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MICROVASCULAR ENDOTHELIAL DYSFUNCTION
IN VASCULAR SENESCENCE AND DISEASE

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Cardiovascular disease (CVD) is the leading cause of death worldwide. According to the World Health Organization, it accounts for approximately 17.9 million deaths annually (WHO, 2019). Endothelial dysfunction is one of the earliest signs of CVD before clinical diagnosis. Research suggests that vascular senescence is a major initiator of cardiovascular disease.

Pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs) are important inflammatory signals. PAMPs arise from microbial action, whereas DAMPs are released during tissue damage. Their binding to pattern recognition receptors (PRRs) can induce oxidative stress, disturbs redox balance, and promotes chronic inflammation. Excess reactive oxygen species (ROS) can also modify self-proteins, creating DAMP-like signals that trigger immune responses.

Another key mediator is the nuclear factor erythroid 2-related factor 2 (Nrf2). Together with heme oxygenase-1 (HO-1), it protects against oxidative stress and cellular senescence. Oxidized low-density lipoprotein (OxLDL) and Toll-like receptor 4 (TLR-4) activate inflammatory pathways, including NF- κ B, leading to the release of IL-1 β and IL-18, inflammation, and pyroptosis.

The gut microbiota also influences blood pressure and vascular health. Beneficial metabolites, produced from butyrate-producing bacteria, improve vascular tone, reduce inflammation, and increase arterial elasticity. Greater microbial diversity is associated with lower arterial stiffness. Studies have also linked gut bacteria to cardiovascular risk in patients undergoing hemodialysis (Menni et al., 2018; Biruete et al., 2019).

Aging reduces endothelial repair capacity and contributes to vascular dysfunction. Genetic factors, diabetes, and arterial wall thickening further worsen endothelial function. Studies have shown that regular exercise, dietary control, and some nutritional factors, such as soy-derived equol, may help reduce arterial stiffness and improve endothelial function (Abd et al., 2020; Lee et al., 2021). Low- and moderate-intensity exercises may be especially beneficial for older adults and patients with type 2 diabetes.

These findings suggest that microcirculation may become an important target for both pharmacological and non-pharmacological treatments of arterial hypertension and other cardiovascular diseases.