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Response to Yin et al regarding: "Conservative vs. operative treatment for humeral shaft fractures: a meta-analysis and systematic review of randomized clinical trials and observational studies"

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In reply:

We thank Yin et al for their interest and comments regarding our recently published meta-analysis comparing conservative vs. operative treatment of humeral shaft fractures. They raised several concerns regarding the outcome parameters, subgroup analysis, and heterogeneity of the studies included in the meta-analysis. We would like to provide more insight and share our thoughts on these concerns.

It was pointed out that the results of randomized controlled trials (RCTs) and observational studies are inconsistent for the analysis on nonunion rate and time to union. In our opinion, this only applies to the secondary endpoint, union time. Determining the exact moment of union is a highly subjective matter and is also influenced by the interval between follow-up visits. This may contribute to results being inconsistent both within and between studies. Furthermore, it is unclear how a difference in union time between treatments would impact clinical practice. There is frequently a discrepancy between radiologic and clinical signs of healing.⁴ Results regarding time to union should therefore be interpreted with caution. Regarding the primary endpoint, nonunion rate, both RCTs and observational studies consistently showed a lower nonunion rate for operative treatment, with minimal heterogeneity for both study designs.

Yin et al remarked that only 2 RCTs were included in the subgroup analysis, making the pooled estimates of RCTs unreliable.^{2,3} As already described in the “Discussion” section of our article, it is a known limitation of our meta-analysis that we were able to include only 2 RCTs. However, the validity of the results of the meta-analysis depends on the quality of the included studies, both of which are of high quality (Methodological Index

for Non-Randomized Studies [MINORS] scores of 17 and 23). Ideally, more RCTs would have been included, had these been available.

Yin et al also advised us to conduct a subgroup analysis of plate use and non-plate use vs. conservative treatment because various operative techniques exist for humeral shaft fractures (nailing, minimally invasive osteosynthesis, and open reduction–internal fixation) and each has its specific merits and demerits when compared with conservative management. At the time of our analysis, we investigated whether such a subgroup analysis was possible. However, because the majority of studies did not describe results for each surgical modality separately, this was not possible.

Finally, Yin et al pointed out that the heterogeneity in the analysis on union time was high ($I^2 = 84\%$). They made the effort to perform an additional analysis by removing the study by Westrick et al,⁵ after which the level of heterogeneity indeed was reduced (to $I^2 = 8\%$, not to $I^2 = 0\%$ as was claimed). The measure of heterogeneity used (I^2) depends on the variation in effect estimates between studies. Therefore, it should be no surprise that this measure is reduced when excluding a relatively outlying effect estimate (as in the study of Westrick et al). In accordance with the *Cochrane Handbook for Systematic Reviews of Interventions*, we think studies should not be excluded based on their results; instead, such exclusion should be based on clinical or methodologic arguments.¹ We could not identify any obvious reason for the “outlying” result found by Westrick et al and therefore did not exclude this study from our meta-analysis.

We appreciate the observations made about our article. We agree that the results regarding the secondary outcome, union time, should indeed be interpreted with caution.

However, we believe that overall the results of the meta-analysis are reliable and represent the highest level of available evidence on this controversial topic.

Disclaimer

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