**Comment on ‘’Polypharmacy and Kidney Function in Community-Dwelling Adults**

**Age 60 Years and Older: A Prospective Observational Study’’**

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Dear Editor,

We read with interest the study by Rahel Ernst et al., in which they aimed to investigate whether there was a relationship between intake of total number of drugs or nonsteroidal anti-inflammatory drugs (NSAIDs) and kidney function. The authors found that each additional medication taken cumulatively for 24 months decreased renal function and, in a high-risk subgroup, per NSAID taken cumulatively for 24 months, renal function decreased by 1.21 mL / min / 1.73 m2 eGFR. (1) In the present study, the cumulative uptake of NSAIDs was found to be associated with a nearly 3-fold reduction in renal function. We think that some methodological issues should be taken into consideration while determining the relationship between chronic NSAIDs use and the renal disease in older adults. (1)

NSAIDs are used frequently in older people, both in acute pain and mainly in cases such as Knee Osteoarthritis, which causes chronic pain. (2) However, NSAIDs have numerous adverse side effects, such as hypertension, congestive heart failure, electrolyte imbalance, and edema. According to the Beers criteria, long-term use of NSAIDs due to gastrointestinal complications, including gastroduodenal ulcer, gastrointestinal bleeding, and perforation, should be avoided; however, it is emphasized that NSAIDs should be used in combination with proton-pump inhibitors (PPI) if pain cannot be controlled by other alternative analgesics. (3) This means that in Rahel Ernst's study, these patients who used NSAIDs for more than 24 months had been probably or should have been receiving PPI at the same time. (1)

PPIs are one of the most commonly prescribed drugs in older people, and it is estimated that between 25% and 70% of the prescriptions have no appropriate indication. (4) The use of chronic NSAIDs is on the top of the indications for which PPIs are recommended. However, in recent years, increasing evidence has shown that PPIs are not innocent drugs and, like NSAIDs, cause both acute and chronic kidney damage.(4) For example, in a large sample-based population-based cohort study, PPI increased the incidence of chronic kidney disease (CKD) by 20% -50%; NSAIDs intake was higher in PPI users than non-PPI users; however, it was found that PPIs increased the risk of CKD by 1.35-fold after adjustment to NSAIDs. (4) Therefore, in the study of Rahel Ernst et al, who investigated the effect of polypharmacy and NSAIDs on renal function, it is an important limitation that PPIs, which are the most common drugs to cause polypharmacy, were not evaluated simultaneously with NSAIDs.(1,5) In that study, it should have been checked whether PPI use contributed to the 3-fold cumulative deterioration in renal function or to what extent it was responsible. In order to establish a clear relationship between NSAIDs and kidney damage, especially in older adults, the simultaneous evaluation of other drugs, particularly PPIs, which affect renal function, and the potential impact on outcomes, should be statistically neutralized.

In conclusion, the study contributes valuable data to medical literature; however, given the above-mentioned issue, they will provide a clearer picture to the readers.

**Conflict of Interest:** No

**References**

1. Ernst R, Fischer K, de Godoi Rezende Costa Molino C, Orav EJ, Theiler R, Meyer U, et al. Polypharmacy and Kidney Function in Community-Dwelling Adults Age 60 Years and Older: A Prospective Observational Study. J Am Med Dir Assoc. 2019 Sep;

2. Nash DM, Markle-Reid M, Brimble KS, McArthur E, Roshanov PS, Fink JC, et al. Nonsteroidal anti-inflammatory drug use and risk of acute kidney injury and hyperkalemia in older adults: a population-based study. Nephrol Dial Transplant. 2019 Jul;34(7):1145–54.

3. American Geriatrics Society 2019 Updated AGS Beers Criteria(R) for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674–94.

4. Lazarus B, Chen Y, Wilson FP, Sang Y, Chang AR, Coresh J, et al. Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease. JAMA Intern Med. 2016 Feb;176(2):238–46.

5. Unutmaz GD, Soysal P, Tuven B, Isik AT. Costs of medication in older patients: Before and after comprehensive geriatric assessment. Clin Interv Aging. 2018;13.