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General review

Diffusion magnetic resonance imaging in cerebral small vessel disease

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ABSTRACT

Cerebral small vessel disease (SVD) is frequent in the elderly, and accounts for a wide spectrum of clinical and radiological manifestations. This report summarizes the most important findings obtained using diffusion MRI (DWI) in SVD. With DWI and apparent diffusion coefficient (ADC) maps, recent ischemic lesions can easily be detected after acute stroke in SVD, while even multiple simultaneous lesions may be observed. Microstructural changes are frequent in SVD, with increases in diffusivity and decreases in anisotropy being the most reliable findings observed, mainly in white matter. These tissue changes are associated with clinical severity and especially executive dysfunction. They can also precede the usual MRI markers of SVD, such as white matter hyperintensities, microbleeds and lacunes. Thus, DWI may reveal surrogate markers of SVD progression and offer a better understanding of their underlying mechanisms.

1. Introduction

Cerebral small vessel disease (SVD) is responsible for functional and structural alterations of the cerebral perforating arteries, arterioles and capillaries. SVD accounts for a wide spectrum of clinical manifestations, ranging from mild symptoms, such as mild cognitive impairment to stroke, gait disturbances and dementia [1]. SVD is responsible for multiple types of cerebral lesions identified by conventional magnetic resonance imaging (MRI), including recent small subcortical infarcts, lacunes and white matter hyperintensities (WMH) of presumed vascular origin, cerebral microbleeds (MB), perivascular spaces and brain atrophy [2].

Diffusion is a physical phenomenon related to the random movements of water molecules in cerebral tissue, and mainly hindered by cell barriers and macromolecules. Water molecules also diffuse differently according to the direction of their measurement in cerebral tissue, and a phenomenon called 'anisotropy' is related to the various geometric, spatial arrangements of cell barriers and macromolecules. Thus, diffusion measures can be used to probe the microstructural changes [3,4] that occur within cerebral tissues in SVD, particularly those related to the cell membrane and/or myelin

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changes detected in both gray matter and white matter (WM). Diffusion-weighted MRI (DWI) techniques can also assess changes in cerebral connectivity [5] in SVD for a better understanding of the mechanisms underlying disability and cognitive decline [6,7].

The present review summarizes the most important results obtained with DWI in SVD. References were identified through searches of PubMed up to November 2016, using the following search terms: MRI diffusion AND small deep infarcts OR small artery disease OR small vessel disease OR cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoaraiosis (CADASIL) OR arteriolosclerosis OR subcortical ischemic vascular dementia OR leukoaraiosis OR perforating artery OR cerebral amyloid angiopathy (CAA). After all original papers published in English were reviewed ($n = 569$), one author (A.L.I.) screened all the abstracts; 105 papers were ultimately selected for review after the exclusion of general technical reviews and single-case studies.

2. DWI for assessing small ischemic brain lesions

The first clinical application of DWI in SVD patients was to identify recent, small ischemic lesions characterized by an acute reduction of diffusion easily confirmed on apparent diffusion coefficient (ADC) maps. As soon as the technique became available, DWI was found to be much more sensitive for detecting recent small ischemic lesions than computed tomography (CT) [8–10], and was particularly helpful in demonstrating that the clinical presentation of lacunar syndromes was rarely specific to the lesion site, which was contrary to what had been assumed previously [11]. In addition, in the acute stage of stroke, DWI was able to detect multiple small and recent ischemic lesions in SVD patients at a rate of 8% in sporadic cases and 10.5% in CADASIL [12]. Multiple 'silent infarcts' were also detected in 15% of patients with probable CAA [13] and in up to 38% of patients with vascular dementia [14]. In addition, multiple hyperintense lesions found on DWI proved to be more closely related to SVD markers, such as lacunes and MB, than to cardioembolic sources, such as atrial fibrillation [15], thereby suggesting that multiple silent infarcts may actually be part of the SVD spectrum. Observations of multiple silent infarcts in CADASIL long before the appearance of atrial fibrillation is in line with this interpretation (Fig. 1) [16]. Some authors even demonstrated that such DWI lesions turned into cavities in 61% of cases and that a significant proportion of subcortical infarcts can lead to T2-weighted hyperintensities after 20 months of follow-up [17]. Thus, asymptomatic focal ischemic lesions may sometimes secondarily merge with WMH and contribute to the progression of WM lesion load in SVD [18].

