

Reviewer #1:

We would like to thank the reviewer for his constructive comments.

Reviewer #2:

We would like to thank the reviewer for his valuable comments and suggestions. We would like to underline that all comments were taken into account and all necessary changes were clearly marked in the text with blue color.

1. This case study was not registered as a clinical trial, because it did not include any experimental interventions. All patients underwent a very common procedure in orthopedics (arthroplasty) and received anticoagulants for prevention of thrombosis, which is a standard prophylactic procedure. In addition, this study received a research grant from the National Association of Orthopaedic Surgery and Traumatology.
2. A. Thank you for your comment concerning bone cement. It is known from the relevant literature that bone cement does not predispose to thrombosis, on the contrary it may have a prophylactic effect to air-embolism in cases of cemented arthroplasties (ref. 12, 14). However, in order to clarify - in relation to your comment - that the patients had a high level of control, we have added some further information about our methodology in the patients and methods section, page 7, 1st paragraph.
B. Concerning tourniquet time, one of the exclusion criteria already described in Patients and Methods section was a threshold (tourniquet time) exceeding 100 min. Thus, all patients included in this study had a tourniquet time of less than 100 min. This is additionally stated at the Patients and Methods section (page 7) as following: “operative time with the use of tourniquet was less than 100 min for all patients included in this study, as defined above”.
C. All surgeries were performed by the same group of four experienced surgeons sharing the same surgical principles, with the same rate of participation per type of arthroplasty and anticoagulation selection postoperatively. This is additionally stated at the Patients and Methods section (page 7) as following: “All surgeries were performed by a group of four experienced surgeons sharing the same surgical principles.”
D. In addition, all patients -independently of type or arthroplasty- followed the same rehabilitation protocol, as stated in Patients and Methods section (page 7): “Drainage was used in all cases and patients were encouraged to start flexing the ankle joint and contracting the quadriceps muscle as soon as possible and to begin ambulation with the help of crutches or ambulator the first postoperative day.”

3. According to the comment about the calculation of sample size in our study, the following clarifying statement was added in statistical analysis section, (page 8), 1st paragraph: “After the enrollment of 50 patients in the study, sample size estimations showed that the required sample size to have adequate power to detect potential statistically significant differences should be approximately 200 patients. A post hoc power analysis showed that the power of the final sample of the study equaled 0,71. The Gpower v.3.1 was used in both cases.”

Science Editor:

Thank you very much for your beneficial comments and suggestions regarding our study.

- a. According to the comment about the calculation of sample size in our study a clarifying statement was added in the 1st paragraph of statistical analysis section (page 8).
- b. The questions raised by the reviewers were answered in detail and clarity.
- c. In order to resolve all language issues in the manuscript, based on the peer review report, we authorized a native-English speaker (Mrs Teresa Jane Carr is referred in ACKNOWLEDGEMENTS section) to edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript’s language will meet your direct publishing needs.
- d. We have completed the Conflict-of-Interest Disclosure Form and the STROBE checklist with page numbers.
- e. We have provided the approved grant application document by Hellenic Association of Orthopaedic Surgery and Traumatology.
- f. Apart of the inclusion of figures in the main text, we prepared separate files with the figures using PowerPoint and/or png format to ensure that all graphs or arrows or text portions can be reprocessed by the editor.
- g. We added the “article highlights” section at the end of the main text according to your recommendations.