PROTON PUMP INHIBITORS USE IS ASSOCIATED WITH AN INCREASED RISK OF FRACTURES: RESULTS FROM THE DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY (DOPPS).

Maria Fusaro[1], Maurizio Gallieni[2], Arianna Pitino[1], Graziella D'Arrigo[3], Sabrina Molinaro[1], Giorgio Iervasi[1], Andrea Aghi[4], Mario Plebani[5], Sandro Giannini[4], Fabio Malberti[6], Loreto Gesualdo[7], Brian Bieber[8], Keith McCullough[8], Giovanni Tripepi[3], Francesca Tentori[8]

[1]Institute of Clinical Physiology, National Council of Research (CNR), Pisa, ITALY, [2]Nephrology and Dialysis Unit, San Carlo Borromeo Hospital, Biomedical and Clinical Science 'L.Sacco', University of Milano, Milano, ITALY, [3]Clinical Epidemiology and Physiopatology of Renal Disease and Hypertension, IFC-CNR, Reggio Calabria, ITALY, [4]Clinica Medica 1, University of Padova, Padova, ITALY, [5]Laboratory Medicine Unit, University of Padova, Padova, ITALY, [6]Division of Nephrology and Dialysis, Istituti Ospitalieri di Cremona, Cremona, ITALY, [7]Nephrology, Dialysis and Transplanation Unit, 'Aldo Moro' University of Bari, Bari, ITALY, [8]Arbor Research, Arbor Research Collaborative for Health, Ann Arbor, MI.

INTRODUCTION AND AIMS

Proton pump inhibitors (PPIs) are extensively used for the chronic treatment of common gastrointestinal disorders in dialysis patients. PPIs interfere with the active transport of magnesium causing hypomagnesemia. Magnesium is essential for bone health and contributes severe osteoporosis in patients on chronic PPI treatment. We evaluated the association between PPI use and bone fractures in hemodialysis patients in the DOPPS study.

METHODS

Among 50411 (58% male) hemodialysis patients from the DOPPS dataset, 39% of patients received PPI treatment, aged 62.5±15 years, dialysis duration 588 days, BMI 25±6 Kg/m^2. Comorbidities were the following: 39% diabetics, 80% hypertensives, 43% coronary artery disease (CAD), 32% congestive heart failure (CHF), 33% cardiovascular (CaV) disease, 16% cerebrovascular (CeV) disease, 26% peripheral vascular disease (PVD), and 70% of patients showed CAD or CHF or CaV or CeV or PVD (**Table 1**). Bone fractures requiring hospitalization were considered. Hip fractures were analyzed as a subset. The median and the interquartile range of follow-time is 19 months (interquartile range: 9-27 months).

Table 1: Main Characteristic of the patients.

Demographic	
Gender	58 % male
PPI tratment	39 %
Age	62.5±15 years
Dialysis Duration	588 days
BMI	25±6 Kg/m^2
Comorbidities	
Diabetics	39%,
Hypertensives	80%
Coronary artery disease (CAD)	43%
Congestive heart failure (CHF)	32%
Cardiovascular (CaV) disease	33%
Cerebrovascular (CeV) disease	16%
Peripheral vascular disease (PVD)	26%
Patients showed CAD or CHF or CaV or CeV or PVD	70%

