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Pattern of cognitive deficit in vascular dementia

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Abstract

Background: Vascular dementia (VaD) is the second most common cause of dementia after Alzheimer's disease. Vascular dementia has heteregeneous manifestation due to varying infarct location and subtypes. Despite quite frequent in Indonesia due to high incidence of stroke, the study about pattern of cognitive deficit in vascular dementia are still limited. *Methods:* This study is an observational cross-sectional consecutive sampling study conducted at the Memory Clinic of Provincial General Hospital Prof. Dr. R.D.Kandou, Manado, North Sulawesi, Indonesia during the period 1 January 2023 to 31 March 2024. Vascular dementia was diagnosed based on NINDS-AIREN criteria, and further classified based on Vascular Impairment of Cognition Classification Consensus Study (VICCCS). Cognitive examinations were done by using the Indonesian version of the Montreal Cognitive Assessment instrument (MoCA-INA) and other cognitive examinations. *Results:* There were 100 subjects who met the inclusion and exclusion criteria. The mean MoCA-INA in the study subjects was 12.2 (SD ± 6.0), with the lowest value found in mixed type dementia followed by multiple infarction/cortical and subcortical vascular dementia. Memory was the domain that most frequently impaired in vascular dementia. Impairments in the language domain were more common in the multiple infarct/cortical subtype, while executive function deficits were more frequently found in the subcortical subtype of vascular dementia ($p<0.001$). Attention, memory and visuospatial disorders did not show any significant differences in the three subtypes of vascular dementia.
Conclusion: Language disorders are more common in multiple infarction or cortical subtypes, while executive function is more dominantly impaired in the cortical subtype.

Keyword: Vascular, dementia, cognitive impairment

INTRODUCTION

Vascular dementia (VaD) is neurocognitive disorder that represents a decline in cognitive function due to decreased blood flow in the brain.[1] In 15% to 20% of dementia cases, vascular dementia is the second most prevalent subtype of dementia after Alzheimer's disease. It has been discovered that in Asian countries, particularly in developing countries, this percentage is larger and can even exceed 30%.[2] VaD is highly prevalent in Indonesia due to the country's high stroke incidence. An earlier study in Indonesia found that dementia affected 0.29% of elderly individuals, with vascular dementia accounting for 56% of cases.[3] Compared to Alzheimer's disease, VaD has a more varied clinical presentation because the symptoms differ according to the site of the infraction. The subtypes of VaD, namely small vessel disease, large vessel disease, and mixed dementia, also influence the profile of cognitive impairments.[4]

Based on previous studies, cognitive characteristics in VaD show varying patterns of impairment, especially in small vessel VaD. A study by Sengupta *et al*. revealed that attention impairment was substantially more implicated in small vessel dementia than large vessel dementia4, while according to Ying *et al*., patients with small vessel VaD had higher levels of executive dysfunction than those with large vessel and mixed vessel VaD ($P<0.05$). Visuospatial and language-verbal domains were also more involved in patients with large artery VAD ($P<0.05$).[5] The aim of this study was to describe the profiles

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of cognitive function in relation to domain impairment in various VaD subtypes.

METHODS

This study was carried out in the Provincial General Hospital Prof. Dr. R. D. Kandou's Memory Clinic in Manado, North Sulawesi, Indonesia, from January 1, 2023, to March 31, 2024. It is an observational cross-sectional study with consecutive sampling. Subjects who met the criteria for vascular dementia based on the International Workshop of the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) (Table 1), aged greater than eighteen, and were eligible to participate in this study. Subjects with psychiatric disorders like depression, schizophrenia, and conversion reactions were excluded, as were those with other conditions that cause dementia, such as normal pressure hydrocephalus, subdural hematoma, intracranial tumors, central nervous system infections, and drug intoxication. Subjects who could not undergo cognitive function examinations were also excluded from this study.

