Correspondence on 'Concomitant use of oral glucocorticoids and proton pump inhibitors and risk of osteoporotic fractures among patients with rheumatoid arthritis: a population-based cohort study'

We read with great interest the article by Abtahi *et al*,[1] which reported that concomitant use of oral glucocorticoids (GCs) and proton pump inhibitors (PPIs) is associated with a positive risk (1.6-fold) of osteoporotic fractures compared with their non-use in patients with rheumatoid arthritis (RA). In addition, this risk was significantly higher when compared with the single use of GCs or PPIs. Increased fracture risk associated with concomitant GC and PPI use was observed for fractures of the hip, clinical vertebrae, pelvis and ribs, but not for those of the humerus or forearm. Although the findings of this study are relevant to clinicians, some issues remain unaddressed in this regard. Therefore, we attempted to explore these grey areas.

First, there is a need to examine why the Disease Activity Score 28 erythrocyte sedimentation rate (DAS28-ESR) or DAS28-C reactive protein (CRP) was employed in the clinical evaluation.[2 3] The ability to assess the severity of RA disease and the changes over time in a standard, reliable, and valid manner is essential to evaluate the need for and response to healthcare interventions.[2 3] Standard assessments of severity have increasingly been devised to focus on RA diseases, so as to respond particularly to the changes in an individual's clinical status. Many reports recommend the use of DAS28-ESR >5.1 or DAS28-CRP >4.6 to define high disease activity, since these cut-off points have been previously validated.[4] Moreover, this will enable more accurate measurement of disease activity when DAS28-ESR and DAS28-CRP are used. Patients with higher disease activity may have an increased risk of osteoporotic fracture and be more prone to concomitant use of oral GCs and PPIs.[5 6] Otherwise, a stable clinical status (lower disease activity) may not have led to the use of GCs or PPIs, as well as lower osteoporotic fracture rates. Thus, the observed associations of the concomitant use of oral GCs and PPIs with the risk of osteoporotic fracture reported in this study may be underestimated or overestimated.

Second, postmenopausal osteoporosis is the most common osteoporosis that occurs in women, which subsequently resulted in osteoporotic fractures, even under slight trauma.[7] Also, statins are widely used for the treatment of hyperlipidaemia and recent in vitro and animal data suggest that statins promote bone formation and increase bone strength.[8 9] Numerous observational studies have demonstrated that the use of statins is associated with lower risk of osteoporotic fractures.[10 11] However, postmenopausal status and statins use were not described in the baseline characteristics of these four groups. Therefore, there may be a limited possibility of drawing accurate or reliable conclusions.

Third, this study enrolled 33 369 patients with RA initially, but only 12 351 (37%) patients who met the inclusion criteria were used to further analysis. The patients having a definite RA diagnosis, based on Muller's algorithm, were excluded. We suggested that patients having a definite RA diagnosis based on Muller's algorithm should also be included as a comparison group and that time-dependent Cox proportional-hazard models should also be used to investigate the risk of osteoporotic fracture. Therefore, selection bias may be excluded in this study.

In conclusion, although we share some concerns about this article with Abtahi *et al*, we compliment the authors for their commendable work and hope that this study would benefit the readers.

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