Editorial Commentary

Gait Decline
The Role of Cerebral Small Vessel Disease and Biomarkers

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With the global increasing aging of our societies, there is a growing interest in understanding the mechanisms explaining mobility limitations and poor physical performance in elderly population. Epidemiological studies report that, in community-dwelling older adults, the prevalence of abnormal gait could be ≈30% after the age of 70 years. One of the most obvious complications of poor physical performance is an increased risk of falls, which may have tragic consequences. After an hip fracture, for example, the 1-year risk of mortality is ≈30%3; higher than after an acute myocardial infarction. Overall, poor physical performance is associated with an increased risk of disability, institutionalization, and death.3 The simple measurement of short-distance usual gait speed (usually over a distance of 4–10 m) has progressively emerged as a simple and reliable measure of physical performance, requiring only a chronometer and a few seconds, leading some authors to propose it as a new vital sign in the geriatric examination, together with other parameters, such as blood pressure or heart rate.4

The causes of mobility limitations are complex and multifactorial, involving many systems such as osteoarticular or cardiovascular systems, sensorial abilities, or the central nervous system.5 A growing number of studies have focussed on the role of cardiovascular risk factors, by analogy with cognitive function. Dyslipidemia, diabetes mellitus, and hypertension have all been shown to be associated with poor physical performance. Slow gait speed is associated with cardiovascular risk,7 and with an increased risk of stroke and cardiovascular mortality.8 One of the explanations for the association between cardiovascular risk factors and poor physical performance involves the role of cerebral small vessel disease, that is, brain white matter abnormalities,9 silent infarcts, and gray matter atrophy.10 Cardiovascular risk factors are associated with cerebral small vessel disease, which impairs brain connectivity and the pathways controlling cognition, balance, and motor function. These associations may reinforce themselves in a vicious circle, as mobility limitations may generate sedentary behavior, thereby promoting cardiovascular risk factors (Figure).

In this issue of Hypertension, Tchalla et al11 have examined the association between plasma levels of Soluble Vascular Cell Adhesion Molecule-1 (sVCAM-1)—a biomarker of systemic endothelial dysfunction—and mobility impairment, assessed through a gait speed measure and the occurrence of falls >1 year. sVCAM-1 promotes the adhesion of inflammatory cells to the vascular endothelial wall, in particular in the cerebral microvasculature, and facilitates their migration through the endothelium. According to the authors, the resulting inflammatory response may result in impaired cerebral blood flow regulation, especially endothelium-dependent vasodilatation in response to changes in blood end-tidal Pco2, and ischemic damage to the cerebral microvasculature that manifests as white matter hyperintensities in brain imaging studies. In this work, ≈700 community-dwelling participants aged ≥65 years were included as part of the MOBILIZE (Maintenance of Balance, Independent Living, Intellect, and Zest in the Elderly) Boston Study. The authors found that elevated levels of sVCAM-1 were cross-sectionally associated with slower gait speed, and with an increased risk of incident falls, including injurious falls, over the 1-year follow-up. Furthermore, a transcranial Doppler ultrasound was available for 60% of the participants: sVCAM-1 levels were associated with decreased resting blood flow velocity and cerebral vasomotor range, therefore, suggesting, according to the authors, that plasma sVCAM-1 is a marker of chronic cerebral blood flow dysregulation secondary to endothelial dysfunction.

Critics will dispute the specificity of sVCAM-1 as a marker of cerebral blood flow dysregulation and regret the absence of brain magnetic resonance imaging to assess the presence of cerebral small vessel disease. The reader is also left with the question of whether hypertension and slow gait speed were associated in this population, and, if yes, whether s-VCAM1 explained part of the association. In addition, the association between sVCAM-1 and slow gait speed was characterized by a complex pattern: higher sVCAM-1 levels were associated with slow gait speed only among participants with a history of controlled or uncontrolled hypertension (79% of all participants), while there was no association among normotensive subjects. Additional studies will be necessary to replicate this finding and better understand the mechanisms underlying this interaction. The authors also claim that they used a longitudinal design to examine the association of sVCAM-1 with incident falls.

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However, the follow-up was short (1 year), and, more importantly, participants with a history of falls were not excluded from this analysis; therefore, their findings may be explained by those participants who walked slowly and had already fallen at the time of the sVCAM-1 measure.

Nevertheless, sVCAM-1 may rejoin the previous list of plasma inflammatory biomarkers, such as interleukin 6, which have shown to be associated with both cardiovascular risk and mobility limitations in elderly people. The availability of 1 or several plasma biomarkers associated with the vascular component of mobility limitations presents a large interest, as they may contribute to identify subjects who may benefit from targeted interventions.

Mobility limitations in elderly people represent a major challenge for public health. The findings of Tchalla et al add to an increasing literature that pleads for a contribution of vascular risk factors to mobility impairment and offers an opportunity for prevention. Whether vascular drugs, such as antihypertensive drugs or statins, could have a protective effect for mobility in elderly people needs to be tested in randomized clinical trials. Repeated measures of gait speed and plasma biomarkers will be particularly valuable in the design of such studies.

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