

Prof. Massimiliano Leigheb
Editor-in-Chief
World Journal of Orthopedics
18th May 2021



Dear Prof. Massimiliano Leigheb and the World Journal of Orthopedics Editorial Office,

RE: Manuscript 64320 (Submission number from World Journal of Critical Care Medicine)

Thromboelastography in elective total hip arthroplasty.

On behalf of our co-authors, we would like to sincerely thank you for considering our revised manuscript for publication in the *World Journal of Orthopedics*.

Please find attached a detailed, point-by-point summary for each Reviewer comment, in addition to the Editor's comments.

Response to Reviewer 1

We thank Reviewer 1 for the detailed and insightful analysis and expert constructive suggestions. Please find attached our detailed point-by-point response.

Comment 1. Age and co-existing disease play a role in complications after total hip arthroplasty. I suggest the addition of data regarding comorbidities along with relevant regression analysis.

We thank the reviewer for this comment.

We agree that age and comorbidities play a role in the rate and extent of complications post-operatively. However, we would like to reiterate our study was an observational study only and inadequately powered to examine for complications. We did however collect data on a number of comorbidities including ischemic heart disease, cerebrovascular disease, diabetes, smoking and hypertension. We excluded patients ASA 4 or greater, as well as excluding those with renal impairment (eGFR <60mL/min, KDIGO stage 3A or greater) and significant atherosclerotic disease.

We have updated Table 1 to include this additional demographic information regarding the patients studied, and this has been included in our revised manuscript.

We again thank the reviewer for this comment.

Comment 2. Please add marginal lines for the tables.

We thank the reviewer for this comment.

The appropriate changes have been made to the tables and this is now reflected in the revised manuscript.

We once again thank Reviewer 1 for their comments and hope we have addressed them satisfactorily.

Response to Reviewer 2

We thank Reviewer 2 for reviewing our manuscript and providing their expert comments and constructive suggestions. Please find below our detailed point-by-point response.

Major Comments

Comment 1. Only 52 patients were enrolled, and given the retrospective nature of the study it would be easy to collect more patients

We thank the reviewer for this comment.

We acknowledge that 52 patients is a limited sample size, however we would like to illustrate that this study was observational only, and powered only to examine trends in coagulation in this patient cohort only, not explore clinical outcomes or investigate observations.

Due to the observational nature of this work, the sample size of greater than 50 patients provides clear data regarding these coagulation trends, and achieves the objectives of this pilot observational study. Further, we have acknowledged our sample size as a limitation within our limitations section, however do not believe it detracts from the overall validity of this work.

Once again, we thank the reviewer for this important comment.

Minor Comments

Comment 1. I would like to know at least the protocol behind the choice between general or spinal anesthesia.

We thank the reviewer for this important comment and appreciate the opportunity to elaborate on this protocol. All patients were recruited from our orthopedic perioperative clinics. We included all adult patients (>18 years old), undergoing primary elective THA with an ASA score of 2 or 3.

The protocol in our institution used to guide appropriate selection of patients for either general or spinal anesthesia was standardized for all patients. All patients scheduled for surgery underwent routine pre-operative investigations in dedicated orthopedic pre-operative anesthesiology clinic. This included a multidisciplinary review by an anesthesiologist, pharmacist, perioperative nurse and orthopedic medical officer. Routine preoperative investigation included electrocardiogram, chest x-ray and pathology testing (including full blood count, urea and electrolytes and coagulation studies). Comorbidities were optimised, which included smoking cessation, optimization of hypertension and ischemic heart disease and other comorbidities, as well as optimization of perioperative anemia and glycemic control. These were managed in accordance with National Australian Guidelines.

Patients were provided with full informed consent in the pre-operative anesthesiology clinic and were counselled regarding anesthetic technique. Anesthesia preference included spinal anesthesia, unless contraindicated (previous spinal surgery, aortic stenosis, or patient refusal). Routine intraoperative anesthesia monitoring included continuous EKG and arterial saturation monitoring and non-invasive blood pressure monitoring. Continuous blood pressure monitoring via an arterial line was used in select patients (e.g., significant cardio-respiratory comorbidity).

