

Association between proton pump inhibitors therapy and fracture risk in patients with rheumatoid arthritis

Proton pump inhibitors are commonly prescribed for the treatment of acid-related gastrointestinal diseases. The association between proton pump inhibitors therapy and other subsequent comorbidities has been extensively explored.¹ Recently, a cohort study in USA conducted by Ozen *et al* published in the *Annals of the Rheumatic Diseases* reported that proton pump inhibitors therapy was not associated with increased fracture risk in patients with rheumatoid arthritis (HR=0.92; 95% CI 0.80 to 1.06).² Ozen *et al*'s study is an important one and deserves a practical value. Some points not shown in the original article are shared with the readers. First, in order to test this issue in a different country, a preliminary population-based cohort study was conducted using the 2005–2012 database of the Taiwan National Health Insurance Program with 23 million residents living in Taiwan.³ Patients ≥ 20 years old with a diagnosis of rheumatoid arthritis were included in the study. In order to reduce the biased results, those patients who had a cumulative period of proton pump inhibitors therapy < 3 months were excluded from the study. The main outcome was a new diagnosis of any major osteoporotic fractures including fractures of the spine, humerus, forearm, wrist and hip. Table 1 shows that the incidence of major osteoporotic fractures is 1.33-fold higher in patients with proton pump inhibitors therapy than those without use, but it does not reach statistic significance (1.24 vs 0.94 per 100 person-years; 95% CI 0.86 to 2.06, $p=0.2049$) which was compatible with Ozen *et al*'s study reporting that no association could be observed between proton pump inhibitors therapy and fracture risk in patients with rheumatoid arthritis.² Second, previous research has suggested that no significant association can be detected between proton pump inhibitors therapy and fracture risk in older adults.⁴ Ozen *et al*'s and our studies further confirm that even in patients with rheumatoid arthritis, such an association still does not exist. Third, I agree with Sugiyama's comments published in the *Annals of the Rheumatic Diseases* reporting that no conclusive evidence supports a cause–effect relationship between proton pump inhibitors therapy and fracture risk, regardless of the population studied.⁵ Fourth, currently no research definitely proves that proton pump inhibitors therapy can change bone mineral density. So, the American Gastroenterological Association does not recommend that patients on long-time therapy of proton pump inhibitors need to routinely assess bone mineral density.⁶ Fifth, based on the above discussion, patients with rheumatoid arthritis who are on long-time therapy of proton pump inhibitors do not need to routinely examine bone mineral density and do not need to worry about fracture risk.

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Table 1 Incidence of major osteoporotic fractures between proton pump inhibitors use group and non-use group in ≥ 20 years old adults with rheumatoid arthritis, in 2005–2012

Variable	Proton pump inhibitors use				Non-use				Incidence rate ratio (95% CI)*	P value
	N	Event	Person-years	Incidence	N	Event	Person-years	Incidence		
All	558	22	1760	1.24	5299	204	21 690	0.94	1.33 (0.86 to 2.06)	0.2049

Incidence: per 100 person-years.

*Incidence rate ratio: proton pump inhibitors use vs non-use (95% CI).