Neuroimaging of Vascular Dementia

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KEYWORDS

• Vascular dementia • MR imaging • Subcortical vascular dementia • CADASIL
• Cerebral amyloid angiopathy (CAA)

KEY POINTS

- Vascular dementia (VaD) is the third leading cause of progressive and irreversible dementia after Alzheimer disease (60%–70%) and dementia with Lewy bodies (10%–25%).
- Because of the high variability of cerebrovascular pathologic conditions and its causative factors, there are no accepted neuropathologic criteria for diagnosing VaD.
- Brain pathology may show diffuse confluent age-related white matter changes, multi-lacunar state (état lacunaire), multiple (territorial) infarcts, strategic cortical-subcortical or watershed lesions, cortical laminar necrosis (granular cortical atrophy), and delayed postischemic demyelination and hippocampal sclerosis.
- Subcortical VaD is the most common subtype of small-vessel VaD and constitutes approximately 50% of VaD cases.

INTRODUCTION

Cerebrovascular disease (CVD) is the second most prominent cause of dementia either alone or in combination with Alzheimer disease (AD).[1] In the past, the term *vascular dementia* (VaD) was used to define the cognitive impairment resulting from CVD and ischemic or hemorrhagic brain injury.[2] The definition and diagnostic criteria of VaD remains unclear and generates much confusion in clinical practice. In addition, it was not able to classify patients who develop a cognitive impairment that does not fulfill the traditional criteria for dementia but that nonetheless has a significant impact on the patients' quality of life and ability to carry out activities of daily living. The term *vascular cognitive impairment* (VCI) was introduced to encompass all of the effects of vascular diseases or lesions on cognition and incorporate the complex interactions between vascular causes, risk factors, and cellular changes within the brain and cognition.[3] VCI refers to "a syndrome with evidence of clinical stroke or subclinical vascular brain injury and cognitive impairment affecting at least one cognitive domain." VCI also includes both pure (CVD alone) and mixed (CVD with other pathologic conditions, such as that of AD). It is important to understand that VCI is not a disease like AD but is rather a syndrome or phenotype that results from CVD, subsequently leading to vascular brain injury that disrupts the brain network for memory and thinking. VaD is a subset of the broader designation VCI.

PREVALENCE

Dementia from all causes has a prevalence of about 8% in individuals aged more than 65 years.[1,3] In the Western literature, VaD is the third leading cause of progressive and irreversible

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dementia after AD (60%–70%) and dementia with Lewy bodies (10%–25%).[4] The incidence of VaD shows a wide variation in the patient population (age, sex), geographic location, and use of clinical methods. Of all causes of dementia, 13% to 19% are from pure vascular causes, whereas mixed dementia whereby vascular causes are part of the disease is seen in 11% to 43%.[3,4] The proportion of cases caused by VaD decreases with increasing age, but the prevalence of all dementia increases so rapidly with age that the prevalence of VaD also increases, from 0% to 2% in the 60- to 69-year-old age group and up to 16% (3%–6% for men) in individuals aged 80 to 89 years.[5] Globally, VaD seems to be more common in men, especially before 75 years of age. The incidence in women and men aged 85 years and older is around 9.3% and 15.9%, respectively. Epidemiologic studies suggest that the incidence of VaD in Europe accounts for about 15% to 20% of the cases, whereas in Japan it accounts for around 50% of the cases.[1,6] VaD is also more prevalent in populations affected by cerebral small-vessel disease (SVD), such as Asians, African Americans, and Hispanics.

The introduction of the new term *VCI* encompasses all of the effects of vascular disease on cognition leading to a change in the epidemiology. In patients younger than 74 years, VCI may be the single most common cause of cognitive impairment. In those individuals aged 75 to 84 years, cases of pure VCI, VaD, and those with a vascular component in the context of mixed disease outnumber those with pure AD.[7] In a Canadian study, the prevalence of VCI has been estimated at 5% in people older than 65 years.[1,5] The cognitive outcome of patients with VaD may be as severe as in AD, but their morbidity and mortality are usually worse.

DIAGNOSTIC CRITERIA

The concept of CVD leading to cognitive decline and dementia has been recognized since the seventeenth century. In the latter half of the nineteenth century, Kraepelin and colleagues coined the term *atherosclerotic dementia*.[8] In 1974, Vladimir Hachinski and colleagues[9] introduced the term *multi-infarct dementia* (MID). Since then, because of the advances in imaging techniques, our understanding of the disease process has significantly evolved. Unfortunately, because of the high variability of cerebrovascular pathologic conditions and its causative factors, there are no accepted neuropathologic criteria for diagnosing VaD or VCI, as agreed for AD or dementia with Lewy bodies. Unlike AD, vascular lesions are classified based on the morphologic characteristics rather than by their pathogenesis. The criteria from the *Diagnostic and Statistical Manual of Mental Disorders*, (Fourth Edition) (*DSM-IV*) for VaD were proposed by the American Psychiatric Association from a general definition of dementia (**Box 1**).[10] The major limitations for these criteria are the following: They are purely clinical. No neuroimaging findings are incorporated. No criteria are mentioned to establish a causal relationship between dementia and vascular disease. The cross-sectional neuroimaging modalities computed tomography (CT) and magnetic resonance (MR) imaging have significantly improved our understanding of SVD, MID, and VaD. In 1993, the National Institute of Neurologic Disorders and Stroke (NINDS)–Association Internationale pour la Recherche et l'Enseignement en Neurosciences (AIREN) formulated criteria that incorporated the structural neuroimaging as a crucial element for the diagnosis of VaD (**Box 2**).[11] To enhance their clinical implementation, operational definitions for the radiological part of the NINDS-AIREN's criteria were subsequently modified in 2003.[12] To diagnose VaD, the current criteria require the presence of the syndrome of dementia and a pathophysiologic mechanism.

Box 1
***DSM-IV* criteria for VaD**

a. There are multiple cognitive deficits manifested by both memory impairment and one or more of the following cognitive disturbances: aphasia, apraxia, agnosia, or disturbance in executive functioning.

b. The cognitive deficits cause significant impairment in social or occupational activities and represent a significant decline from a previous level of functioning.

c. There are focal neurologic signs and symptoms (eg, exaggeration of deep tendon reflexes, extensor plantar response, pseudobulbar palsy, gait abnormalities, weakness of an extremity) or laboratory evidence indicating CVD (eg, multiple infarcts involving the cortex and the underlying white matter) that are judged to be etiologically related to the disturbance.

d. The deficits do not exclusively occur during the course of a delirium.

From American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th edition. Washington, DC: American Psychiatric Association; 1994. p. 9–36; with permission.