Response to Letter Regarding Article, “Proton Pump Inhibitors, Platelet Reactivity, and Cardiovascular Outcomes After Drug-Eluting Stents in Clopidogrel-Treated Patients: The ADAPT-DES Study”

We appreciate the interest by Pacheco et al in our article detailing the association between proton pump inhibitor (PPI) use, platelet reactivity, and cardiovascular outcomes within the Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) study.1 We share the authors’ concern regarding the potential for residual confounding within this analysis (as well as in all of the other previously published observational analyses examining outcomes associated with PPI usage). What was unique about the present analysis is that platelet reactivity was systematically measured in a large cohort of patients who were also queried for PPI usage. As such, the analysis allows further mechanistic observations within this observational cohort study, although not implying causation.

The observation that PPI was associated with high platelet reactivity (HPR) in both univariable and multivariable analyses was initially demonstrated, and we then performed multivariable modeling of discharge PPI use both with and without HPR in the final multivariable modeling of out-of-hospital outcomes. The rationale to include HPR as a covariate stemmed from a desire to determine whether any of the effect of PPI on outcomes was independent of HPR. We performed both a propensity-stratified analysis that did not include HPR and a propensity plus covariates analysis that included HPR, as well as other clinical covariates. The estimates for discharge PPI use were consistent, but we presented the latter results which were slightly more conservative (perhaps because of PPI’s effect on HPR, but also possibly because of other reasons).

Although these findings are intriguing, we must be circumspect regarding any definitive conclusions that can be drawn from this analysis, and residual confounding can clearly play a role. Patients prescribed PPIs at discharge are inherently different from those not prescribed PPIs. From our analysis, though, it does seem safe to conclude that there is residual risk in these patients that is not well-explained by HPR alone, which is an important observation.

Disclosures

Dr Weisz is on the advisory board of AngioSlide, AstraZeneca, Calore, Corindus, Medivizer, and Medtronic. Dr Kirtane received institutional research grants to Columbia University from Boston Scientific, Medtronic, Abbott Vascular, Abiomed, St Jude Medical, Vascular Dynamics, and Eli Lilly. Dr Rinaldi is a consultant for Abbott Vascular, Boston Scientific, St Jude Medical, and Volcano. Dr Stuckey is on the advisory board of Boston Scientific and received speaker honoraria from Boston Scientific and Eli Lilly/Daiichi-Sankyo. Dr Maehara received grant support from and is a consultant for Abbott Vascular, Cordis, IDEV, Medtronic, and Volcano. Dr Henry is on the scientific advisory board of Abbott Vascular, Boston Scientific, and The Medicines Company; and is on the steering committee of TRANSLATE sponsored by Eli Lilly and Company/Daiichi-Sankyo. Dr Cox is a consultant for Abbott Vascular and Boston Scientific. Dr Duffy received speaker honoraria from Volcano. Dr Mehran received institutional research grant support from The Medicines Company, Bristol-Myers Squibb/Sanofi, and Eli Lilly and Company/Daiichi-Sankyo; and is a consultant for Abbott Vascular, AstraZeneca, Boston Scientific, Covidien, Janssen Pharmaceuticals, Regado Biosciences, Maya Medical, Merck & Co, and The Medicines Company. The other authors report no conflicts.

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