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Editorial

The big problem of small vessel disease

In this issue of *American Heart Journal Plus: Cardiology Research and Practice* small vessel disease, a ubiquitous pathologic process, is discussed from a variety of different perspectives. Small vessel disease is a driving force for organ dysfunction involving the heart, lung, kidney, eye, brain, and peripheral muscle. Individuals with small vessel disease share predisposing factors including hypertension, diabetes, hyperlipidemia, and smoking, and can manifest signs and symptoms of the disease in more than one organ, supporting the notion that it is a global pathologic process [1]. While small vessel disease is associated with significant morbidity and mortality, there is no specific effective treatment due, at least in part, to insufficient understanding of the mechanisms involved. By sharing what is known amongst investigators who study small vessel disease in different organs, improved understanding of the disease can ultimately inform novel treatments.

In this issue, Iyer and colleagues review data on small vessel disease of the eye, namely, diabetic retinopathy, a significant cause of blindness [2]. They discuss the results of several large clinical trials that report small vessel remodeling in the retina as an independent risk factor for the development of cardiovascular disease, including myocardial infarction and death, especially in women. Microvascular changes in diabetic retinopathy occur secondary to chronically uncontrolled blood sugar levels and lead to structural and functional abnormalities of the endothelium. As with small vessel disease of the brain, kidney and heart, inflammation and ischemia are key pathologic processes, and the mainstay of systemic treatment is to control blood pressure and blood sugar levels.

Small vessel disease of the brain is discussed by Meariman and colleagues [3]. Clinically, this manifests as stroke, hemorrhage, and dementia. Similar to small vessel disease of the eye, there is strong correlation with traditional vascular risk factors including hypertension, diabetes, tobacco use and increased age, and risk factor modification is of paramount importance. They discuss an inherited cerebral small vessel disease linked to mutations of the NOTCH3 gene in which patients present with stroke and dementia. Interestingly, concomitant heart involvement including evidence of coronary microvascular dysfunction and myocardial infarction has been reported in this inherited condition. Treatment for cerebral small vessel disease is focused on aggressive management of risk factors, primarily, smoking cessation and lowering of blood pressure and cholesterol.

Concomitant small vessel disease of the heart and the lungs is seen in patients with pulmonary hypertension. Vahdatpour and colleagues present data suggesting shared pathophysiologic mechanisms between pulmonary microvascular dysfunction and coronary microvascular dysfunction [4]. In both conditions, endothelial dysfunction and smooth muscle proliferation results in vasoconstriction and ischemia with resultant adverse remodeling and fibrosis. Abnormal coronary flow reserve has been documented in patients with pulmonary hypertension, and right ventricular failure is a shared pathologic endpoint in both coronary microvascular dysfunction and pulmonary microvascular dysfunction.

Singh and colleagues review data that supports a strong association between chronic kidney disease and cardiovascular disease, which accounts for half of all deaths in patients with kidney disease [5]. A direct correlation between chronic kidney disease and abnormal coronary flow reserve in the heart has been reported, with progressive worsening in coronary microvascular function paralleling the decline in kidney function. On histologic evaluation, microvascular rarefaction and fibrosis are seen in both coronary microvascular dysfunction of the heart and small vessel disease of the kidney. Small vessel disease of the retina, an independent predictor of the development of chronic kidney disease, underscores the global nature of this disease process.

After ischemic heart disease, peripheral arterial disease is the second most common complication of systemic atherosclerosis, yet this condition remains under-recognized and under-diagnosed [6]. As noted by Bethel and Annex, peripheral arterial disease is viewed as a disease of large vessels from the perspective of both diagnosis and treatment [7]. However, evidence suggests that abnormalities of the microvasculature play an important role in this disease. Parallels to that of coronary microvascular disease are presented, and approaches toward future therapeutics for peripheral arterial disease that target the microvasculature are discussed.

Lastly, Prakash and colleagues review the spectrum of coronary microvascular dysfunction of the heart ranging from the classical presentation of patients (predominantly women) with ischemia with non-obstructive coronary artery disease, angina with no obstructive coronary arteries, and myocardial infarction with non-obstructed coronary arteries, to men and women with obstructive coronary artery disease [8]. They discuss the role of coronary microvascular disease in other cardiac conditions where it is considered an “innocent” bystander, but plays a crucial pathologic role including hypertension, cardiomyopathies, aortic stenosis, HIV, and chronic autoimmune diseases. Microvascular dysfunction of the heart, they contend, is an expression of a systemic illness that worsens with age and is accelerated by vascular risk factors.

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Declaration of competing interest

None.

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