

Name of journal: World Journal of Orthopedics

Manuscript NO: 47801

Title: Advanced septic arthritis of the shoulder treated by a two-stage arthroplasty

Dear Prof. Bao-Gan Peng, Dr. Jin-Zhou Tang, Dr. Ruo-Yu Ma, and reviewers,

Thank you for the time spent on our manuscript and for your valuable comments.

We have addressed all the comments below and hope that the modifications made to the manuscript improved its quality and made it suitable for publication in World Journal of Orthopedics.

Sincerely,

The authors

Reviewer's code: 01220036

SPECIFIC COMMENTS TO AUTHORS

Good approach!

Author response : Thank you!

Reviewer's code: 04424227

SPECIFIC COMMENTS TO AUTHORS

The manuscript by Goetti P et al. indicates that Short interval two-stage approach for septic shoulder arthritis is an effective treatment option. Overall, the results are interesting but there is still room for improvements. The characteristics of arthritis should be further explained. Please refer to relevant literatures. e.g. Journal of Agricultural and Food Chemistry 2018, 66, 6073–6082; Food & fuction 2018, 9, 2070–2079; Journal of Agricultural and Food Chemistry 2019, 67(10):2856–2864.

Author reponse : First, thank you for the kind words regarding our submission.

Thank you for this comment. The manuscript focusing on septic arthritis, we subsequently modified the manuscript adding this relevant information in the text as follows:

Introduction, first paragraph

~~«Primary management consists of arthroscopic or open irrigation and debridement and is usually combined with local and systemic antibiotherapy to eradicate the infection»~~

«Primary management consists of arthroscopic or open irrigation and debridement and is usually combined with local and systemic antibiotherapy to eradicate the infection. Even after successful elimination of bacteria, cartilage and bone destruction is the consequence of prolonged inflammatory arthritis mediated by pro-inflammatory cytokines^[2-6]. »

And added the five following references

2 **Sultana S**, Dey R, Bishayi B. Dual neutralization of TNFR-2 and MMP-2 regulates the severity of *S. aureus* induced septic arthritis correlating alteration in the level of interferon gamma and interleukin-10 in terms of TNFR2 blocking. *Immunol Res* 2018; **66**: 97-119 [PMID: 29218573 DOI: 10.1007/s12026-017-8979-y]

3 **Farrow L**. A systematic review and meta-analysis regarding the use of corticosteroids in septic arthritis. *BMC Musculoskelet Disord* 2015; **5**; 16:241 [PMID: 26342736 DOI: 10.1186/s12891-015-0702-3]

4 **Zhai KF**, Duan H, Cui CY, Cao YY, Si JL, Yang HJ, Wang YC, Cao WG, Gao GZ, Wei ZJ. Liquiritin from *Glycyrrhiza uralensis* Attenuating Rheumatoid Arthritis via Reducing Inflammation, Suppressing Angiogenesis, and Inhibiting MAPK Signaling Pathway. *J Agric Food Chem* 2019; **67**: 2856-2864 [PMID: 30785275 DOI: 10.1021/acs.jafc.9b00185]

5 **Zhai KF**, Duan H, Chen Y, Khan GJ, Cao WG, Gao GZ, Shan LL, Wei ZJ. Apoptosis effects of imperatorin on synoviocytes in rheumatoid arthritis through mitochondrial/caspase-mediated pathways. *Food Funct* 2018; **9**: 2070-2079. [PMID: 29577119 DOI: 10.1039/c7fo01748k]

6 **Zhai KF**, Duan H, Khan GJ, Xu H, Han FK, Cao WG, Gao GZ, Shan LL, Wei ZJ. Salicin from *Alangium chinense* Ameliorates Rheumatoid Arthritis by Modulating the Nrf2-HO-1-ROS Pathways. *J Agric Food Chem* 2018; **66**: 6073-6082 [PMID: 29852739 DOI: 10.1021/acs.jafc.8b02241]

