

Cerebral Small Vessel Disease: Are the  
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## Editorial

Some medical disorders have an insidious development with an asymptomatic period which may represent the authentic therapeutic window. Probably, this is the case of the Cerebral Small Vessel Disease (CSVD). This term includes several pathological processes of different aetiologies which cause an increase of parietal thickness in arterioles, capillaries and venules. This phenomenon affects basically the basement membrane and it is associated with the narrowing of the lumen and the weakening of the wall. The consequences of these alterations are the loss of proteins to interstice and the slowness of blood flow, which increase the risk of ischemia and tissue bleeding [1,2].

The most prevalent form of CSVD is the one called type 1 or arteriolosclerosis. This condition has a 6 to 10 times higher prevalence than stroke and it is related to aging and classical vascular risk factors, like arterial hypertension and diabetes mellitus. In the brain, the main pathological findings of arteriolosclerosis are loss of smooth muscle cells in the media, accumulation of fibrohyaline material, fibrinoid necrosis, and development of microatheromas and Charcot-Bouchard microaneurysms [3]. The parenchymatous consequences of arteriolosclerosis are both ischemic (white matter lesions, lacunes) and haemorrhagic (microhaemorrhages, intracerebral haemorrhages). Clinically, arteriolosclerosis is associated with cognitive deterioration, dementia, mood disorders, gait and motor disturbances, lacunar strokes, and disability. However, this condition may be “silent” and it is a frequent incidental finding in some individuals [4]. Similarly to other diseases, only histology gives a definitive confirmation and in vivo diagnosis may be supported by neuroimaging findings (lacunes, leukoaraiosis, white matter lesions, microhaemorrhages), especially magnetic resonance [5].

The therapeutic management of patients with diagnosis of microangiopathy has three main considerations. First, these patients have specific risks during standard clinical management of acute ischemic stroke. An increased risk of intracranial bleeding after thrombolytic therapy for acute stroke or during chronic anticoagulant treatment for secondary prevention of stroke has been reported in several studies. In patients who underwent carotid endarterectomy, the presence of leukoaraiosis raised the probability of peri-operative stroke or death. Globally, the presence of leukoaraiosis reduces the benefit from these treatments, but it is not a contraindication [6,7].

Second, the symptomatic management of patients with cognitive impairment related to CSVD. Currently, the therapy of cognitive manifestations is based on memantine and acetylcholinesterase inhibitors used in Alzheimer’s disease (galantamine, donepezil, and rivastigmine). A meta-analysis of clinical effects in patients with vascular dementia including all drugs used to treat Alzheimer’s disease concluded that cholinesterase inhibitors and memantine produce small benefits in cognition of uncertain clinical significance in patients with mild to moderate vascular dementia. The current data are insufficient to support the widespread use of these drugs in patients with dementia related to CSVD [8].

Third, the specific therapy directed to vessel pathology and parenchymatous consequences. This therapy includes the use of antiaggregant drugs and the control of vascular risk factors associated with microangiopathy. The ischemic strokes related to CSVD have aetiopathogenic characteristics different from strokes due to large vessels atherosclerosis or cardiac disorders, but no randomised clinical trial has independently assessed the effects of antiplatelet agents in these patients. Only some trials evaluating antiaggregant drugs in secondary prevention of stroke assessed subgroups of patients with CSVD. The study drugs were aspirin, ticlopidine, aspirin plus clopidogrel, dipyridamol plus aspirin, and cilostazol. All drugs showed efficacy in prevention of stroke related to CSVD and the available data support the use of antiaggregants to reduce the risk of recurrence of ischemic events. There were no significant differences among drugs and there was no evidence of an increased risk of intracranial haemorrhage [9-11]. The control of risk factors related to CSVD includes the use of antihypertensive and hypolipemiant drugs. The evidence supports the lowering of blood pressure for the prevention of stroke. However, there are still capital questions without a definitive response which need to be assessed. First, if clinical effects observed in previous clinical trials can

be obtained in patients with CSVD. Second, if the goal of therapeutics is an intensive or a standard blood pressure control. Third, which specific drug or class should be preferentially used? The results of trials assessing atorvastatin, pravastatin and simvastatin were not consistent and new data are needed [3].

In summary, the presence of CSVD is extremely frequent in patients with stroke, cognitive complaints and some asymptomatic individuals with vascular risk factors. The management of this condition includes the secondary prevention with antiplatelet agents and antihypertensive drugs and the symptomatic treatment with anti-Alzheimer therapies. Probably, the efficacy of these treatments could be greater if an early (pre-symptomatic) diagnosis is done. Therefore, the challenges for the management of patients with CSVD are the precise knowledge of the natural history of disease (from the presence of vascular risk factors in asymptomatic individuals to clinical manifestations in patients), the early pre-clinical diagnosis, and the definition of the optimal preventive strategies. Currently, some ongoing trials are trying to evaluate different drugs and therapeutic goals (cilostazol plus aspirin, aggressive versus standard blood pressure control) and new strategies emerge to answer some of these questions [10,11].

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