

Caffeine Consumption Linked to A Longer Life for CKD Patients

Consuming caffeine—the more the better—may help reduce the risk of early death among patients with chronic kidney disease, suggests a study presented at Kidney Week.

Drinking coffee has previously been shown to reduce the risk of an early death among the general population. Caffeine consumption has also been linked to better outcomes from some chronic diseases. For example, studies have shown that coffee and tea consumption help reduce the risk of death in patients with liver disease (Modi AA, et al. *Hepatology* 2010; 51:201–209), by exerting beneficial effects on the liver (Louise JM, et al. *J Hepatol* 2017; 67:339–348). Now, Miguel Bigotte Vieira, MD, of the Centro Hospitalar Lisboa Norte in Portugal, and his colleagues show that regular caffeine consumption may also yield life gains for CKD patients.

In their study, Bigotte Viera and colleagues looked at mortality rates in 2328 patients with CKD who participated in the National Health and Nutrition Examination Survey

(NHANES) between 1999 and 2010. The NHANES collects detailed health and nutritional data on a nationally representative sample of the US population.

Caffeine consumption was assessed based on reports of 24-hour consumption at the outset of the survey. The study grouped patients into 4 categories of caffeine consumption. The first consumed less than 29.5 mg/day of caffeine. That amount is less than the amount found in an iced tea, based on estimates from the Center for Science in the Public Interest. The second consumed between 30.5 to 101.0 mg/day—about the amount found in a soda or a cup of instant coffee. The third consumed between 101.5 and 206.0 mg/day—about the amount found in a cup or two of coffee. The fourth group consumed 206.5 to 1378.5 mg/day—the equivalent of multiple cups of coffee a day.

Compared with those in the lowest group of caffeine consumption those in the second group had a 12% reduction in the risk of dying (HR 0.88, 95% CI, 0.68–1.44). The

benefits were even larger for the 3rd and 4th groups with a 22% (95% CI, 0.60–1.01) and 24% (95% CI, 0.59–0.97) lower risk of dying, respectively.

“Our study showed a dose-dependent protective effect of caffeine consumption on mortality among patients with CKD,” said Bigotte Vieira. He noted the benefit persisted even when they adjusted for potential confounders like socioeconomic status, health factors, and other nutritional habits. He cautioned, however, that this observational study can’t prove the survival benefit was caused by caffeine consumption.

“These results suggest that advising patients with CKD to drink more caffeine may reduce their mortality,” he suggested. “This would represent a simple, clinically beneficial, and inexpensive option, though this benefit should ideally be confirmed in a randomized clinical trial.” ●

“Caffeine consumption and mortality in chronic kidney disease” (Abstract 2784081)

Proton Pump Inhibitors Increase Risk of Developing CKD

Using proton pump inhibitors (PPIs) increases the risk of developing chronic kidney disease (CKD) or kidney failure by 33%, according to a meta analysis presented at Kidney Week.

PPIs are one of the most commonly prescribed medications worldwide. They are used to treat gastroesophageal reflux disease (GERD). But a growing number of studies have linked them to serious adverse effects including kidney disease, fractures, *Clostridium difficile* infections, and vitamin deficiencies (Wilhelm SM, et al. *Expert Rev Clin Pharmacol* 2013; 6:443–451).

To assess the potential kidney risks, Charat Thongprayoon, MD, of the Bassett Medical Center in Coopers-town, New York, and his colleagues analyzed data from studies that compared the risk of developing CKD or kidney failure among PPI users and non-users. They included 5 studies with 536,902 participants. The relative risk of kidney disease was one-third higher among PPI users (RR 1.33 95% CI, 1.18–1.51).

“This study demonstrates a significant association between the use of PPIs and increased risks of chronic

kidney disease and kidney failure,” said Thongprayoon.

He acknowledged that such observational data cannot prove that PPIs cause kidney injury, but he said the evidence is compelling enough to warrant more cautious use of these drugs.

“Although no causal relationship has been proven, providers should consider whether PPI therapy is indicated for patients,” Thongprayoon said. “Chronic use of PPIs should be avoided if not really indicated.”

Nephrologist Ziyad Al-Aly, MD, director of clinical epidemiology at VUS Department of Veterans Affairs St. Louis Health Care System, said the meta analysis helps synthesize the evidence to date linking PPIs with kidney disease. He noted there are a variety of potential mechanisms that might explain kidney-related adverse events in PPI users. The most plausible is that the drugs impair the ability of organelles called lysosomes, which act as the cell’s “garbage incinerator,” he explained.

