

Use of PPIs associated with higher risk of death than use of H₂ blockers

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Patients who use proton-pump inhibitors (PPIs) may have a 25% higher risk of death than those who use H₂-receptor antagonists (H₂ blockers), according to a recent study.

Using inpatient and outpatient data from the U.S. Department of Veterans Affairs, researchers assessed risk of all-cause mortality in a primary cohort of new users of PPIs or H₂ blockers ($n=349,312$), as well as in cohorts of PPI users versus non-PPI users ($n=3,288,092$) and PPI users versus users of neither PPIs nor H₂ blockers ($n=2,887,030$). Median follow-up was 5.71 years.

Results were published online on July 4 by *BMJ Open*.

Compared with use of H₂ blockers, use of PPIs was associated with increased risk of death (adjusted hazard ratio [HR], 1.25; 95% CI, 1.23 to 1.28). Mortality risk was also higher with PPI use versus no PPI use (adjusted HR, 1.15; 95% CI, 1.14 to 1.15) and with PPI use versus use of neither PPIs nor H₂ blockers (adjusted HR, 1.23; 95% CI, 1.22 to 1.24).

Among 166,098 new users of PPIs, mortality risk increased with duration of PPI use. Compared to participants exposed to PPIs for 30 days or fewer, those exposed to PPIs for longer durations had a higher risk of death (adjusted HR for 31 to 90 days, 1.05 [95% CI, 1.02 to 1.08]; for 91 to 180 days, 1.17 [95% CI, 1.13 to 1.20]; for 181 to 360 days, 1.31 [95% CI, 1.27 to 1.34]; and for 361 to 720 days, 1.51 [95% CI, 1.47 to 1.56]).

The authors noted limitations to their study, such as its observational design, the possibility of residual confounding, and its population of mostly older, white male veterans. In addition, they defined drug exposure as having a prescription for PPIs or H₂ blockers but noted that some participants' exposure may have gone undetected if they obtained the medications over the counter.

“Although our results should not deter prescription and use of PPI where medically indicated, they may be used to encourage and promote pharmacovigilance and emphasise the need to exercise judicious use of PPI and limit use and duration of therapy to instances where there is a clear medical indication and where benefit outweighs potential risk,” the study authors wrote.