Renal Consult

Do PPIs Pose a Danger to Kidneys?

Q Is it true that PPI use can cause kidney disease?

Proton pump inhibitors (PPIs) have been available in the United States since 1990, with OTC options available since 2009. While these medications play a vital role in the treatment of gastrointestinal (GI) conditions, observational studies have linked PPI use to serious adverse events, including dementia, community-acquired pneumonia, hip fracture, and *Clostridium difficile* infection.[1-4]

Studies have also found an association between PPI use and kidney problems such as acute kidney injury (AKI), acute interstitial nephritis, and incident chronic kidney disease (CKD).[5-7] One observational study used the Department of Veterans Affairs (VA) national databases to track the renal outcomes of 173,321 new PPI users and 20,270 new histamine H2 receptor antagonist (H2RA) users over the course of five years. Those who used PPIs demonstrated a significant risk for decreased renal function, lower estimated glomerular filtration rate (eGFR), doubled serum creatinine levels, and progression to end-stage renal disease (ESRD).[8]

Another study of 10,482 patients (322 PPI; 956 H2RA; 9,204 nonusers) and a replicate study of 248,751 patients (16,900 PPI; 6,640 H2RA; 225,211 nonusers) with an initial eGFR ≥ 60 mL/min/1.73m^2 also found an association between PPI use and incident CKD, which persisted when compared to the other groups. Additionally, twice-daily PPI use was associated with a higher CKD risk than once-daily use.[9]

The pathophysiology of PPI use and kidney deterioration is poorly understood at this point. It is known that AKI can increase the risk for CKD, and AKI has been an assumed precursor to PPI-associated CKD. However, a study by Xie and colleagues reported an association between PPI use and

increased risk for CKD, progression of CKD, and ESRD in the absence of preceding AKI. Using the VA databases, the researchers identified 144,032 new users of acid-suppressing medications (125,596 PPI; 18,436 H2RA) who had no history of kidney disease and followed them for five years. PPI users were found to be at increased risk for CKD, and a graded association was discovered between length of PPI use and risk for CKD.[10]

While these studies are observational and therefore do not prove causation, they do suggest a need for attentive monitoring of kidney function in patients using PPIs. Evaluating the need for PPIs and inquiring about OTC use of these medications is highly recommended, as research has found 25% to 70% of PPI prescriptions are not prescribed for an appropriate indication.[11] Considerations regarding PPI use should include dosage, length of use, and whether alternate use of an H2RA is appropriate. **—CAS**

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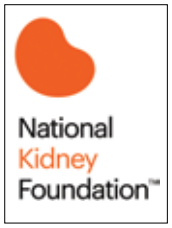

The National Kidney Foundation Council of Advanced Practitioners' (NKF-CAP) mission is to serve as an advisory resource for the NKF, nurse practitioners, physician assistants, clinical nurse specialists, and the community in advancing the care, treatment, and education of patients with kidney disease and their families. CAP is an advocate for professional development, research, and health policies that impact the delivery of patient care and professional practice. For more information on NKF-CAP, visit **www.kidney.org/CAP**.

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How to Interpret Positive Troponin Tests in CKD

Q Recently, when I have sent my patients with chronic kidney disease (CKD) to the emergency department (ED) for complaints of chest pain or shortness of breath, their troponin levels are high. I know CKD increases risk for cardiovascular disease, but I find it hard to believe that every CKD patient is having an MI. What gives?

Cardiovascular disease remains the most common cause of death in patients with CKD, accounting for 45% to 50% of all deaths. Therefore, accurate diagnosis of acute myocardial infarction (AMI) in this patient population is vital to assure prompt identification and treatment.[1,2]

Cardiac troponins are the gold standard for detecting myocardial injury in patients presenting to the ED with suggestive symptoms.[1] But the chronic baseline elevation in serum troponin levels among patients with CKD often results in a false-positive reading, making the detection of AMI difficult.[1]

With the recent introduction of high-sensitivity troponin assays, as many as 97% of patients on hemodialysis exhibit elevated troponin levels; this is also true for patients with CKD, on a sliding scale (lower kidney function = higher baseline troponins).[2] The use of high-sensitivity testing has increased substantially in the past 15 years, and it is expected to become the benchmark for troponin evaluation. While older troponin tests had a false-positive rate of 30% to 85% in patients with stage 5 CKD, the newer troponin tests display elevated troponins in almost 100% of these patients.[1,2]

Numerous studies have been conducted to determine the best way to interpret positive troponin tests in patients with CKD to ensure an accurate diagnosis of AMI.[2] One study determined that a 20% increase in troponin levels was a more accurate determinant of AMI in patients with CKD than one isolated positive level.[3] Another study demonstrated that serial troponin measurements conducted over time yielded higher diagnostic accuracy than one measurement above the 99th percentile.[4]

The American College of Cardiology Foundation task force found that monitoring changes in troponin concentration over time (3-6 h) is more accurate than a single elevated troponin when diagnosing AMI in symptomatic patients.[3] Correlation between elevated troponin levels and clinical suspicion proved helpful in determining the significance of troponin results and the

probability of AMI in patients with CKD.[2]

The significance and interpretation of elevated troponin levels in patients with CKD remains an important topic for further study, as cardiovascular disease continues to be the leading cause of mortality in patients with kidney dysfunction.[1,2] More definitive studies need to be conducted on patients with CKD as high-sensitivity troponin assay testing becomes standard for diagnosing AMI.

So, the reason you see more positive troponin results in your CKD population is due to both the increased accuracy of the newer tests and the fact that CKD often causes a false-positive result. Monitoring your patients with serial troponins for at least three hours is essential to confirm or rule out an AMI. **—MS-G** **CR**

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