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 colleagues[1] 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 authors[1] 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 guideline[2] 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 evidence[1 3–6] 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 use[6] as shown by the unadjusted HR 1.36 (95% CI 1.19 to 1.55).[1]

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