Dear Editor:

We have recently read with great interest the clinical report by Liu T and colleagues [1] concerning “Increased serum HMGB1 level may predict the fatal outcomes in patients with chronic heart failure”. They indicate that serum HMGB1 levels were inversely correlated with LVEF and positively correlated with NT-pro-BNP and may be an alternative indicator in the risk stratification of patients with chronic HF (heart failure).

In this paper, although the authors come to a conclusion that serum HMGB1 levels were correlated with the risk stratification of patients with chronic HF, the exact mechanisms are totally unknown. Besides, the enrolled 94 patients are all due to ischemic cardiomyopathy, it actually provides a link between HMGB1 and ischemic heart disease. Here we propose that endothelial cells may mediate the effect of HMGB1 in ischemic heart disease. Besides, HMGB1 is a redox sensitive protein with three cysteine residues at positions 23, 45 and 64, and can also inhibit the migration of endothelial cells. Actually, to some extent, the suppressed migration of endothelial cells may account for the bad effects of HMGB1 in ischemic heart disease. However, recently, we found that HMGB1 can impair endothelial cell function by increasing the permeability of endothelial cells through TLR4/caveolin-1 pathway [9], which gives us a novel insight of HMGB1’s role in ischemic heart disease. So the coronary artery endothelial cells or the microcirculation endothelial cells in myocardium from patients of ischemic heart disease could be affected directly by increased serum HMGB1. Subsequently, it is possible that HMGB1 impairs the function of coronary artery endothelial cells and the microcirculation endothelial cells in myocardium at least increase their permeability through TLR4 pathway and increased permeability can promote more cytokines (tumor necrotic factor-α (TNF-α) and the interleukin (IL)-6) migrating to myocardium tissues from microvessel system, which can damage myocardium further. The higher the serum HMGB1 is, the worse the prognosis of ischemic heart disease patients is. This may explain the increased mortality rates in patients with ischemic heart disease in one aspect [3].

So, endothelial cells can be as an important object to research in HMGB1 mediated ischemic heart disease. Besides, HMGB1 is a redox sensitive protein with three cysteine residues at positions 23, 45 and 106. Its activity can be different with different redox states [10]. Some activities can be different with different redox states [10]. However, we do not know the exact state of the increased serum HMGB1 in ischemic heart disease, which will bring us difficulties in investigating the specific mechanisms underlying such phenomenon. Thus, the redox state of serum HMGB1 should also be clarified in the future studies, which can help us in knowing this biomarker well.

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Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

References