Editorial

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Impaired Phenotype of Endothelial Cell-Derived Micro Particles: The Missed Link in Heart Failure Development?

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Abstract

Chronic heart failure (HF) is considered important clinical setting associated with increased morbidity and mortality rates. Biomarkers are widely used aimed improve diagnostics and prediction of HF, while several biomarkers, i.e., natriuretic peptides, galectin-3, ST2, might exhibit similar prognostication for both HF with reduced (HFrEF) and preserved ejection fraction (HFpEF). Based on the currently available data, endothelial cell-derived micro particles (MPs) may consider a biomarker of endothelial dysfunction. Moreover, imbalance between endothelial cell-derived MPs predominantly associated with increased apoptotic derived MPs and decreased MPs shedded from activated endothelial cells (determined as "impaired phenotype") might be a maker of HF development and progression. Probably, "impaired phenotype" of circulating endothelial cell-derived MPs could independently predict clinical outcomes in HF beyond traditional cardiovascular risk factors.

Keywords: Heart failure; Micro particles; Endothelial cells; Endothelial dysfunction; Prediction; Biomarkers

Editorial

Heart failure (HF) is concerned a major health problem associated with high prevalence, morbidity, mortality, and financial expenditures [1], whereas mortality rate have exhibited a tendency to decline over the past decade in the developing countries [2]. Over the last decade substantial changing in HF phenotype' presentation has found [3]. Recent studies have revealed that the newly diagnosed incidences of HF with reduced ejection faction (HFrEF) have declined, although frequency of HF with preserved ejection fraction (HFpEF) appears to be araised [4-6]. Most interestingly, the clinical outcomes including mortality and re-admission in patients with HFpEF were not better than in individuals with HFrEF [7, 8]. Nevertheless, both HF phenotype' presentations have sufficiently distinguished in CV risk factors, metabolic co-morbidities, and aging [9]. Whether cardiovascular (CV) and metabolic risk factors may substantially change the incidence of HF remains to be controversial [10, 11].

Current HF clinical guidelines are recommended to use limited numerous of biomarkers (natriuretic peptides, galectin-3, cardiac troponins, ST2) to risk stratify the patients with acute, acutely decompensated, and chronic HF, as well as probably to biomarker-guided therapy [12, 13]. However, biomarker determinations for individuals with both HF phenotypes (HFrEF and HFpEF) undoubtedly require prospective validation due to concerning in clarification of useful regarding predicting prognosis [14, 15]. In this context, the discovery of novel biomarkers, which could have higher predictive value irrespective recently defined limitations suitable for "old" biomarkers, appears to be attractive.

Micro particles (MPs) are defined small phospholipid-rich micro vesicle (diameter less 100 nm) realized from various types of cells due to apoptosis or activation by several stimuli [16]. Depending of their origin (deriving from activated cells or apoptotic cells) MPs may exhibit controversial effects [17]. Indeed, activated endothelial cell MPs contribute to repair capabilities regarding vasculature, whereas apoptotic endothelial cell MPs may directly and indirectly worse endothelial integrity and functionality [17, 18]. MPs are involved in pathophysiology of wide spectrum states including inflammation, blood coagulation/thrombosis, cell cooperation, cell differentiation/growth, malignancy/tumor progression, metastasis, angiogenesis/neovascularization [17, 19-21].

High circulating levels of MPs deriving mainly from erythrocytes, mononuclears, endothelial cells and platelets were found in individuals who were suspected to have CV disease or exhibited CV/metabolic risk factors, as well as in patients with known CV disease. Although erythrocytes- and platelets-derived MPs widely contributed to coagulation cascade and inflammation that are considered a clue of atherothrombosis, myocardial infarction, ischemia-induced cardiac dysfunction [20, 21], endothelial cell-derived MPs were found to be a marker of endothelial dysfunction and predictor of HF advance and development [17]. Therefore, recent studies have shown a causality role of circulating MPs derived from endothelial cells in atherosclerosis, endothelial dysfunction, HF, myocardial infarction, thromboembolism, diabetes-induced vasculopathy, renal disease [22-26]. It has been suggested that some triggers, i.e., neurohormones, active molecules, growth factors, cytokines, free radicals, might effect on repair ability of progenitor cells through epigenetic modifications contributing to MP secretion. Finally,

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MPs may link activity of endogenous repair systems and CV risk factors [27].

Recently it has been reported that imbalance in numerous of circulating MPs derived from apoptotic and activated endothelial cells (determined as "impaired phenotype") might be not only biomarker of endothelial dysfunction in HF patients and predictor of HF phenotypes' development, but it exhibited predictive value in individuals with cardiac dysfunction [23, 28-30]. Indeed, elevated level of apoptotic endothelial cell-derived MPs associated with decreased number of angiogenic MPs shadding from activated endothelial cells are discussed a common attribute of cardiac dysfunction beyond etiology and concomitant risk factors. Interestingly, impaired phenotype of MPs pattern might determine in several states including non-CV disease, such as metabolic syndrome, obesity, insulin resistance [29]. Whether impaired phenotype of MPs might play a causality role in CV disease including HF or, in contrast, underdiagnosed CV disease are prior imbalance in MPs' pattern is not fully clear [31].

Updating our knowledge, pattern of endothelial cell-derived MPs might be a secondary target of HF medical care to improve clinical outcomes and individualize the treatment strategy of cardiac dysfunction depending on HF phenotypes. Unfortunately, there is not clinical evidence regarding useful of impaired MPs' pattern in prediction of HF phenotype development in greater patient cohort. Therefore, direct comparison of predictive values regarding MPs' pattern and other HF biomarkers are needed to be performed. The large clinical trials are required to explain the role of endothelial cell-derived MPs' pattern as biomarker of HF phenotypes, HF development, and probably HF-related outcomes.

In conclusion, endothelial cell-derived MPs have promise in the clinical aspects linking epigenetic regulation of HF phenotypes, CV risk factors, and individual prognostication toward HF evolution. The practical use of measurements of MPs' numbers appears to be interesting, whereas there are several limitations regarding standardization of the appropriate methods and interpretation of data received. However, endothelial cell-derived MPs interact in HF manifestation and development and may probably have independent predictive value. More investigations are needed to identify an unequivocal association between "impaired phenotype" of endothelial cell-derived MPs and prognosis in HF individuals.

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