

In their letter to the editor, the authors highlighted several points to clarify. We would like to reply to all issues raised in their letter.

1. We have indicated all current and possible limitations of our study with clear and definite expressions in our manuscript as; "Although a lack of invasive measurements was the major limitation of our study, we did not consider invasive assessment, since it might cause ethical problems if performed in cases of mild-to-moderate MS. Central venous pressure and inferior vena cava diameters, which remain other important study limitations, were also not recorded in our study. Because right ventricular systolic function was preserved, this issue was overlooked. Male gender was also found to be a predictor of WRF (worsening renal function); however, it is better not to generalize about this, since there were relatively few male patients in the cohort, which is another limitation of this study. The number of patients enrolled in this study was another limitation; therefore, our findings should not be generalized. These findings should be supported by further studies conducted with a sufficient number of patients".
  2. We were in hope that, our published data would support future research aimed at elucidating the pathophysiology leading to worsening renal function in mitral stenosis, therefore a better understanding of the mechanisms of the cardiorenal interaction.
  3. On the contrary of the authors' expression, there was no any attempt to consolidate our results in related manuscript. The reason for citing an experimental study was the lack of any clinical study on this topic. As our study results represent very first findings in this subject, the mentioned citation was aimed to explain the problem and targeted to point possible underlying mechanism.
  4. As we did not evaluate "venous congestion" in our study, we kindly suggest reading related references in our manuscript to get more in detail.
  5. We have published to share a small group of patients' results. Therefore, a statement as "a selection bias" is unmeritorious. Using such expression requires a previous experience or performing a larger study.
- In conclusion; the manuscript itself may give all related answers of possible questions. Mankind always sets itself only such tasks as it can solve; since, looking at the matter more closely.

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## Aggregation of lipoprotein(a) to apolipoprotein A-I and coronary artery problem

To the Editor,

Sir, the recent report on aggregation of lipoprotein(a) to apolipoprotein A-I and coronary risk factor is very interesting published in September issue of The Anatolian Journal of Cardiology 2013; 13: 543-51 (1). Onat et al. (1) concluded that "Lp (a) may aggregate in a pro-inflammatory milieu to apoA-I, rendering apoA-I atherogenic." The mechanism underlying the atherogenic is an issue for discussion. Aggregation might lead to a bigger complex molecule but this cannot be sufficient for explanation for triggering the atherogenic. There should be some vascular insult that will be the starting point of atherogenic. A possible mechanism to be mentioned is the energy fluctuation during formation of intravascular lipoprotein complex. In fact, many previous reports confirming the formation of complex can result in energy insult to the vessel and lead to vascular disorder [the good example is the formation of hemoglobin A1C (2)].

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## Author's Reply

To the Editor,

We appreciated to learn the comment by Wiwanitkit to our prospective population-based study published in September issue of The Anatolian Journal of Cardiology 2013; 13: 543-51 (1) indicating that aggregation of lipoprotein (Lp) (a) in a proinflammatory setting to apolipoprotein (apo) A-I, the major protein constituent of HDL particles, may lead to impairment of the antioxidant and atheroprotective functions of apoA-I, which may ultimately become diabetogenic or atherogenic, a process representing HDL dysfunction and autoimmune activation. The author points out that the aggregation process per se may be inadequate to induce atherogenicity which may require the mediation of energy fluctuation in the course of intra-

vascular lipoprotein complex formation resulting in endothelial dysfunction, as best observed in the instance of the formation of hemoglobin A1c.

Such mediation may well be so, though we have no own investigations in this regard. Nonetheless, it is recognized that impaired function of HDL particles may promote the development of adverse outcomes (2). Moreover, elevated plasma levels of macrophage migration inhibitory factor (MIF), an immunoregulatory cytokine, are closely linked to oxidative stress and endothelial activation in patients with chronic kidney disease (3) to levels of which also a potential role has been ascribed in the development of insulin resistance in humans (4). We have, further, as yet unpublished prospective evidence that hemoglobin A1c may be involved in prediabetic individuals in similar autoimmune complex, resulting in increased all-cause mortality.

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## The relationship between mean platelet volume and high on-treatment platelet reactivity

To the Editor,

We read the article by Jakl et al. (1) published in February issue of *The Anatolian Journal of Cardiology* 2014; 14: 85 with great interest. They assessed the relationship between mean platelet volume (MPV), platelet count, platelet hematocrit and high on-treatment platelet reactivity (HTPR) in patients with acute coronary syndrome treated by percutaneous coronary intervention. Study patients were divided into groups according to their response to antiplatelet treatment: normal response to antiplatelet treatment, poor responsiveness to aspirin (PRA), poor responsiveness to clopidogrel (PRC), and dual (both aspirin and clopidogrel) poor responsiveness (DPR). MPV and platelet hematocrit were increased in patients with DPR, PRA and PRC. Platelet count was increased only in patients with PRC. Moreover, they found that MPV and platelet count was predictors of HTPR.

This is an interesting study. However, we want to make minor criticism about this study from methodological aspect.

Firstly, the method used for MPV assessment is not clear. They didn't mention about the tube (EDTA or citrate) that blood sample collected. It is clear that MPV increases over time in EDTA-anticoagulated samples and this increase was shown to be proportional with the delay in time between sample collection and laboratory analysis (2). With impedance counting, the MPV increases over time as platelets swell in EDTA, with increases of 7.9% within 30 min and an overall increase of 13.4% over 24 h, although the majority of this increase occurs within the first 6 h (3). The recommended optimal measuring time of MPV is 2 h minutes after venipuncture (3). It would be better if they clarified this situation in the paper.

Secondly, it has to be kept in mind that there are significant associations of MPV with some cardiovascular conditions like smoking, obesity, hyperlipidemia, hypertension, coronary artery disease, metabolic syndrome, statin use and atrial fibrillation (4-6). They only compared the groups (DPR or not, PRA or not and PRC or not). We can suspect higher incidence of associated cardiovascular risk factors in patients with acute coronary syndrome treated by percutaneous coronary intervention. It has been shown that obesity, hypertension, hyperlipidemia, smoking, metabolic syndrome and atrial fibrillation increase MPV values (4-6). It has also been shown that statin use can affect MPV values (7). Absolutely, these factors should have been considered in assessment. The difference of MPV between groups might be due to these associated factors in patients with acute coronary syndrome treated by percutaneous coronary intervention. Otherwise regression analysis must have been done to eliminate effect of these factors on MPV.

MPV is universally available with routine blood counts by automated hemograms and a simple and easy method of assessing platelet function. In comparison to smaller ones, larger platelets have more granules, aggregate more rapidly with collagen, have higher thromboxane A2 level and express more glycoprotein Ib and IIb/IIIa receptors (4, 8). We believe that MPV can be affected by many inflammatory and cardiovascular risk factors. Because of that all confounding factors must be taken into account. Also standardized methods should be used for assessment of MPV.

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