Other authors have suggested that DWI can be used to differentiate SVD from other causes of stroke. However, no clear lesion size cut-off has been found specifically for SVD. Some have reported that a diameter < 15–20 mm is a good predictor of SVD [19,20], whereas others could find no size differences between small ischemic lesions related to SVD and those secondary to middle cerebral artery occlusion [21]. In any case, a diameter of 20 mm is generally considered the extreme limit on DWI, and is larger than the 15-mm diameter size limit of a residual cavity [2]. Also, a distal location of small hyperintense DWI lesions in the perforating territory of large intracranial arteries was more specific to SVD than proximal lesions, albeit only in a few studies [22,23]. However, the

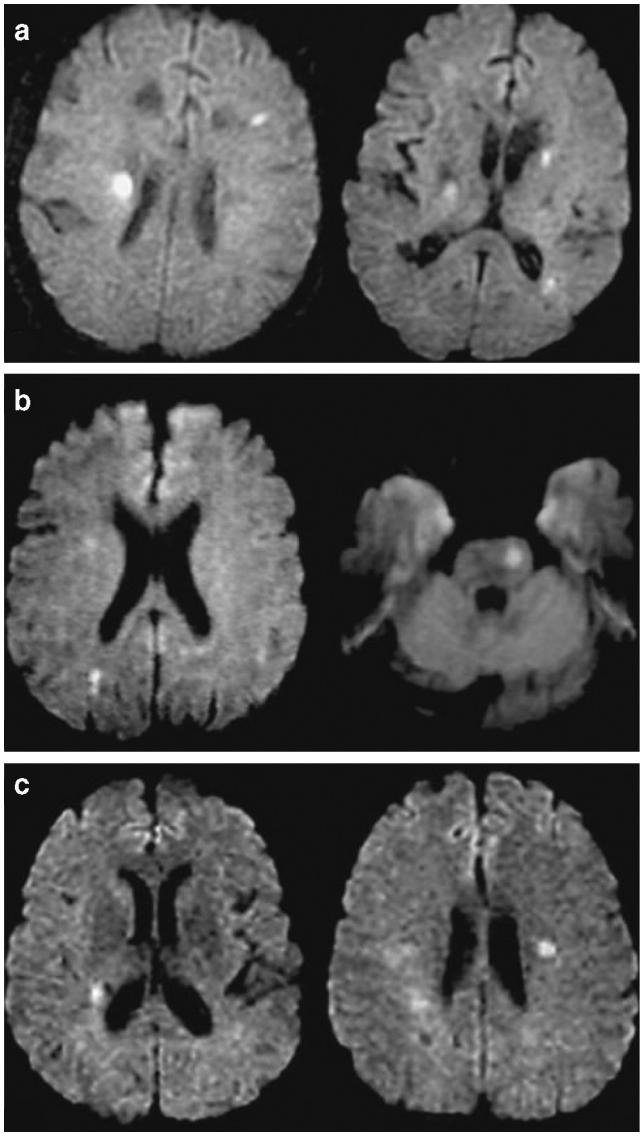

Fig. 1 – Multiple acute cerebral infarcts in three patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoaraiosis (CADASIL): (a) 51-year-old man with left hemiplegia, motor aphasia and pseudobulbar palsy shows left caudate and right corona radiata lacunar infarcts, and severe leukoencephalopathy on T2-weighted imaging; (b) 44-year-old man with transient left hemiparesis, dysarthria, and acute left pontine and right occipitoparietal infarcts shows mild leukoencephalopathy on T2-weighted imaging; and (c) 54-year-old woman with right facial paresthesia shows infarctions in the right posterior limb of the internal capsule and left corona radiata.
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