February 25, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2429-review.doc).

Title: Can periprosthetic hip joint infections be successfully managed by debridement and prosthesis retention? A literature review

Author: Konstantinos Anagnostakos, Cornelia Schmitt

Name of Journal: *World Journal of Orthopedics*

ESPS Manuscript NO: 7660

We have thoroughly read all comments made by the reviewers. The manuscript has been improved according to the suggestions of reviewers as followed (all revisions are underlined in the text):

Reviewer 1

- The article is well written. The analysis of the literature well-conducted , precise, but limited. The materials and methods are adequate in a retrospective study . The analysis of the data obtained is acceptable. I would have preferred that the authors enfatizzassero their personal results as opposed to those in the literature , instead of inserting them into the analytic discourse generally.

  In the invitation that we received from the World Journal of Orthopedics we were asked to provide a review article and not an original work. Therefore, we

did not include any personal experience which was then compared with literature data. Here, we did not change anything in the manuscript.

- The literature reviewed is definitely part since it is only 11 studies with a total of 292 cases. And only 52 cases of late infections are quite a few . In addition, the treatment procedures are certainly very different from each other , so it is difficult to draw more conclusions precise and safe to drive in a unique treatment of infection in hip replacements . Moreover, even the authors write: " Although single studies Demonstrated high success rate exceeding 90% , the relative small number of patients treated as well as the low level of evidence does not allow for generalization of Conclusions . " . The authors also write : "Due to the relative small power of the included cases and inhomogenities in the treatment procedures and collectives Themselves it can not be stated Which antibiotic treatment is the optimal" and also " The current literature does not allow for generalization of conclusion with regard to the best treatment modality . " . But then comes to the conclusion that the work done by the authors has been absolutely useless if you can not give definite indications for treatment in case of infection of the hip , on the basis of the literature.

  We do not think that our work is useless only because definite indications cannot be stated based on the current literature data. On the contrary, we think it is important to emphasize that current literature data is insufficient and more future work is needed on this area in order to clarify such problems. Similar conclusions have been also made on the International Concensus Meeting on Periprosthetic Joint Infection, which took place last year in Philadelphia. Therefore, we did not change anything in the manuscript.

- In light of all these considerations , I therefore consider that the article can be published with modifications. That is expanding and looking for articles literature considered homogeneous . In addition , the authors should better highlight their type of treatment performed and their personal results.

  We have addressed to these points before (no changes made).

Reviewer 2

Thank you for giving me the opportunity to review the manuscript entitled "Can periprosthetic hip joint infections be successfully managed by debridement and prosthesis retention? A systematic literature review". Here are my comments.

- ABSTRACT I do believe that systematic review has to include search of at least two data bases. As only one base was searched here (PubMed), this cannot be a systematic review.

  We have removed the word "systematically" from the Abstract but also from the Title.

- Results: I find presented percentages (21%; 75%; 70.4%; 92.8 %; and 89.6%) confusing there. That requires additional explanation.

  After each percentage we have added "infection eradication rate" in order to clarify what the percentages state.

- KEY WORDS Why were the terms "irrigation" and "retention" left out from the key words list? The terms were used to search the PubMed base.

  We have added the term "irrigation" to the key words. The term "retention" already appears in "prosthesis retention".

- MATERIALS AND METHODS If the abbreviation is DAIR, wouldn't it be expected to have order "Debridement, Antibiotics, Irrigation, and Retention" instead of "Debridement, Irrigation, Antibiotics, and Retention"?

  This is correct. The abbreviation "DAIR" stands for "Debridement, Antibiotics, Irrigation, and Retention" instead of "Debridement, Irrigation, Antibiotics, and Retention". We have used the latter one because it is used more often in the literature. However, we have corrected it now to the correct order.

- As I am curious, could the author explain me why the studies with <10 patients were excluded from the review?

