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EDITORIAL

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All disease stems from vessels

Although rapid advances in vascular biology and therapeutics in the last several decades have brought revolutionary improvement to morbidity and mortality of cardiovascular disease (CVD), vascular dysfunction still plays a central role in the vast majority of diseases. We here put forward a novel concept "all disease stems from vessels,"[1] and discuss the importance of vascular function in relation to the pathogenesis of range of various diseases.

1 | THE BLOOD VESSEL IS THE CANDLE OF LIFE

The blood vessel is a remarkable organ of the human body, where nutrients and metabolites are exchanged and transported. Its normal structure and function play a critical role in the maintenance of homeostasis of the body. With advancing age and the accumulation of diverse risk factors, the structure and function of blood vessels undergo a series of degenerative or pathological alterations, which lead to vascular structural remodeling and dysfunction, and eventually the occurrence of numerous diseases. That is, the health of blood vessels determines the health of individuals. Therefore, a better understanding of the vascular dysfunction process in different diseases is principle to finding and evaluating both lifestyle and pharmacological countermeasures to treat vascular injury.

2 | THE BLOOD VESSEL IS THE VITAL BRIDGE CONNECTING ALL SYSTEMS AND TISSUES OF THE HUMAN BODY

Throughout the eight systems of the human body, blood vessels are ubiquitous and serve as a huge bridge tying all the tissues together. Blood passes through the vessels from heart to brain, lungs, gastrointestinal tract, kidneys, and bones and muscles in order to facilitate the rapid distribution and efficient transport of nutrients, including glucose, amino acids, or lipids, and the removal of waste products for processing elsewhere, such as lactic acid to the liver or urea to the kidneys (Figure 1). A slight alteration in vessels may affect the situation as a whole.

3 | VASCULAR DYSFUNCTION AND STRUCTURAL ABNORMALITY LEAD TO ALL DISEASE

Vascular dysfunction and structural abnormality, characterized by large elastic artery stiffening and endothelial dysfunction, are independent predictors of future CVD diagnosis and an early finding of the development of CVD. In fact, not limited to traditional CVD, these structural and functional changes in the vessels also contribute to other diseases that affect the life span and health span of humans, including cancer, diabetes, neurodegenerative diseases, kidney diseases, and eye disease. Thus, vascular dysfunction serves as a common basis of different kinds of diseases.[1]

CVD is the most terrible killer that endangers people's health and is closely bound with vascular dysfunction. Interestingly, vascular dysfunction is present in the absence of clinical CVD and conventional CVD risk factors. Before the onset of CVD, endothelial cells (ECs) and vascular smooth muscle cells (VSMCs) are under oxidative stress, inflammatory cells are activated, and inflammatory adhesion molecules are secreted (IL-6, TNF-α, ICAM-1, VCAM-1, MCP-1, etc). In the subcellular organelles, mitochondrial dysfunction plays a fundamental role in atherosclerosis etiology, with imbalance of reactive oxygen species production, respiratory chain disorder, and defective mitophagy.[2,3] All of these lead to vasodilation and vasoconstriction dysfunction and eventually result in the occurrence of CVD.

Cancer is another huge health issue that threatens our lives. Vascular endothelial cells located in the tumor microenvironment are involved in tumor vascularization for tumor cells growth, infiltration, and recurrence, by releasing a series of chemokines and cytokines (VEGF, FGF, MMP, IL, TGF-β1, etc) and interacting with tumor stem cells and immune cells. The important role of vessels and vascular cells strongly supports the concept that vascular dysfunction may be a precursor to the development of cancer.[4]

Diabetes is a serious and widespread condition with more than 500 million prevalent cases worldwide. ECs in a high-sugar environment showed abnormal metabolic state: the oxidation of glucose results in the formation of glucuronide, accompanied by a large amount of reactive oxygen species production. Non-enzymatic glycosylation of proteins generates a large number of advanced glycation end-products, which further leads to EC injury and deterioration

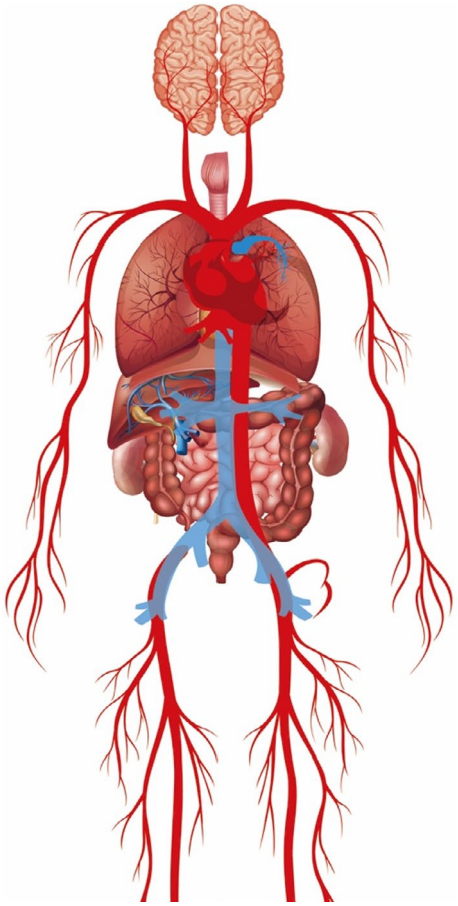

FIGURE 1 Blood vessels serve as a huge bridge connecting all the tissues and organs of human body. [Colour figure can be viewed at wileyonlinelibrary.com]

of endothelial function.[5] It is concluded that vascular dysfunction is a primary effect of elevated glucose levels.

Neurodegenerative diseases, such as Alzheimer's disease and vascular dementia, are closely associated with cerebrovascular dysfunction, including structural changes of vascular wall, degenerated capillaries, vascular fibrosis, and calcification, while treatment targeting vascular ECs shows a favorable effect on alleviating the symptoms of the disease.[6]

Patients with kidney disease develop microinflammation at an early stage, which is due to the release and activation of inflammatory factors mediated by $CD14^+/CD16^+$ cells and the exacerbation of oxidative stress response, and finally results in EC apoptosis and vascular dysfunction.[7]

Based on current literature and our studies, we highlight the central role of vessels and propose that vascular dysfunction and structural abnormality are the sources of all diseases. Collectively, vascular dysfunction leads to circulating factors disorder and aberrant molecular and cellular processes. The hierarchical regulatory cascade promotes the development of a wide range of pathophysiological manifestations.

5 | FUTURE DIRECTIONS AND PERSPECTIVES

All disease stems from vessels. Taken together, instead of targeting a single disease, interventions that target fundamental vascular dysfunction can potentially prevent and treat a range of vascular pathologies and various diseases simultaneously. Accordingly, a brand new discipline system of pan-vascular diseases should be established. The discovery and development of more pharmacological and non-pharmacological interventions aimed at vascular function are urgently needed. Further basic research and translational studies should identify and develop appropriate countermeasures against vascular dysfunction.

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CONFLICTS OF INTEREST

Nothing to disclose.

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