Cognitive Impairment in Lacunar Strokes

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Abstract
Vascular cognitive impairment is closely related to stroke. Each condition is a risk factor for the other. Cognitive impairment is a symptom that makes it difficult for a stroke patient to live at home. In this review paper, different types of vascular cognitive impairment are discussed, with emphasis on cognitive impairment related to lacunar strokes (LACS). Symptoms, diagnostics, epidemiology, treatment, and prognosis are surveyed. LACS are often associated with leukoaraiosis, which is related to subcortical ischemic vascular dementia. Even if LACS often are mild, they may therefore be associated with cognitive impairment on longer term.

Definitions
According to ICD-10, a diagnosis of dementia requires: (1) impairment in short- and long-term memory; (2) impairment in abstract thinking, judgement, higher cortical function, or personality change; (3) memory impairment and intellectual impairment, which cause significant social and occupational impairments; and (4) the occurrence of these traits when patients are not in a state of delirium.

Cognitive impairment is a continuum, affecting different cognitive domains at different rates, from different causes. The definition of dementia requires memory impairment plus involvement of at least one other cognitive domain. This definition is less appropriate for vascular cognitive impairment (VCI), because in VCI memory is often less affected than executive functions. In this paper, the terms cognitive impairment and VCI are used whenever possible.

Delirium, or confusional state, is a more or less acute disorder of attention and global cognition (memory and perception), which is reversible. Delirium is almost always caused by a provoking event, such as an infection, a metabolic condition, or a psychotropic drug. People with pre-existing cognitive impairment are at higher risk for developing delirium.

LACS result from occlusion of the penetrating arteries that provide blood to the brain’s deep structures. A corresponding infarction is often small, within 10 mm and affects the deep nuclei of the brain or different neural pathways to and from the cortex. Compared to larger infarctions that involve the cortex, patients with LACS often have a lower grade of stroke severity and a better short-time prognosis. Therefore, LACS have been considered as relatively benign. On the other hand, LACS are often seen together with leukoaraiosis or cerebral white matter changes. These are radiologic findings with bilateral patchy or diffuse areas of hypointensities of the cerebral white matter on T2-weighted MRI. Leukoaraiosis is probably caused by chronic ischemia in the white matter, leading to loss of myelin and axons, and ultimately to gliosis and atrophy. Leukoaraiosis is related to cognitive impairment.

Classification of Cognitive Impairment
Not so many years ago, a rather strict distinction was made between the primary degenerative forms of dementia, such as Alzheimer’s disease (AD), and vascular forms of dementia, such as multi-infarct dementia. Mixed forms of dementia were recognized, but were considered as exceptions. In later years, this classification of dementia has been re-evaluated. This re-evaluation is based partly on pathologic-anatomic studies, partly on the fact that there is considerable overlapping in pathophysiology, risk factors and symptoms between the primary degenerative and vascular forms of dementia. For example, there often is significant vascular pathology in AD, and hypoperfusion may play a significant role. By some authors, mixed dementia is now considered as the most common type. In the Swedish Kungsholmen project, initially only 5% of the patients were diagnosed with mixed dementia, but after re-evaluation 55% of patients were diagnosed as having mixed dementia. With this background it has...
been proposed that the concept of dementia is obsolete, because “it combines categorical misclassification with etiologic imprecision”.4 We should therefore think in terms of a continuum of cognitive impairment, and focus on causes instead of effects.4

**Vascular Cognitive Impairment**

Vascular cognitive impairment (VCI) may roughly be divided into two types, namely the cortical and subcortical types. The cortical type is caused by stenosis of larger vessels, leading to multiple, strategic, or larger infarcts that have impact on cognition. The number of and distribution of such infarcts jointly contribute to cognitive impairment.19

The subcortical type is caused by stenosis of smaller vessels in the white matter. This may give rise to multiple complete infarcts, leading to the lacunar state (état lacunaire), or to hypoperfusion which leads to leukoaraiosis. In recent years, the term SIVD has been coined as a name of dementia that is associated with small vessel disease.

