vascular lipoprotein complex formation resulting in endothelial dysfunction, as best observed in the instance of the formation of hemoglobin $A1_c$.

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 We have, further, as yet unpublished prospective evidence that hemoglobin A1c may be involved in prediabetic individuals in similar autoimmune complex, resulting in increased all-cause mortality.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 be 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 to taken into account. Also standardized methods should be used for assessment of MPV.

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Author`s Reply

To the Editor,

We are pleased by interest and valuable comments by authors. They correctly pointed out some unclarities in our letter, as some information were not presented due to limited extend of scientific letter format (1). We are glad to supplement this information here.

The first remark was about the method used for blood sample collection. EDTA containing tubes were used for mean platelet volume and platelet count examination. All samples were processed in less than 2 hours. According to the literature (2) and our experience in such settings the mean platelet volume increase does not excess 10%. Moreover, using a citrate can result in changes of mean platelet count (2). Samples for aggregometry were collected in hirudine, which seems to produce better results than citrate or lepirudine and is generally available for this method (3).

Another remark concerned the potential bias caused by impact of comorbidities on mean platelet volume. In his letter a detailed summary of such confounding factors, namely smoking, obesity, hyperlipidemia, hypertension, coronary artery disease, metabolic syndrome, statin use and atrial fibrillation is presented. These associations correlate with finding that patients with higher mean platelet volume are in higher risk of ischemic heart disease (4) suggests that such bias must be excluded.

We analyzed the influence of smoking, diabetes, atrial fibrillation, left ventricle systolic dysfunction (5) [ejection fraction <40% and inflammation (6) (hs-CRP >20 mg/L (7)]. C-reactive protein was measured using CRPL3 Tina-quant C-Reactive Protein Gen. 3 assays by Roche Diagnostics, Germany. Statin use was not added in statistical analysis, because only three patients were not treated using these agents. None of risk factors mentioned above was associated with increased mean platelet volume (Table 1). Regression analysis was not beneficial either.

Therefore we expect that the relation of mean platelet volume to both high on-treatment platelet reactivity and increased mortality is rather based on alteration of platelet functions than by concomitant association with another risk factor. Unfortunately, number of patients is insufficient for detailed statistical evaluation. This study also cannot explain the exact etiology of platelet function impairment. Despite these limitations the study suggests that mean platelet volume can be used as marker of high on-treatment platelet reactivity and for risk stratification.

Table 1. Mean platelet volume according to presence of comorbidities

	Mean platelet volume (f)		
	Risk factor present	Risk factor not present	*P*
LV EF <40% (n=52)	10.9±0.8	10.7±1.2	NS
Atrial fibrillation (n=22)	11.1±0.9	10.6±1.2	NS
Diabetes mellitus (n=48)	10.8±1.7	10.6±0.9	NS
Smoking habit (n=104)	10.7±0.9	10.5±1.3	NS
hs-CRP <20 mg/L (n=27)	10.8±1.5	10.6±1.0	NS

LV EF - left ventricle ejection fraction

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Factors influencing the use of ambulance among patients with acute coronary syndrome: results of two centers in Turkey

Dear Editor,

We have read article published in the Anatolian Journal of Cardiology about the use of ambulance among patients with acute coronary syndrome (ACS) by Demirkan et al. (1) with a great interest. In this article, it was determined that large proportion of patients with ACS were transported to hospitals in unsafe conditions instead of using ambulance. In the conclusion part; the importance of health educational programs for the formation of a behavioral changes in using ambulance and the need for a larger study were emphasized.

We are working in the Department of Paramedics, in our Eskişehir Osmangazi University, which had been founded 16 years ago. After reading the article; we decided to mention about paramedics, who are educated for working in ambulance services.

Paramedic profession was found in USA in 1970's in prehospital emergency settings. Paramedics work on the scene of emergencies to assess a patient's condition, provide medical care at an advanced life support level in the pre-hospital environment at the point of illness or injury and also transport the patient to a hospital if necessary (2).