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Proton pump inhibitors in cirrhosis: a marker of morbid conditions or cause of mortality

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To the Editor,

We read with interest the study by Nardelli et al., which adds to a growing literature on the potential ills of proton pump inhibitors (PPIs) in patients with cirrhosis.¹ Their prospective design allowed for assessment of minimal HE (MHE) and they reported that PPI use was independently associated with MHE, overt HE and mortality. While we applaud the authors' efforts, we are concerned about residual confounding that may have led to misinterpretation of mortality results.

The authors outline that decreased gastric acid provides biologic plausibility for the association between PPIs and *C. difficile* colitis, spontaneous bacterial peritonitis and pneumonia, which could explain some increased mortality in PPI users.² However, infections accounted for just over a third of deaths overall, type of infection was unreported and cause of death stratified by PPI use was not included. PPI use was weakly associated with overt HE but this is unlikely to account for their reported mortality, even when considered in combination with infections. This begs the question whether other explanations may exonerate PPIs.

It is possible that PPI use may merely be a marker of patient comorbidities. Increased health care utilization, smoking, obesity, NSAID use and vascular disease are all potential confounders of PPI use and death.³ These factors were not assessed. Furthermore, 42% of PPI users had “an appropriate” indication which included recent gastrointestinal bleed and/or endoscopic ligation of varices, both of which may increase mortality independent of MELD or Child-Pugh score. It would therefore be worthwhile to examine the mortality among PPI users with strong vs weak indications.

Despite these limitations, this study provides a valuable addition to the literature on PPIs and HE and provides important data arguing for the judicious discontinuance of PPIs in cirrhosis patients. However, we have a difficult time accepting PPIs as an independent risk factor for all the deaths observed without knowing more about the causes of death and comorbidities that come with PPI use.

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Conflicts of Interest: None

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References

1. Nardelli S, Gioia S, Ridola L, Farcomeni A, Merli M, Riggio O. Proton pump inhibitors are associated to minimal and overt hepatic encephalopathy and increase mortality in cirrhotics. *Hepatology*. 2018.
2. Nehra AK, Alexander JA, Loftus CG, Nehra V. Proton Pump Inhibitors: Review of Emerging Concerns. *Mayo Clin Proc*. 2018;93(2):240–246. [PubMed: 29406201]
3. Hvid-Jensen F, Nielsen RB, Pedersen L, et al. Lifestyle factors among proton pump inhibitor users and nonusers: a cross-sectional study in a population-based setting. *Clin Epidemiol*. 2013;5:493–499. [PubMed: 24348070]