“They impair the action of those organelles and they accelerate aging of the cells,” he said.

Currently, many physicians who prescribe PPIs moni-

tor their patients for signs of acute kidney injury, Al-Aly noted. However, a recent study by Al-Aly and his colleagues showed that even PPI-using patients without signs of acute kidney injury may be at risk of renal disease (Xie Y, et al. *Kidney Int* 2017; 91:1482–1494).

“It could be happening insidiously without that warning sign,” he said.

He agreed that more caution should be used in prescribing these drugs. When they are indicated, such as when a patient has a bleeding ulcer, he said the lowest dose should be used for the shortest duration of time. He questioned why the drugs are being so widely prescribed and used, noting that data suggest 30–60% of PPI users may not need the drugs.

“When people who don’t have a medical need to be on a PPI in the first place, all they are getting is the side effects,” he said. “In that instance, the risks outweigh the benefits.” ●

“Proton Pump Inhibitors and Risk of Chronic Kidney Diseases: A Meta-Analysis” (Abstract 2763180)

Excess Accumulation of Bone Drug in Rats With Compromised Kidneys

By Bridget M. Kuehn

A drug used to treat osteoporosis accumulates excessively in the bones of rats with chronic kidney disease, (CKD), according to a study presented at Kidney Week.

Bisphosphonates are currently not recommended in patients with CKD—despite the elevated risk of osteoporosis—because of potential safety concerns. The drug is cleared by the kidney, so in patients with impaired kidney function there is a concern about excess accumulation of the drug, said Mohammad Walid Aref, an MD/PhD candidate at the Indiana University-Purdue University-Indianapolis School of Medicine. But other experts point to the risk of more brittle bone rather than reduced excretion.

“The main concern about using these drugs is that they cause very low bone formation (adynamic bone), which could eventually result in more brittle bone,” said bone disease specialist Susan Ott, MD, a professor of medicine at the University of Washington in Seattle.

Limited data are available on the use of this class of drugs in CKD because patients with the condition were excluded from clinical trials (Ott S. *Intl Soc Nephrol* 2012; 82:833–835). Some studies, however, have documented a risk of acute kidney injury in patients without kidney disease who

are taking intravenous bisphosphonates. Others have suggested a potential benefit for patients with stage 3 disease, but no clear benefit has been shown for patients with later stages of disease (Ott SM. *Semin Dial* 2015; 28:363–369).

To better understand the dynamics of these drugs, Aref and his colleagues administered fluorescently labeled zolendronate to 25-week-old rats with CKD or without. Blood flow to the bones was measured using an injection of fluorescent microspheres. The rats were later euthanized, some 24 hours later, others 5 weeks out from the treatment. The animals’ radius/ulna, distal femur, tibia, and 3rd lumbar vertebra were then examined using whole bone fluorescence imaging.

The animals with CKD had levels of blood urea nitrogen twice as high as the normal animals. The kidney-impaired animals also had higher levels of zolendronate in their bones at 24 hours and 5-weeks posttreatment. The authors also found nonsignificant differences in blood flow in the CKD animals compared with the normal controls. The results suggest that the accumulation of bisphosphonate may be caused by more blood flow and more bone surface, Aref said.

“It may be due to increased turnover and increased blood flow rather than a damaged kidney that can’t filter them out,” he noted.

The results add to the preclinical evidence on the dynamics of bisphosphonate in the setting of kidney disease, said Ott.

“This [finding] is consistent with the previous studies and has used a different technique which is interesting, and studied a different bisphosphonate that is known to have a stronger binding to the bone mineral,” Ott wrote.

Ott noted that there are many more questions to be answered including how kidney disease affects skeletal uptake and whether worsening kidney disease impacts blood flow or whether the zolendronate itself may affect blood flow. She also questioned whether parathyroid hormone also may play a role since zolendronic acid would be expected to increase the hormone.

Aref and his colleagues are currently studying whether lower doses or different patterns of administering zolendronate change its accumulation in rats with CKD.

The study doesn’t yet have implications for clinical care, Ott cautioned. “We still don’t have any studies that show any benefit with these drugs in late stages of CKD on fractures,” Ott said. ●

“Bisphosphonate Skeletal Accumulation is Increased in Early and Mid-Stage CKD” (Poster 0897)