Response to Letter Regarding Article, “Cardiovascular Events as a Function of Serum Bilirubin Levels in a Large, Statin-Treated Cohort”

Mascitelli and Goldstein propose that lower levels of redox-active iron could explain some of the observed relationship between low serum bilirubin and the increased incidence of cardiovascular disease. Biliverdin/bilirubin, ferritin, and carbon monoxide are produced in equal quantities by heme-oxygenase–1, and the vascular effects of raised carbon monoxide may also contribute to the relationship between bilirubin and cardiovascular disease reported in our article.1 Disentangling the individual role of HO-1 products in cardiovascular disease will be difficult, although an independent effect of bilirubin is somewhat supported by Mendelian randomization designs using genetic variation strongly associated with bilirubin clearance.2,3 However, we should point out that these findings are not consistently replicated.4 We are not convinced that the results of our study can provide particularly strong support for the iron hypothesis, which remains an interesting area for research and debate.5,6

Disclosures

None.

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References

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