**Subcortical Ischemic Vascular Dementia**

The concept SIVD was introduced around the year 2000 and is a further development of the concepts vascular dementia andBinswanger’s disease.20 SIVD results from complete or incomplete occlusion of small arteries in the white matter, leading to hypoperfusion. If the occlusion is complete, a lacunar infarct becomes the consequence, but if it is incomplete, leukoaraiosis is the result.21 These two conditions commonly occur together.20

The risk factors for SIVD are the common vascular risk factors; e.g., hypertension, diabetes, cigarette smoking, and hypercholesterolemia. Additional risk factors in elderly people are heart failure, arrhythmias, and orthostatic hypotension. These are believed to promote hypoperfusion. Major surgery in the elderly, especially coronary bypass surgery and surgery due to hip fracture, is also believed to worsen SIVD through hypoperfusion.20

Although a recent review article has shown that all major cognitive domains may be involved,24 the symptoms and course of SIVD differ in many ways from AD. A psychomotor slowness (bradyphrenia) is typical, including a verbal response latency. This slowness is a part of a dysexecutive syndrome caused by interruption of prefrontal-subcortical neural circuits. Other features of this syndrome include impairment of goal formulation, initiation, planning, organizing, ranking, deciding, and change of strategies. Early in the course of the disease, memory may be relatively intact, but memory functions tend to fluctuate, because of fatigue and other factors. Nocturnal confusion is common, with a disturbed circadian rhythm (a tendency to sleep at daytime and be awake in the night). Psychiatric symptoms are also common, including indifference, depression, lack of initiative and interest, and emotional lability. Contrary to patients with AD, language functions are relatively intact, as well as recognition capability and ability to count.

The motor features of SIVD are typical. Symptoms from the lower extremities dominate. In the beginning of the 20th century, French neurologists coined the term ‘marche à petits pas’, which refer to the typical somewhat broad-based gait, with small shuffling steps, and relatively preserved function in the upper limbs. Extrapyramidal symptoms, such as hypokinesia and rigidity, are common, but not tremor. Often a patient freezes when trying to walk and there are also turning difficulties. The risk for falls and fractures is high. Cortical symptoms are not a part of the syndrome, but may occur if the patient also has cortical lesions.

Not uncommonly, urgency incontinence also is present. The triad cognitive impairment, a broad-based gait and urgency incontinence may also bring normal pressure hydrocephalus (NPH) to mind. If imaging gives rise to the suspicion of NPH, an infusion test may be needed in order to exclude this condition.

**Epidemiology**

Several studies show that cognitive impairment increases the risk for stroke later in life. Compared to healthy persons, the relative risk for persons with dementia to later have a stroke, is between two and three.23–25 Not unexpectedly, the prevalence of cognitive impairment and dementia before a stroke incidence is increased and lies between nine and 16 percent in different studies.26–29 Stroke is also a risk factor for cognitive impairment. In cohort studies, the relative risk for dementia after stroke is between two and four compared to age-matched healthy persons.30–32

Regarding LACS, the severity of cognitive impairment seems to be related to the severity of leukoaraiosis.19,33 Even if LACS often are mild, they may be associated with cognitive impairment on longer term, more so than other types of strokes.24 Within the Secondary Prevention of Small Subcortical Strokes (SPS3) study, nearly half of the participants had mild cognitive impairment between 2 weeks to 6 months after the qualifying stroke.35 A recent review paper, which included 24 studies, found that 24 % of patients with lacunar stroke who had cognitive impairment (mild cognitive impairment or dementia) post stroke. In that review, there was no significant difference between lacunar and non-LACS with regard to prevalence of cognitive impairment after stroke, however.36

The European multicenter Leukoaraiosis and Disability Study (LADIS) has focused on the role of leukoaraiosis and to some extent of lacunes, in predicting disability. The main result of LADIS was that leukoaraiosis more than double the risk for being dependent after 3 years of follow-up.37 Increasing severity of leukoaraiosis and number of lacunes were each related to worse cognitive performance.38 Regarding lacunes, their location within subcortical grey matter (thalamus, putamen, pallidum) is a determinant of cognitive impairment, independently of the extent of leukoaraiosis.38

**Cognitive Assessment**

The most important information regarding a patient’s cognitive ability originates from observations of daily activities in the hospital ward, or in the patient’s own house. Activities such as dressing, toileting, kitchen routines, counting money, and spatial orientation, may often give more information than a psychometric test can do. Such information may give a more positive image of the patient’s capabilities than a test instrument. When choosing a test instrument, it is preferable to choose one that is able to test all relevant cognitive domains. A disadvantage with the often-used Mini Mental State Examination (MMSE),39 is its relative
loading on verbal skills, versus visuospatial, constructional and executive functions. Use of MMSE only may fail to identify subjects with VCI. Amendments and modifications to MMSE have been suggested, but they have not gained widespread use.

