

# Biosensing of periprocedural events in acute ST-segment elevation myocardial infarction patients with the erythrocyte-derived microparticles

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## Abstract

The short commentary is depicted the role of the circulating number of red blood cell (RBC) microparticles (MPs) as predictive biomarker in acute myocardial infarction patients after primary percutaneous coronary intervention (PCI). The commonly used cardiac biomarkers (i.e., troponins, creatine kinase-myocardial band isoenzymes, myoglobin, heart-type fatty acid-binding protein, copeptin and B-type natriuretic peptide) have now exhibited broad spectrum limitations regarding short-term and long-term mortality rate. Recent clinical studies have shown that the number of RBC-MPs has increased in acute myocardial infarction as compared to healthy volunteers and patients with unstable angina, associated with the extent of myocardial damage and have potential adverse vascular and thrombotic effects. It has been suggested that the number of RBC-MPs might be better predictor compared to other cardiac biomarkers in scintigraphically measured infarct size, periprocedural left ventricular ejection fraction and survival rate.

Microvascular obstruction has remained a prognostic importance for short-term and long-term periprocedural survival after acute ST-segment elevation myocardial infarction (STEMI) [1,2]. Although there is a large body of evidence regarding utility of biomarkers of cardiac injury in predicting myocardial functional recovery [3-5], the prognostic information of commonly used cardiac biomarkers (i.e., troponins, creatine kinase-myocardial band isoenzymes, and their combinations) regarding mortality rate is still controversial [6-8]. Indeed, troponin I is an highly sensitive marker of myocardial necrosis or even very minor reversible myocardial injury caused by percutaneous coronary intervention (PCI), which did not influence the death rate [9].

However, in the Selective Inhibition of Delta-protein Kinase C for the Reduction of Infarct Size in Acute Myocardial Infarction (PROTECTION-AMI) trial were determined that only baseline left ventricular ejection fraction (LVEF), infarct size and infarct heterogeneity independently predicted 90-day LVEF, though other biomarkers did not [3]. In the EVOLVE (Evaluation Of MCC-135 for Left Ventricular Salvage in Acute Myocardial Infarction) trial, elevated troponin T level was associated with increased 180-day composite clinical events and independently predicted several adverse events, but not death [10]. In contrast, Gollop *et al.* [11] reported that an elevation in CK-MB was best predictor of adverse events including death compared with troponins in post-PCI individuals. Thus, actual findings suggest that cardiac biomarker of injury (i.e., troponins, creatinine kinase MB isoenzyme, and probably myoglobin) might no longer be the optimal early predictors in STEMI patients undergoing primary PCI, while they are able to depict worsening myocardial perfusion, myocardial infarct size, cardiac function and postponed left ventricular remodeling. Moreover, as a prognostic marker, creatinine kinase MB isoenzyme measured on admission was superior to cardiac troponin using a high-sensitivity assay, NTproBNP measurement on admission, but myoglobin, heart-type fatty acid-binding protein, copeptin and B-type

natriuretic peptide were prognostically equivalent [12]. Consequently, to improve predictive approaches based on biomarker measurement in PCI patients, discovery of novel biomarkers maximally attributed solely to each individual after PCI is required. Formerly cell-derived microparticles (MPs) were determined as cell debris without any diagnostic and predictive information, but now they are considered biomarkers in cardiovascular and metabolic disease including atherosclerosis, unstable angina pectoris, hypertension, heart failure, arrhythmia, thromboembolism, metabolic syndrome, and diabetes, as well as in subjects with implanted cardiac assist devices [11,13-22].

The majority investigations have now addressed to the endothelial cell-derived MPs, which are marker of endothelial dysfunction and cardiovascular death [23,24], while MPs originated from other cells (i.e., red blood cells) have exhibited a relation to severity of atherosclerosis and coronary obstruction [25]. Recent studies have shown that the circulating number of endothelial cell-derived MPs originated from activated or apoptotic cells may be markers with powerful independent predictive value in patients with acute myocardial infarction after PCI, although utility of endothelial cell-derived MP measurement is not strongly determined [26]. However, it has suggested that endothelial cell-derived MP assay could be incorporated into multiple biomarkers strategy based on troponins and creatinine kinase MB isoenzyme measurement to improve risk stratification for cardiovascular events

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in patients at high risk for cardiac death and cardiovascular events [27].

The number of red blood cell (RBC) MPs has increased in acute myocardial infarction as compared to healthy volunteers and patients with unstable angina and probably associated with the extent of myocardial damage. RBC-MPs have potential adverse vascular effects and they have been shown to be elevated in ST elevation myocardial infarction (STEMI) [28]. There is evidence regarding close relationship between circulating number of RBC-MPs and biochemical infarct size, circulating troponins and reverse of ischemia-induced myocardial dysfunction [28], although the exact pathophysiologic routes for these interactions remain to be uncertain. Probably, pro-coagulant thrombotic activity of RBC-MPs and their ability inducing platelet activation and aggregation might explain the role of them in the pathogenesis of periprocedural microvascular obstruction and left ventricular remodeling [29,30]. Therefore, RBC-MPs are able to activate endothelium in visceral organs and thereby influence vasoconstriction and direct injury of them [31,32]. Finally, RBC-MPs are player in the myocardial reperfusion injury, which attenuates the benefit of PCI after acute myocardial infarction. Whether RBC-MPs would be potentially useful for risk stratification after primary PCI is not fully clear. Therefore, it is not understood whether RBC-MP count would be prognostically superior to high-sensitivity cardiac troponins, creatinine kinase MB isoenzyme, myoglobin, natriuretic peptides, copeptin, heart-type fatty acid-binding protein, and scintigraphically measured infarct size, which remains a better correlate of 1-year mortality than either biomarkers. However, measurement of circulating RBC-MP number after primary PCI appears to be promising because lack of individualized biomarkers with predictive value regarding survival in subjects with microvascular obstruction remains to be challenged. All these findings require more investigations in future.

## Conclusion

There are no strong evidence regarding the advantages of periprocedural use of RBC-MPs compared to widely used biomarkers including high-sensitivity cardiac troponins, creatinine kinase MB isoenzyme during PCI to provide prognostic information about the degree of myocardial injury and risk of morbidity and mortality. However, the need of discovery of novel biomarker with higher predictive value is obvious fact. RBC-MPs could be discussed as attempt to individualize risk stratification amongst acute ST-segment elevation myocardial infarction patients after primary PCI, because other routinely used biomarkers have exhibited some serious limitations. In future, more investigations are required to explain in detail the role of the number of RBC-MPs in prediction of survival amongst acute ST-segment elevation myocardial infarction patients after primary PCI.

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## Conflict of interests

None declared

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