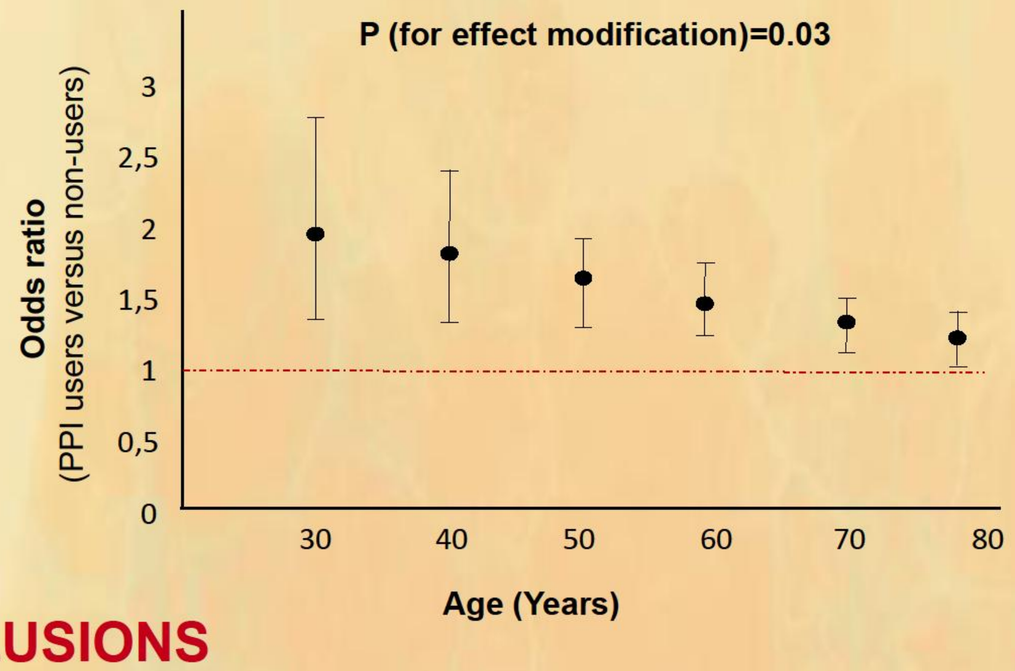
RESULTS

Overall, 6.5 (95% CI: 5.9-7.1) hip fractures every 1000 patients-years (PY) and 21 (95% CI: 20-22) bone fractures every 1000 PY were observed. On univariate logistic regression analyses, PPI use was related to an increased risk of hip (odds ratio: 2.27, 95% CI: 1.89-2.73, P<0.001) and bone fractures (odds ratio: 1.56, 95% CI: 1.41-1.72, P<0.001). In two logistic regression models (adjusting for confounding variables), a strong relationship was confirmed between PPI use with hip (odds ratio=1.68, 95% CI: 1.38-2.05, P<0.0001) and bone (odds ratio=1.34, 95% CI: 1.20-1.50, P<0.0001) fractures (**Table 2**). Furthermore, a significant and inverse effect modification by age (P=0.03) on the relationship between PPI treatment with any bone fractures (but not with hip fractures) was found, so that the odds of bone fractures associated with PPI use was high in younger patients and progressively lower in older patients (**Figure 1**).

Table 2: Univariate and multivariate model adjusted for confounding variables.

	HIP FRACTURE	BONE FRACTURE
PPI Use (Univariate)	OR: 2.27, (95% CI: 1.89-2.73, P<0.001)	OR: 1.56, (95% CI: 1.41-1.72, P<0.001)
	HIP FRACTURE	**BONE FRACTURE**
PPI Use (Multivariate)	OR: 1.68, (95% CI: 1.38-2.05, P<0.0001)	OR: 1.34, (95% CI: 1.20-1.50, P<0.0001)

Figure 1: Inverse effect modification by age on the relationship between PPI treatment with any bone fractures.



CONCLUSIONS

In hemodialysis patients, PPI use is associated with a +34% and a +68% excess risk for bone and hip fractures as compared to those untreated. Although we controlled for a series of well-known potential confounders, the possibility of residual confounding by indication cannot be excluded. The risk of bone fractures associated with PPI use was higher in younger patients.

*** Corresponding Author**
Maria Fusaro, M.D., Ph.D.
National Research Council (CNR) – Institute of Clinical Physiology (IFC), Pisa, Italy and Department of Medicine, University of Padua, Padova, Italy

E-mail: dante.lucia@libero.it

References

1. Maria Fusaro, Marianna Noale, Giovanni Tripepi, et al. Long-Term Proton Pump Inhibitor Use is Associated with Vascular Calcification in Chronic Kidney Disease: A Cross-Sectional Study Using Propensity Score Analysis. Drug Saf. May 2013. DOI: 10.1007/s40264-013-0062-6.
2. Yu EW, Bauer SR, Bain PA, Bauer DC. Proton pump inhibitors and risk of fractures: a meta-analysis of 11 international studies. Am J Med. 2011;124(6):519–26.
3. Ngamruengphong S, Leontiadis GI, Radni S, Dentino A, Nugent K. Proton pump inhibitors and risk of fracture: a systematic review and meta-analysis of observational studies. Am J Gastroenterol. 2011;106(7):1209–18.

53 ERA
559--SP
Dialysis. Epidemiology, outcome research, health services research.
Maria Fusaro
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA MAY 21-24 2016 AUSTRIA
PosterSessionOnline.com