Every research subject had a neurological examination as well as a history taking. The study collected demographic data on age, gender, and education. Hypertension, diabetes mellitus, dyslipidemia, heart disease (myocardial infarction, atrial fibrillation, mitral stenosis, prosthetic heart valve, and endocarditis), and a history of stroke were among the conditions covered by the medical history. The medical history also included questions about past smoking and alcohol consumption. We used the Vascular Impairment of Cognition Classification Consensus Study (VICCCS) to categorize subtypes of vascular dementia into three groups: (1) ischemic subcortical vascular dementia, which includes Binswanger's disease, white matter ischemic

Table 1: Vascular dementia diagnosis criteria based on NINDS-AIREN

	Criteria	Feature
1.	Dementia	Impairment of memory Impairment of memory and ≥2 deficit in cognitive impairment: • Orientation • Attention • Language • Visuospasial • Executive function, motor control, praxia
2.	Cerebrovascular disease	Focal signs on neurological examination (hemiparesis, lower facial weakness, babinski sign, sensory deficit, hemianopia, and dysathria) Evidence of relevant cerebrovascular disease by brain imaging (CT-scan) : • Infarct of large vessel • Single strategically placed infarct • Multiple basal ganglia and white matter lacunes • Extensive periventricular white matter lesions • Combinations thereof
3.	A relationship between the above disorders	Manifested or inferred by the presence of ≥1 of: • Onset of dementia within 3 months after a recognized stroke • Abrupt deterioration in cognitive functions • Fluctuating, stepwise progression of cognitive deficits
4.	Clinical features consistent with the diagnosis of probable vascular dementia	Early presence of gait disturbances History of unsteadiness of frequent, unprovoked falls Early urinary incontinence Pseudobulbar palsy Personality and mood changes
5.	Feature that make the diagnosis of vascular dementia uncertain	Early onset of memory deficit and progressive worsening of memory and other cognitive functions in the absence of focal neurological signs and cerebrovascular lesions on CT or MRI.

lesions, and lacunar infarcts primarily located in subcortical areas; (2) multiple infarcts vascular dementia, which includes multiple large cortical infarctions; and (3) mixed dementia, which includes vascular and neurodegenerative diseases like Alzheimer's disease and dementia with Lewy body. The study excluded the post-stroke dementia classification because the temporal onset of dementia conflicted with the NINDS-AIREN criteria.[6] The Hachinski scoring, with a value of 4–7, was used to determine the mixed subtype of vascular dementia and Alzheimer's dementia (Table 2).

The Montreal Cognitive Assessment Instrument in Indonesian (MoCA-INA) as well as other cognitive tests were used to conduct cognitive evaluations. The MoCA-INA consists of 30 items that assess visuospatial, naming, memory, attention, language, abstraction, delayed recall, and orientation. Scores range from 0-30, with scores above 25 considered normal, otherwise considered cognitive impairment.[7] MoCA-INA's application stems from earlier studies that found a stronger correlation between MoCA and the Mini Mental Stage Examination (MMSE) and the extent of white matter damage in vascular dementia.[8] The following methods were used to test attention: the random A letter test, the forward and backward digit span, and the subtraction of seven. The animal naming test, token test, Boston naming test, repetition, reading aloud, and sentence composition were all used to assess language skills. Semantic and episodic long-term memory, orientation, and delayed recall of a five-word list were used to assess memory. The clock drawing test, block design, copying images, and drawing on request were used to assess visuospatial skills. Trail-making tests A and B, general knowledge, solving a series of ideas, proverb comprehension, equation solving, and computations were used to assess executive function. The lipid profile, HbA1c, and fasting blood sugar were examined in a laboratory. All participants underwent imaging evaluations using a non-contrast head MRI and/or head CT scan. The procedures for digital subtraction angiography and magnetic resonance angiography were followed based on indication.