Details of this protocol have been included within the methods section of our manuscript, and we thank the reviewer again for the opportunity to clarify this point.

Comment 2. The author stated that the study was not designed to investigate clinical outcomes or incidence of venous thromboembolic events, but it would be interesting to at least see mentioned these data, as they are the final endpoint of the topic.

We thank the reviewer for this comment.

After careful review of the data, we note that there were zero cases of clinically significant venous thromboembolic events. However, we acknowledge that we did not actively investigate our entire patient cohort for venous thromboembolic events complications with lower limb ultrasound or computed tomography pulmonary angiography (CTPA). Within our manuscript, we do note that one patient in the spinal cohort complained of dyspnoea and chest pain three days postoperatively but had a negative CTPA, while one patient in the general anesthesia cohort had unilateral calf swelling postoperatively with negative ultrasound.

Again, we thank the reviewer for this comment, and have updated our limitations section accordingly.

Comment 3. In the results section the authors stated that 52 patients were enrolled, it would be interesting to know how many patients were excluded for the absence of TEG or any other reason.

We thank the reviewer for this comment. Zero patients were eliminated from this study secondary to a lack of availability of TEG. Our methods section has been updated to reflect this (Page 6, line 1).

Our study enrolment used a convenience sampling method, and therefore, beyond the exclusion criteria listed in our manuscript, no patient was excluded secondary to patient or equipment factors beyond what is stated. We again thank the reviewer for this comment and hope the addition to our methods section adds clarity.

Comment 4. - in the result section, the authors stated that there were no differences in patient weight nor sex based on type of anaesthetic used. I would suggest to consider other factor in the analysis, to better describe the two population, such as ASA class.

We thank the reviewer for this comment. We agree this information would be useful for the reader.

A similar comment was also made by Reviewer 1. In response, we have including additional demographic data, including ASA class in Table 1.

This new information has been provided in our revised manuscript.

Table 1

	Spinal (n=32)	GA (n=20)	P value
Median Age	74	61	<0.01
Median weight (kg)	70	70	0.67
Sex (Male)	14	7	0.23
ASA class 2	17	13	0.56
ASA class 3	15	7	
Ischaemic heart disease	1	0	>0.99
Cerebrovascular disease	0	0	
Diabetes	3	1	
Hypertension	6	4	
Smoking history	4	4	

Comment 5. - lines 19-21 of page 3 and the whole page 4, describing study design and aims, should be placed in methods section.

We thank the reviewer for this comment. We have updated our manuscript accordingly and have moved these components to the methods section.

We once again thank Reviewer 2 for their comments and hope we have addressed them satisfactorily.

Comments

Comment 1. The title is too long, and it should be no more than 18 words.

We thank the editor for this constructive comment.

Our revised title is “*Thromboelastography in elective total hip arthroplasty*”.

This has been reflected in our revised manuscript.

Comment 2. PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

We thank the editor for this comment.

We have made the necessary revisions as required and this has been reflected in the revised manuscript.

Comment 3. The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.

We thank the editor for this comment.

Article highlights have been added appropriately and included within the revised manuscript at the end of the main text.

Comment 4. The STROBE statement needs to be added to the page number.

We thank the editor for this comment.

We have added the page numbers (of where each checklist item appears within the manuscript) to our STROBE statement. We have included a new table detailing this, and included this as Appendix 1 in our revised manuscript.

We thank the editor for this comment and hope we have addressed all editorial concerns satisfactorily.

Once again, we are very appreciative of the Reviewers and the Editorial team for their time, expertise, and opinions.

We hope we have addressed all the key points and comments raised by the expert reviewers and are grateful for the opportunity to resubmit our revised manuscript for consideration by *World Journal of Orthopedics*.

Dr Patryck Lloyd-Donald



Dr Wen-Shen Lee



Address for correspondence

A/Prof Laurence Weinberg

Email: laurence.weinberg@austin.org.au

Department of Anaesthesia

Austin Hospital, 145 Studley Rd, Heidelberg, Melbourne,
Victoria 3084, Australia