1. As requested we uploaded an mp3 audio file of the core tip.
2. Following your guidelines we modified figure 2 and a decomposable figure of all the figures, whose parts are all movable and editable, were also uploaded in a PowerPoint file.
3. We rearranged authors' affiliations adding the postcode as follows
«**Patrick Goetti, Nicolas Gallusser, Alexander Antoniadis, Diane Wernly, Frédéric Vauclair, Olivier Borens, Department** of orthopedic surgery and traumatology, Lausanne University Hospital and University of Lausanne, Lausanne **1010**, Switzerland »
4. We rearranged «Author contribution as follows » as follows:
«**Goetti P and Gallusser N** designed the study and wrote the manuscript;
Antoniadis A and Wernly D compiled the data and reviewed the literature,
Vauclair F and Borens O critically reviewed the manuscript. »
5. We added a «biostatic statement »:
«**The current manuscript reports only descriptive data from a collective of 5 patients. Due to the small sample size no biostatistical analysis was conducted.** »
6. As well as a «Data sharing statement»:
«**Due to the small collective of patients, no data set was created.** »
7. We rearranged « Corresponding author information » by adding organization real-name mailbox and modifying phone numbers as follows
Corresponding author: **Patrick Goetti, MD, Department** of orthopedic surgery and traumatology, Lausanne University Hospital and University of Lausanne, Avenue Pierre-Decker 4, Lausanne **1010**, Switzerland. patrick.goetti@chuv.ch
Telephone: +41-79-5569044
Fax: +41-21-3142755
8. As requested we added our names at the end of the core tip as follows:

Goetti P, Gallusser N, Antoniadis A, Wernly D, Vauclair F, Borens O. Advanced septic arthritis of the shoulder treated by a two-stage arthroplasty. *World J Orthop* 2019; In press

9. As requested we added the article Highlights section as follows:

ARTICLE HIGHLIGHTS

Research background

Septic arthritis of the glenohumeral joint is a relatively rare entity representing 3% to 15% of septic arthritis. It can nonetheless lead to major complications such as bone and cartilage destruction if treatment is delayed. Early treatment is therefore mandatory to alleviate pain and restore optimal function. Open or arthroscopic irrigation and debridement associated with targeted intravenous antibiotic therapy is effective to eradicate the infection. However, in patients with advanced osteoarthritic changes and/or massive rotator cuff tendon tears, infection eradication can be challenging to achieve and the functional outcome is often not satisfying even after successful infection eradication.

Research motivation

The motivation behind this study was to evaluate a two-stage approach with initial resection of the native infected articular surfaces, implantation of a cement spacer before final treatment with a total shoulder arthroplasty in a second stage. While this treatment option is gaining popularity in recent years, the evidence in the literature remains limited.

Research objectives

The available studies which deal with the topic of two-stage revision are focused on infected TSA. The results of patients with native advanced septic arthritis which are merged in these cohorts, with no separate analysis provided for this specific subgroup. The aim of our study was report our results of a short interval two-stage arthroplasty approach for septic arthritis with concomitant advanced degenerative changes of the shoulder joint.

Research methods

We retrospectively included five consecutive patients over a five-year period and evaluated the therapeutic management and the clinical outcome assessed by disability of the arm, shoulder and hand (DASH) score and subjective shoulder value (SSV). All procedures were performed through a deltopectoral approach and consisted in a debridement and synovectomy, articular surface resection and insertion of a custom made antibiotic enriched cement spacer. Shoulder arthroplasty was performed in a second stage.

Research results

Mean age was 61 years (range, 47-70 years). Four patients had previous surgeries ahead of the septic arthritis. All patients had a surgical debridement ahead of the index procedure. Mean follow-up was 13 months (range, 6-24 months). Persistent microbiological infection was confirmed in all five cases at the time of the first stage of the procedure. The shoulder arthroplasties were performed six to twelve weeks after insertion of the antibiotic-loaded spacer. There were two hemi and three reverse shoulder arthroplasties. Infection was successfully eradicated in all patients. The clinical outcome was satisfactory with a mean DASH score and SSV of 18.4 points and 70% respectively.

Research conclusions

Our study indicates that short interval two-stage approach for septic glenohumeral arthritis is a valid alternative treatment option for patient with advanced degenerative condition and/or irreparable rotator cuff tears. The main advantage of this novel approach is that by treating the underlying bony pathology in terms of resecting the arthritic bone the chances of successful infection eradication are increased and at the same time it allows for adequate pain control and improvement of functional outcomes. In our opinion, it should be reserved for selected patients with higher stage of infection, who failed to heal with arthroscopic or open lavage and debridement

Research perspectives

The rising number of shoulder procedures performed in aging population with inherent higher risk factors could potentially lead to a growing number of septic glenohumeral arthritis. Multicenter studies are necessary to achieve a higher case load and evidence regarding these rare indications.

10. We reformatted the references according to the provided guidelines
11. The English Editing Certificate was uploaded
12. Finally, we signed the new version of the license agreement