Author’s response to reviews

Title: Immediate versus delayed surgery for hip fractures in the elderly patients: a protocol for a systematic review and meta-analysis

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Author’s response to reviews:

Dear Dr. Fedorowicz,

We would like to thank you and the reviewers for the valuable and constructive feedback that we received in response to our submission “Immediate versus delayed surgery for hip fractures in the elderly patients: a protocol for a systematic review and meta-analysis” (SYSR-D-17-00144). We have revised the paper according to the reviewers’ suggestions and hope that the new version of the article will be suitable for publication.

Below, please find detailed responses to the reviewers’ comments and brief summaries how we addressed them.

If you have any questions, please don’t hesitate to contact us anytime.
Comments of Reviewer #1

1. In the PROSPERO registered protocol (CRD42017058216) the age inclusion is >60 years: "Participants/population: Patients older than 60 years with hip fractures treated surgically." In this protocol is >=65 years: "Patients 65 years of age or older, who undergo surgery for acute hip fracture"

Thank you for pointing this out. This was an error in the manuscript. We changed the inclusion criteria for age throughout the manuscript accordingly. (lines 64, 71, 131, 144, 151 (table 1), 240).

Comments of Reviewer #2

1. Nicole Simunovic review in 2010, beside addressing the mortality benefit of early surgery, she also reported of some of the outcomes intended in your protocol as unadjusted data indicated that earlier surgery also reduced in-hospital pneumonia (RR 0.59, 95% CI 0.37-0.93, p = 0.02) and pressure sores (RR 0.48, 95% CI 0.34-0.69, p < 0.001). (Simunovic N, Devereaux PJ, Sprague S, Guyatt GH, Schemitsch E, Debeer J, et al. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. CMAJ.2010;182(15):1609-16.)

We thank the reviewer for this valid point. We are aware of the fact that Nicole Simunovic found four studies that reported postoperative complications. Besides demonstrating a risk reduction for in-hospital pneumonia and pressure sores among patients undergoing early surgery, timing of surgery did not significantly affect the incidence of deep vein thrombosis or pulmonary embolism. However, Simunovic et al. excluded studies not reporting on mortality. So, studies reporting exclusively on the effect of timing of surgery on peri-operative complications might have been missed. We added a sentence that we will include all relevant studies reporting any of our outcomes of interest (line 120-212)- We agree that Simunovic reported some of the outcomes intended in our protocol and, therefore, deleted the word exclusively (line 117).
Comments of Reviewer #3

1. The exclusion criterion 'patients with initially missed hip fracture' appears a bit vague. The review would benefit from specifying that criterion.

   Thank you. We agree and specified that criterion as:
   
   ¥ Patients with hip fractures not related to an acute trauma
   ¥ Patients with pathological fractures
   ¥ Patients with periprosthetic fractures

   (see table 1).

2. Having exactly the same cut-offs for 'early' and 'delayed' surgery might be difficult given possible deviations from clinical practice guidelines, cross-country differences in clinical practice, and differences between centers within a country/region. It is advisable to make a judgment on the indifference margin for the 'early' and 'delayed' surgery time taking advantage of the clinical expert consultation via Delphi approach. Though the numerical difference will presumably appear, they might not entail significant clinical difference thus precluding from combining studies. Supporting sensitivity and heterogeneity analysis will shed more light on the validity of that approach.

   Thank you for this great suggestion. We will consult with our clinical expert panel via Delphi approach to define what time frames are similar enough to be analyzed together as “early” and “delayed” surgery. We added a sentence (line 216 – 220).

3. I would like to point out the differences between the submitted protocol and PROPSERO with regard to e.g. age (,.60 years in PROSPERO, ,.65 years in the current protocol).

   Thank you. We changed the information within the manuscript (see response to comments if reviewer #1)