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Abstract:

Circulating extracellular vesicles (EVs) have a great impact on human health as biomarkers and messengers in intercellular signalling. We aimed to determine how the miRNA profile of circulating EVs during an acute coronary event interferes with the vasculogenic potential of endothelial cells (EC).

EVs were purified from the plasma of patients in the acute phase of non-ST segment elevation myocardial infarction (NSTEMI, n = 33) and from healthy donors (n = 19) used as a control group. Human ECs were treated with EV suspension (5×10^7 particles/cm^2) and tested for their vasculogenic potential and mRNA expression. The EV miRNA profile was determined by miRNA array. EV levels were markedly increased in the plasma of NSTEMI ($2.3 \times 10^{11} \pm 1.5 \times 10^{10}$ particles/mL) versus control ($1.2 \times 10^{11} \pm 1.1 \times 10^{10}$ particles/mL; p = .02). Treatment of ECs with control EVs increased migration, tube formation, and shaped more branched vessel-like structures in comparison to Sham-treated ECs. Nevertheless, EVs from NSTEMI lacked their vasculogenic potential. Network analysis of EV miRNA and EC mRNA expression revealed a correlation of increased miR-199a-3p and miR-125a-5p expression with a decrease in components involved in EC sprout and stabilization. Combined therapy with miR-199a-3p and miR-125a-5p decreased EC vasculogenic potential. Moreover, anti-miRNA therapy with a combination of anti-miR-125a-5p and anti-miR-199a-3p restored the vasculogenic potential impaired by NSTEMI EVs.

Circulating EVs play an important role in the control of angiogenesis. However, in the acute phase of NSTEMI, intercellular communication via EV is modified and loses its ability to generate new blood vessels. The loss of angiogenic capacity of EVs during NSTEMI may be an important player in the disease progression and outcomes.