A new test, which has been constructed with all relevant cognitive domains in mind and yet is possible to accomplish within 10 minutes, is the Montreal Cognitive Assessment (MoCA). This test may be freely used for clinical purposes. MoCA is recommended by the National Institute for Neurological Disorders and Stroke (NINDS) and by the Canadian Stroke Network (CSN) as a screening test for vascular cognitive impairment. The Hachinski Ischemic Score may also be used in order to identify a vascular component of cognitive impairment.

More subtle cognitive deficits, such as fatigue, stress hypersensitivity, lack of concentration ability and lack of initiative (conation), may be handicapping, but are difficult to measure. Yet, these difficulties may be of great significance and have implications for younger stroke patients ability to return to their occupation. In these cases, a neuropsychologic examination may add to the comprehensive picture. Different neuropsychologic tests are suggested by NINDS and CSN.

The presence of cognitive impairment may also have implications for a patient’s ability to drive a car and other vehicles, as well as for permission to possess firearms. Laws and regulations differ between countries. In Sweden, in addition to the physician’s general assessment, the Nordic version of Stroke Driver Screening Assessment (SDSA) is often used in order to evaluate driving skills. An on-road test, managed by a specially trained driving instructor, is sometimes needed. Driving simulators are still under development and not used in clinical praxis in Sweden.

Treatment and Prevention

Although cholinesterase inhibitors produce small cognitive improvements in patients with vascular cognitive impairment, such improvements are small. Because of their limited effects, adverse effects, and costs, cholinesterase inhibitors are generally not used in patients with vascular cognitive impairment or dementia.

Treatment of vascular risk factors is the only possible way of slowing down the progress of cognitive impairment. In two hypertension trials, it has been shown that ramipril and the combination perindopril/indapamide have beneficial effect on cognitive performance in trials, it has been shown that ramipril and the combination perindopril/indapamide have beneficial effect on cognitive performance. Other studies support these findings. It has also been shown that the progress of leukoaraiosis may be slowed down with proper blood pressure management. As for other vascular risk factors (e.g. diabetes, cigarette smoking, obesity, and low physical activity), it is tempting to believe that targeting them vigorously may prevent or delay dementia.

Prognosis

Several studies have shown that combination stroke and cognitive impairment is unfavorable in several ways. These patients often need a longer stay in hospital. Dementia before a stroke increases the risk for both early death and death within 1 year and also increases the risk of a recurrent stroke. Most likely, the explanation is multifactorial. Stroke patients with dementia may more easily contract complications, including infections, thromboembolic events, and fractures, both in the acute phase of stroke and later on. An important factor may be the attitudes of doctors and nursing staff towards patients with dementia. They may not be chosen for active rehabilitation, or prescribed warfarin in case of atrial fibrillation.

Due to slowness of mental processing (bradyphrenia), these patients may need longer time to communicate. This is often manifested by an increased latency of verbal response. Reduced ability to stand stress, decreased power of initiative, and reduced flexibility are all related to the impaired executive functions. Memory functions may be more or less affected, especially regarding new learning and short-term memory. ADL functions are often impaired. This may be true also for patients with relatively mild cognitive impairment. These patients are therefore in need of more help in their everyday life and many patients are in need of a sheltered living. Due to the gait abnormalities, there is often a high risk for falls. Stroke patients with cognitive impairment have a high risk for hip fractures. Depression and mood disorders are common among these patients. This may be manifested by a so-called vascular depression, manifested by depression, apathy, and irritability.

The treatment outcome and natural course of vascular depression is considered worse than that of the non-vascular depression.

Despite the abovementioned difficulties, patients with vascular cognitive impairment may often function well in everyday life, thanks to a well preserved personality and a well preserved language. The condition often seems to be stationary for a long time. Deterioration may occur step-wise, and ‘steps’ may correspond to a new stroke and loss of compensation mechanisms. Whether deterioration occurs in steps or not, it is unfortunately common that the disease progresses over several years. Loss of interests, inability to associate, and inability to change line of thoughts, which may lead to perseverations, are symptoms that are common. Ultimately, patients get dependent in all domains and nutrition becomes difficult. Not unexpectedly, these patients often die from vascular causes, but many also die from infections or unrelated causes, such as malignancy.