Authors’ reply

We appreciate Dr Sertoglu and colleagues’ interest in reviewing our published article [1]. Here we propose clarifications on the mentioned points.

First, we absolutely admit that assessing serum folate, vitamin B12, and methylmalonic acid (MMA) is beneficial in differentiating the underlying cause of hyper-homocysteinemia (HHcy). However, they have limited applicability, especially in a developing clinical setting such as Iran. Even if readily accessible, we believe that further studies and additional evidence should support the utility and feasibility of further laboratory assessments for the purpose of cardiovascular risk stratification. Besides, in our study even mild increases in serum homocysteine (Hcy) values were associated with increased risk of coronary heart disease, even before development of HHcy. Actually, one may not expect elevated MMA levels in the absence of HHcy [2]. Even so, we share the same opinion that one certain shortcoming of our study is the unavailability of serum folate, vitamin B12, and MMA assessments. The same issue applies to the designated measurement methods for serum C-peptide using mass spectroscopy based techniques that are neither readily available, nor feasible to be performed in our setting.

We agree with the remarks about statistics. In our previous experience we used log transformation for triglycerides (Tg) and homeostatic model assessment of insulin resistance (HOMA-IR) when they had skewed distributions [3]. However, since Cox’s proportional hazard analysis and logistic regression have no pre-assumptions regarding the normality of entered variables, assessment of their distribution was not relevant in our models, in this study. This is one of the advantages of logistic regression modeling in comparison with the other models for statistical discrimination [4]. We described the application, advantages, and drawbacks of similar modeling in a different field and for prediction of a binary outcome, in detail [5]. Additionally, regardless of the distribution of fasting plasma glucose (FPG), Tg, and HOMA-IR, diagnosis of metabolic syndrome (MetS) was made in a binary fashion (1/0; Yes/No) using defined cut-offs for each variable [6]. Nevertheless, we checked our presented descriptive to test the significance of differences using non-parametric comparisons. As a result, we obtained similar significances for comparisons. For instance, even by using non-parametric comparisons, p-values for FPG, Tg, and HOMA-IR remained < 0.001 among the three different Hcy categories, probably due to the substantial between-group difference and the large sample size of our study. Meanwhile, we recall that the presented benefit of testing for Hcy in addition to the traditional risk factors is derived from risk reclassification, rather than mean/median comparisons.

Conflicts of interest

Authors declare no conflicts of interest.

References


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