



## Are Endothelial Cell-Derived Microparticles Predictive Biomarkers in Cardiovascular Diseases?

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Received date: Sep 14,2020;Accepted date: Oct 16,2020;Published date: Oct 23,2020

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### Abstract

Endothelial dysfunction is involved in the various stages of cardiovascular (CV) disease development. Microparticles (MPs) originated from endothelial cells as biological markers of endothelial injury and repair could appear sufficient predictor of clinical outcomes and probable they might use in biomarker-guided therapy. Apoptotic endothelial cell-derived MPs are able to directly mediate a microvascular inflammation and worsening of endothelial integrity. In contrast, endothelial MPs originated from activated endothelial cells might contribute vascular repair and vasodilatation. It has been suggested that endothelial cells release phenotypically and quantitatively distinct endothelial MPs in activation and apoptosis, and that the phenotype of MP pattern can provide useful information reflecting the nature of endothelial injury. Editorial comment is discussed the role of impaired immune pattern of circulating endothelial cell-derived MPs as a personalized marker of vascular remodelling or endothelial dysfunction among CV disease persons.

**Keywords:** Cardiovascular disease; Endothelial dysfunction; Endothelial cell-derived micro particles; Clinical outcomes; Prediction

### Introduction

Endothelial-derived microparticles (MPs) are defined as heterogeneous population of plasma membrane vesicles (diameter 100-1000 nm) produced by apoptotic or activated cells originated from vascular endothelium or circulating endothelial cells [1]. They are derived from cell membrane surfaces via blebbing and shedding in physiological (stress, microenvironmental stimulation) and pathological (coagulation/thrombosis, endotoxemia, endothelial shear stress, ischemic/hypoxic injury, inflammation, and malignancy) conditions and are present in low concentrations in normal plasma [2]. Recent investigations have been shown that endothelial-derived MPs are discussed powerful paracrine regulators of target cell functions affected cell differentiation, tissue growth and reparation, vasculogenesis, vasodilation, inflammation, apoptosis, infection, and malignancy [3-5]. Indeed, MPs acts in intercellular information exchange through transfer of active molecules, microRNA, peptides, hormones, inflammatory factors, growth factors, etc [6,7]. It has been suggested that endothelial cells release phenotypically and quantitatively distinct endothelial MPs in activation and apoptosis, and that the phenotype of MP pattern can provide useful information reflecting the nature of endothelial injury. However, the many phases of biological function of circulating endothelial MPs are still not recognized and requires scrutinises.

There is large body of evidences regarding an association between an immune pattern of MPs originated from endothelial cells and

nature evolution of various diseases including cardiovascular (CV) and rheumatic diseases, cancer, sepsis, eclampsia, autoimmune and metabolic states, etc [8-11]. Elevated level of apoptotic endothelial cell-derived MPs was frequently found in CV diseases including heart failure and was related to endothelial dysfunction [12]. In fact, apoptotic endothelial cell-derived MPs are able to directly mediate a microvascular inflammation and worsening of endothelial integrity [13]. Nevertheless, depletion of potentially pro-angiogenic pool of endothelial MPs originated from activated endothelial cells is discussed a marker of endothelial injury and insufficient repair activity [14]. Recent clinical studies have shown that elevated CD31<sup>+</sup>/annexin V<sup>+</sup> MPs to CD62E<sup>+</sup> MPs ratio is an indicator of impaired immune phenotype of endothelial cell-derived MPs, which allows determining the pattern of MPs in dysmetabolic disorder patients including diabetes mellitus and metabolic syndrome [15]. Therefore, the levels of circulating endothelial cell-derived apoptotic MPs are useful biomarkers for predicting the presence of cardiorenal disease [16], ventricular arrhythmia and sudden cardiac death [17].

Because endothelial dysfunction is involved in the development of CV diseases, MPs originated from endothelial cells as biological markers of endothelial injury and repair could appear sufficient predictor of clinical outcomes and probable they might use in biomarker-guided therapy. Indeed, elevated level of apoptotic endothelial cell-derived MPs have demonstrated their prediction for CV disease development and clinical outcomes [18-20], but the role of decreased circulation level of activated endothelial cell-derived MPs is still not clear. Probably CV disease development is the result of both disease-specific and traditional CV risk factors contributed in imbalance between apoptotic endothelial-derived MPs and activated endothelial cell-derived MPs that leads to impaired immune MP phenotype. Recent clinical studies have shown that high ratio estimated as apoptotic endothelial cell-derived MPs to activated endothelial cell-derived MPs and/or endothelial progenitor cells predicts cardiac failure-related death, all-cause mortality, and risk of recurrent hospitalization due to stable cardiac failure and acutely decompensated cardiac failure [21,22].

Whether impaired phenotype of circulating MPs is useful to predict CV events in patients without previous documented CV and metabolic diseases is not still clear. It has been postulated that pre-existing apoptotic phenotype of endothelial MPs could discuss an individual marker beyond other CV risk factors, such as dyslipidemia, obesity, diabetes, and hypertension. If this assumption is correct, the immune phenotype of endothelial-cell-derived MP is available for the risk stratification among subjects in general population.

In conclusion, impaired immune pattern of circulating endothelial cell-derived MPs might be consider a personalized marker of vascular

remodelling or endothelial dysfunction among CV disease persons, while evidence of predictive value of this marker for patients in general population is limited. More clinical trials with higher statistical power are required to explain these findings and their clinical significance.

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