Reply Letter to Chiavarini et al – "Association between nutritional indices and mortality after hip fracture: a systematic review and meta-analysis"

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Dear Editor,

We thank Chiavarini et al¹ for their comments on our article. We aim to provide clarification on some of the issues as follows:

- 1. The authors have presented data from three studies that were missed by the review. However, there are clear reasons for their non-inclusion. The study of Nuotio et al² was not included as it had overlapping data from the study of Helminen et al³ (both were from the same institution). Since the study of Helminen et al² had a longer study period and larger sample size, it was included. Secondly, the study by Su et al⁴ focused on femoral fractures and not exclusively on hip fractures. The authors in their article have not reported separate data for femoral neck fractures. As per the exclusion criteria of the review, the study conducted by Su et al⁴, involving femoral shaft fractures, was thus excluded. Third, the study cited by the authors from Feng et al⁵ exhibited significant overlap with another study by Feng et al⁶ that was incorporated into the review. However, since the latter had a larger sample size, it was included in the review. Figure 1 of our article mentions the reasons for excluding these studies as overlapping (n=3) and on femoral fracture (n=1).
- 2. The authors point out that the studies of articles Koren-Hakim et al⁷, Miu and Lam⁸, Kotera⁹ and Yokoyama et al¹⁰ were included despite not reporting data as odds ratios (OR)/ risk ratios (RR), / hazard ratios (HR). We computed the OR based on the data pertaining to the numbers of deaths in the low and high-nutrition groups, and subsequently reported this calculated OR in our article without explicitly stating our methodology. We apologize for this inconsistency. The OR was calculated by processing the pool of data by the online software MedCalc, available at https://www.medcalc.org/calc/odds_ratio.php, which generates OR with 95% confidence interval.
- 3. Lastly, regarding the difference in numbers reported in the articles of Hao et al¹¹ and Fujimoto et al¹² and those presented in Figure 2, it is important to understand that these studies compared patients with higher geriatric nutritional risk index (GNRI) scores *vs.* lower GNRI scores, i.e., malnourished patients, as the reference group while calculating the OR. Hence, the ratio was divided by 1 to obtain the association between lower GNRI score *vs.* higher GNRI score (malnourished *vs.* normally nourished), with the latter as the reference group. This was undertaken to ensure consistency in the reference groups used in the meta-analysis. It is not feasible to merge data from studies where some use malnourished patients as the reference group while others use healthy patients. This also explains the difference in numbers in Figure 3 for the studies of Ren et al¹² and Feng et al⁶ and in Figure 4 for the study of Thörling et al¹⁴.
- 4. However, we thank the authors for pointing out an error in Figure 4. We have substituted the unadjusted OR of 11.16 (95% CI: 3.78-32.91) with 4.37 (95% CI: 1.77-10.80) in Figure 4. The amended Figure 4 now has a pooled ratio of OR: 3.00 95% CI: 1.60, 5.64 I^2 =79% p=0.006 instead of OR: 3.61 95% CI: 1.70, 7.70 I^2 =85% p=0.0009 presented in the article. It can be noted that the change is minor, and the results are still statistically significant.

Again, we thank the authors for their interest in our article. As noted from the clarifications, except for a minor non-influencing error in the mini-nutritional assessment-short form (MNA-SF), the review still presents the most robust evidence on the association between nutritional indices and mortality after hip fracture.

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study of Subgroup	log[Ouus Ratio]	36	weight	iv, Kanuoni, 95% Ci	rear	IV, Kanuoin, 95% Ci
Koren-Hakim 2016	2.1277	0.549	15.7%	8.40 [2.86, 24.62]	2016	
lelminen 2017	1.0818	0.2664	24.1%	2.95 [1.75, 4.97]	2017	
Aiu 2017	0.9206	0.6217	13.9%	2.51 [0.74, 8.49]	2017	
lelminen 2019	1.4748	0.4611	18.1%	4.37 [1.77, 10.79]	2019	
horling 2020	0.3853	0.1035	28.1%	1.47 [1.20, 1.80]	2020	-
Fotal (95% CI)			100.0%	3.00 [1.60, 5.64]		•
leterogeneity [.] Tau ² =	= 0.36: Chi ² = 19.0	9. df = 4	(P = 0.00)	008); $I^2 = 79\%$		

Figure 4. Meta-analysis of the association between MNA-SF and mortality after hip fractures.

Conflict of Interest

The authors declare they have no conflict of interest.

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