Response to Letter Regarding Article, “Revisiting the Role of sCD40L as an Inflammatory Biomarker in a Clinical Model of Acute Myocardial Infarction”

Response:

We would like to thank Dr Lee for his valuable comment addressing the important topic of preanalytic factors confounding biomarker measurements. He has recently demonstrated that residual platelets are a source of artifactually high levels of soluble CD40 ligand (sCD40L) in clinical plasma samples. In general, preanalytic conditions are critical in the assessment of sCD40L concentrations and thus should be carefully considered in clinical studies. In this context, our research group showed years ago that plasma, but not serum, samples are appropriate for sCD40L measurements. Furthermore, several factors such as centrifugation of blood at suboptimal force and duration or single low-speed centrifugation under refrigerated conditions can result in contamination by residual platelets and are critical for reliable sCD40L measurements.

With reference to Dr Lee’s letter, the blood samples in our study were centrifuged at 3000 rpm for 10 minutes. The separated plasma was then transferred to polypropylene cryotubes without additives. A portion of the plasma was frozen and then thawed once for the determination of sCD40L. Of course, we cannot entirely exclude the influence of residual platelets, but all plasma samples were managed according to this protocol, which produces consistent sCD40L measurements.

There were 2 patients in our study receiving statin medication. Existing data have demonstrated the interference of statin therapy on sCD40L measurements. We therefore excluded these 2 patients and performed the analysis again without getting divergent results. In all patients there was a significant decrease in the sCD40L concentration compared with the baseline value 60 minutes after induction of myocardial infarction. Nevertheless, sCD40L is known to be upregulated in the presence of cardiac hypertrophy, and an influence of this patient subset on the data cannot be entirely excluded.

We are certainly in agreement with Dr Lee that these preanalytic issues are frequently overlooked and should be considered in future studies. Although methodological considerations may have had a slight effect on the final sCD40L measurements, our results add important information to this field and suggest that sCD40L may well have a future as a useful biomarker.

References

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