemed to me necessary to detail.

Response:

Thank you for this remark. The wording was changed throughout the manuscript.

Changes:

Line 99: “i.e. pain, swelling […]” was changed to “such as pain, swelling […]”.

Line 116: “i.e. Cefazolin” was changed to “for example Cefazolin”

Remark 7.: You have to use a multiple linear model for example like this:

\[
\text{number of procedures} = \text{coefficient}_1 \times \text{age} + \text{coeff}_2 \times \text{sex} + \text{coeff}_3 \times \text{immunosuppression} + \\
\text{coeff}_4 \times \text{time of infection} + \text{coeff}_5 \times \text{type of material used} + \text{coeff}_6 \times \text{type of initial pathology} + \\
\text{coeff}_7 \times \text{type of germs found} + \text{coeff}_9 \times \text{seropositive or seronegative} + \ldots + \ldots
\]

Response:

Thank you for this remark. Due to the retrospective design, the small number of the cases and the heterogenous collective, we believe a multiple linear model will not lead to a relevant conclusion. The presented data is merely a series of purulent infected elbows and the description of the found clinical properties. Please indicate if the reviewers recommend to nevertheless perform a multiple linear model.

Changes:

No changes.