Association of proton pump inhibitors with fracture risk in patients with rheumatoid arthritis

In a recent longitudinal prospective observational study that included more than 10 000 adult patients with rheumatoid arthritis (RA) who had no prior fracture, Ozen and colleagues1 confirmed that proton pump inhibitors (PPIs) were frequently prescribed (approximately 30% of the participants) and showed no association between PPI use and fracture risk; the adjusted HR and 95% CI were 0.92 and 0.80 to 1.06, respectively. This seems to be a timely and clinically meaningful finding.

I agree with the authors1 that higher use of bisphosphonates among the participants with PPI use influenced the aforementioned association. After treatment with bisphosphonates, however, reduction in vertebral fracture risk is obviously larger than that in non-vertebral fracture risk; for example, the latest clinical practice guideline2 described that HR (95% CI) of alendronate was 0.56 (0.46 to 0.67) in vertebral fracture risk and 0.83 (0.74 to 0.93) in non-vertebral fracture risk. Accordingly, the involvement of bisphosphonates is limited, because HR (95% CI) of PPIs was 1.04 (0.85 to 1.27) in vertebral fracture risk and 0.82 (0.69 to 1.00) in non-vertebral fracture risk.1

Here I would like to suggest that accumulating evidence3–6 is unlikely to support a causal relationship between PPI use and fracture risk, regardless of RA, and thus the frequently used drug would not be a modifiable risk factor for fractures, although it is important to note that risk of fractures as well as falls could be higher among many patients with PPI use6 as shown by the unadjusted HR 1.36 (95% CI 1.19 to 1.55).1

Toshihiro Sugiyama

Correspondence to Dr Toshihiro Sugiyama, Department of Orthopaedic Surgery, Saitama Medical University, Saitama 350-0495, Japan; tsugiym@saitama-med.ac.jp

Handling editor Josef S Smolen

Contributors TS is the sole author.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.


Received 20 May 2019
Accepted 21 May 2019
Published Online First 31 May 2019

https://doi.org/10.1136/annrheumdis-2019-215775

ORCID iD Toshihiro Sugiyama http://orcid.org/0000-0001-5551-1340

REFERENCES
4 Sugiyama T. Letter: association between proton pump inhibitor use and fracture risk - causality or confounding? Aliment Pharmacol Ther 2018;47:1569–70.