  The aim of our review was to evaluate how successfully periprosthetic hip joint infections can be managed by DAIR. In most literature reviews, regardless from the topic, case reports and small case series are not included except for those with exceptional results. This is the reason why such case series were not included into our work.

- DISCUSSION The first paragraph of the discussion has to present the main finding of the study. It was not the case here.

  We have added a new paragraph in the begin of the Discussion presenting the main findings of the study.

- Again, this review cannot be attributed as a systematic one. The authors have concluded that the present literature review shows that debridement, irrigation, antibiotic therapy, and prosthesis retention is an acceptable solution in the management of early and acute hematogenous periprosthetic hip joint infections. Where was the change of modular prosthesis components lost?!

  We have added the "change of modular prosthesis components" in the Conclusion paragraph.

Reviewer 3

Poorly written

No comments.

Reviewer 4

- Page 1, title:

  As above mentioned, we have removed the word "systematic" from the tile.

- Page 4, comment [na2]: Pubmed may not include even half of the world literature. Thus this is a limitation of this study.

  This is correct. We have commented on that in the Discussion, adding it as a possible cause for the identification of only 11 relevant studies.

- Page 4, comment [na3]: From what year?

  The literature search was made from the begin of PubMed until September 2013. We have added this information.

- Page 4, comment [na4]: Minimum follow-up included?

  Regarding articles about joint infections, it is common that a minimum follow-up of 12 months (in some journals 24 months) is required before acceptance of the manuscript for publication. Therefore, we did not include minimum follow-up as an exclusion/inclusion criterium.

- Page 4, comment [na5]: Full text or abstracts?

  Through our university library we have access to full texts of almost all medical studies.

- Page 5, comment [na6]: So no high level evidence?

  This is correct. The low level of evidence among the identified studies is commented in the Discussion.

- Page 5, comment [na7]: What was the time frame of late and early infection in these studies?

  This information has been added in Table 1.

- Page 5, comment [na8]: Microbiology spectrum?

Not all studies provide all data about the microbiology spectrum. Moreover, it is almost impossible to provide all available microbiological data from these studies in a Table which is easy to understand for the reader. Therefore, we did not provide these data.

- Page 6, comment [na9]: On the other hand more heterogeneous data may not allow for meaningful conclusion.

  This is correct. We have added this comment to the text.

- Page 7, comment [na10]: wound vac too.

  We have added this information to the text.

- Page 7, comment [na11]: But different indications for acute vs. late infection.

  We have specified this information in the text.

- Page 7, comment [na12]: Staph aureus.

  In their original work, Choi et al. reported "The only risk factor associated with failure of infection control at the latest follow-up was the S. aureus microorganism.". We have added this information to the text.

- Page 7, comment [na13]: However they concluded: Retention treatment can be considered an initial treatment option in selected cases of primary THA, with a single organism, non-S. aureus infection with 50% chance of infection control and no disadvantages in terms of additional procedure, hospital stay, and treatment duration.

  We have added this information to the text.

- Page 7, comment [na14]: MRSA, gram negative infection.

  We have added "MRSA" to the risk factors. Regarding gram-negative infections, available literature data is scarce and therefore we did not add this information to the text.

- Page 8, comment [na15]: Need to differentiate between late infection and acute hematogenous infection after years. Thus using a Tsukayama classification for comparison may be more helpful than the one used by authors: early, delayed, and late infections.

  We have added the definition of acute hematogenous infections to the text. However, we did not change anything in the text because we think it is important to define all kind infections since no classification system is widely established and the readers should know about it.

- Page 8, comment [na16]: The problem then becomes that the surgeon comits that he may have to go in again for removal of beads.

  We have added this information to the text.

- Page 9, comment [na17]: PI summarize the risk high factors for failure.

  We have added this information to the text.

- Page 15, Table 1: comment [na18]: PI specify the definition in each study.

  We have added this information to the text.

We hope our revisions are satisfactory so that our work can now be published in your journal.

With best regards from Germany

PD Dr. Konstantinos Anagnostakos