Highly Sensitive Cardiac Troponin I Assay Leads to Lowered Specificity

To the Editor:

I read with great interest the article of Kavask et al. (1) on the utility of a next-generation high-sensitivity Beckman Coulter cardiac troponin I (cTnI) assay with a 20% CV at 2.95 ng/L. This approach demonstrated a higher diagnostic sensitivity (81% vs 62%) for myocardial injury with a changing pattern of cTnI values, compared with the AccuTnI® assay cleared by the US Food and Drug Administration (1). This high-sensitivity assay had an unexpectedly high prevalence (3%) for interfering heterophilic antibodies compared with the 0.05% prevalence reported in the literature for contemporary assays (2). Heterophilic antibodies usually exhibit weak binding and polyspecificity. These antibodies are involved in the development of high-affinity antibodies, self-tolerance, and idiotypic regulatory processes (2). Critical exclusion of individuals with false-positive results has been reported to be feasible during reference-interval studies (1). How the results for patients in this study were affected by false-positive results and how they may therefore have contributed to the increased diagnostic sensitivity of the test is not known. Interferences by heterophilic antibodies in a cTnI test can be reduced markedly, such as with the revised Dimension cTnI assay with a 20% CV at 0.08 μg/L (3). The high-sensitivity cTnI assay reported by Kavask et al. also deserves such amelioration, if possible. Tests with such a high rate of false positives due to heterophilic antibodies cannot be considered appropriate for routine use because clinicians or laboratory personnel are not always aware of this problem and therefore may not initiate the appropriate follow-up investigations, such as absorption of such heterophilic antibodies or the application of another test. Criteria with greater stringency are necessary to avoid interference by heterophilic antibodies, and the first step is a strict awareness of this problem. An increased diagnostic sensitivity should be feasible, but care must be taken so that negative consequences of false-positive results do not diminish the potential benefits of high-sensitivity assays.

Reference

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To the Editor:

With increasing recognition of the importance of vitamin D deficiency as a risk factor in many common diseases, such as malignancy, diabetes, and cardiovascular disease, there has been growing interest in studies to assess vitamin D concentrations in different populations. Measurement of 25-hydroxyvitamin D (25-OH-D) is accepted as the best estimate of vitamin D status. More than 95% of 25-OH-D is typically 25-OH vitamin D3 (25-OH-D3), with 25-OH vitamin D2 reaching measurable concentrations only in patients taking vitamin D2 supplements (1). Much of the interest in vitamin D status has concentrated on seasonal variation in populations living at high latitudes, with little work done in populations living closer to the equator, perhaps under the assumption that vitamin D deficiency is unlikely in regions of plentiful sunshine. This study describes the range of 25-OH-D3 concentrations seen in a multiethnic Asian population living close to the equator.

We measured 25-OH-D3 concentrations in 240 anonymized leftover fasting venous serum samples from apparently healthy ambulatory outpatients undergoing health screening (40 men and 40...