Clinical significance of white matter lesions – do they predict VCI/dementia?

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Numerous population-based brain imaging studies have shown that the burden of cerebrovascular disease extends far beyond that of clinical stroke. Indeed, a large proportion of older community-dwelling persons have “covert” cerebrovascular lesions, the most common being white matter lesions (WML). In older persons these WML are believed to reflect mostly underlying cerebral small artery disease, although the exact mechanisms remain elusive. These lesions have been associated with lower performance on cognitive tests, especially of executive function and processing speed, gait disturbances, and mood disorders. And in longitudinal population-based studies they are strongly associated with accelerated cognitive decline and increased risk of dementia. This association is less marked among individuals who are already cognitively impaired. WML are strongly correlated with other MRI-markers of small artery disease, such as covert brain infarcts, microbleeds and dilated perivascular spaces, as well as with brain atrophy, and the relative contribution of each on cognitive outcomes may differ according to the clinical setting (e.g. monogenic versus multifactorial disease). Reverse causation due to Wallerian degeneration has also been suggested as a possible explanation of the association between WML and dementia risk, but this is unlikely to be the predominant mechanism at the community level. An important question is whether WML can be used as a tool to prevent the occurrence of dementia. Indeed, WML could represent both a unique window for detecting high risk individuals and an intermediate endpoint for monitoring preventive interventions. However, a number of challenges need to be overcome and additional evidence gathered before this can be efficiently implemented. These include the fact that no treatment has been robustly proven to reduce the progression of WMH, the competing risk of ischemia and bleeding in patients with cerebral small artery disease and the lack of consensus on whom to screen for such lesions and when.