

Proton pump inhibitors associated with risk of chronic kidney disease

January 11 2016

Proton pump inhibitors (PPIs), which are commonly used drugs to reduce acid in the stomach, appear to be associated with an increased risk of chronic kidney disease but more research is needed to determine whether PPI use causes kidney damage, according to an article published online by *JAMA Internal Medicine*.

PPIs are one of the most commonly prescribe medications in the United States and an estimated 25 percent to 70 percent of these prescriptions may have no appropriate indication for use. Other observational studies have linked PPIs to serious adverse health outcomes. However, the authors note that no population-based studies, to their knowledge, have looked at the association between PPI use and the risk of [chronic kidney disease](#) (CKD).

Morgan E. Grams, M.D., Ph.D., of Johns Hopkins University, Baltimore, and coauthors quantified the association between PPI use and incident CKD in the general population using data on self-reported PPI use in the Atherosclerosis Risk in Communities (ARIC) study (10,482 participants followed up for a median of nearly 14 years) or an outpatient PPI prescription in the Geisinger Health System in Pennsylvania (248,751 participants followed up for a median of six years). The results were replicated at Geisinger.

At baseline, PPI users in both groups were more likely to have a higher body mass index and take antihypertensive, aspirin or statin medications.

In the ARIC group, there were 56 incident CKD events among 322 baseline PPI users (14.2 per 1,000-person years) and 1,382 events among 10,160 baseline nonusers (10.7 per 1,000 person-years). PPI use was associated with risk of incident CKD in unadjusted and adjusted analyses. The 10-year estimated absolute risk of CKD among the 322 baseline PPI users was 11.8 percent while the expected risk had they not used PPIs was 8.5 percent, according to the results.

In the replication group at Geisinger, there were 1,921 incident CKD events among 16,900 baseline PPI users (20.1 per 1,000 person-years) and 28,226 events among 231,851 baseline nonusers (18.3 per 1,000 person-years). PPI use was associated with risk of incident CKD in analyses. The 10-year absolute risk of CKD among the 16,900 baseline PPI users was 15.6 percent and the expected risk had they not used PPIs was 13.9 percent, results indicate.

The authors note several study limitations, including that participants who are prescribed PPIs may be at higher risk of CKD for reasons unrelated to their PPI use.

"We note that our study is observational and does not provide evidence of causality. However, a causal relationship between PPI use and CKD could have a considerable public health effect given the widespread extent of use. More than 15 million Americans used prescription PPIs in 2013, costing more than \$10 billion. Study findings suggest that up to 70 percent of these prescriptions are without indication and that 25 percent of long-term PPI users could discontinue therapy without developing symptoms. Indeed, there are already calls for the reduction of unnecessary use of PPIs," the study concludes.

Adam Jacob Schoenfeld, M.D., and Deborah Grady, M.D., M.P.H., of the University of California, San Francisco, wrote a related editorial summarizing recent data on the adverse effects of PPI use.

"A large number of patients are taking PPIs for no clear reason - often remote symptoms of dyspepsia or "heartburn" that have since resolved. In these patients, PPIs should be stopped to determine if symptomatic treatment is needed," they conclude.

More information: *JAMA Intern Med.* Published online January 11, 2016. [DOI: 10.1001/jamainternmed.2015.7193](https://doi.org/10.1001/jamainternmed.2015.7193).

JAMA Intern Med. Published online January 11, 2016. [DOI: 10.1001/jamainternmed.2015.7927](https://doi.org/10.1001/jamainternmed.2015.7927)

Provided by The JAMA Network Journals

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