Plasma-derived exosomes from patients with obstructive sleep apnea contributes to cardiovascular disease through miR-181b-5p-TNF-α signaling

Objective: Obstructive sleep apnea (OSA) is characterized by intermittent hypoxemia with re-oxygenation (IHR) leading to systemic inflammation, and associated increased risk for cardiovascular diseases (CVD). We hypothesized that plasma-derived exosomes may contribute to CVD in OSA through targeting tumor necrosis factor-α via microRNA (miR)-181b-5p.

Method: Exosomes and peripheral blood mononuclear cells (PBMCs) from 38 OSA patients with CVD, 34 OSA patients without CVD and 14 subjects with primary snoring (PS) were assessed.

Results: TNF-α gene expression levels of PBMCs and the release of TNF-α from human umbilical vein endothelial cell lines (HUVEC) in response to stimuli with plasma-derived exosomes were both increased in OSA patients versus PS subjects, and further increased in OSA patients with CVD versus those without CVD, while miR181b-5p gene expression of PBMCs and cell viability of HUVEC were decreased. TNF-α release with exosome stimulation was positively correlated with snoring index and left atrial size, and negatively correlated with minimum oxyhemoglobin saturation. Plasma-derived exosomes from OSA patients inhibited gene expressions of several cell junction-related molecules, including ZO-1, ZO-2, Nectin-3 Occludin, β-catenin, VE-cadherin, PECAM-1, and GJA1, and augmented endothelial monolayer permeability of HUVEC versus PS group.

Conclusions: Exosome-mediated miR-181b inhibition via targeting TNF-α is associated with the development of CVD in OSA patients, probably through destroying cell barrier and enhancing permeability of endothelium.

中文題目：源自阻塞性睡眠呼吸中止症患者血漿的外泌體會透過 miR-181b-5p-TNF-α 訊號傳導途徑導致心血管疾病的發生

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