Table 2: Hachinski ischemic score

Item	Score
Abrupt onset	2
Stepwise detoriation	1
Fluctuating course	2
Nocturnal confusion	1
Relative preservation of personality	1
Depression	1
Somatic complaints	1
Emotional incontinence	1
History of hypertension	1
History of stroke	2
Evidence of associated atherosclerosis	1
Focal neurological symptoms	2
Focal neurological signs	2

The data were presented in numbers (n) along with the average value. Numerical variables were analyzed using the one-way ANOVA test or the Kruska Wallis test. Post-hoc tests were done with the Bonferroni test. We analyzed categorical variables using either Chi-Square or Fisher exact tests. All statistical tests were carried out with a significance value of $p < 0.05$. Statistical analysis was performed with the SPSS 25.0 application (SPSS Inc., Chicago, IL)

RESULTS

During the period of January 1st–December 31th 2023, 218 patients visited the Memory Clinic at Dr. R. D. Kandou, Manado. One hundred subjects fulfilled the inclusion and exclusion criteria. Fifty samples (58%) were men, and the mean age was 61.06 years (SD ± 13.3). A total of 17 (17%) samples had only completed elementary school or less, 56 (56%) had completed high school or junior high school, and the remaining 27 (27%) participants had completed higher education than high school. Fourty one (41%) samples were classified as having subcortical dementia, 48 (48%) as having multiple infarction/cortical dementia, and 11 (11%) as having mixed dementia according to the VICCCS categorization. (Table 3) The cognitive function of each patient was subsequently evaluated. (Table 4)

The research participants' MoCA-INA mean was 12.2 (SD ± 6.0), with mixed type dementia having the lowest value ($p < 0.001$), followed by multiple infarction/cortical and subcortical vascular dementia. The most commonly affected domain in vascular dementia was memory (91%), followed by visuospatial (79%), executive function (77%), language (68.3%), and attention (64%). Language impairments were more common in the multiple infarct/cortical subtype than in the subcortical and mixed subtypes ($p < 0.001$). On the other hand, executive function

Table 3: Demographic study

	n
Gender	
Male	58
Female	42
Age	
≥ 65 years old	58
< 65 years old	42
Education	
Elementary school	17
Junior – senior high school	56
> Senior high school	27
Hypertension	
Yes	64
No	35
Diabetes mellitus (DM)	
Yes	25
No	75
Dyslipidemia	
Yes	38
No	62
History of stroke	
Yes	65
No	35
Smoking	
Yes	19
No	81
Alcohol consumption	
Yes	11
No	89
Demensia subtype	
Subcortical	41
Multipel / cortical infarct	48
Mixed	11

abnormalities were more commonly observed in the subcortical subtype of vascular dementia compared to multiple/cortical and mixed dementia ($p < 0.001$). There were no notable changes seen between the three subtypes of vascular dementia in terms of attention, memory, or visuospatial problems (Table 5).

DISCUSSION

According to our study, 48 cases (48%) of multiple/cortical infarcts were the most common subtype of vascular dementia, followed by subcortical cases (41%), and mixed subtypes (11%). The findings of this investigation are in contrast to those of earlier studies by Sengupta *et al*.[4], which found that small vessel dementia accounted for 40% of cases and large vessel dementia for 24% of cases, respectively, as the most prevalent subtype. This discrepancy is probably due to risk factors and geographic location, as atherosclerosis of the major cerebral arteries is a prevalent cause of stroke in Indonesia. Large artery atherosclerosis accounted for 59.6% of stroke cases, according to a study by Venketasubramanian et al. in 2022. Other etiologies (0.9%), cardio-embolism (2.1%), small vessel disease (26.7%), and unexplained etiology (9.8%) were the next most common causes of stroke.[9]

In the multiple infarction or cortical vascular dementia subtype, language was the domain most significantly affected ($p<0.001$), while in the subcortical subtype, executive function was the domain most significantly damaged ($p<0.001$). This is consistent with other study showing that executive and visuospatial functions were more prevalent in vascular dementia with small vessels, but language was more prevalent in vascular dementia with large vessels.[4] The primary cause of aphasia is recognized to be stroke caused by large vessel occlusion, particularly the middle cerebral artery, either by embolism or thrombosis. These arteries can affect cortical structures, where Wernicke's and Broca's areas were located.[10] According to a 2019 study by Bhat *et al*, cognitive, language, and memory problems were significantly impaired by cortical vascular dementia, particularly in the anterior circulation.[11] Although aphasia due to stroke is strongly associated with left hemisphere damage, previous studies have shown that strokes in the right hemisphere can also cause language disorders. A study conducted by Gajardo-Vidal *et al*. showed that the detrimental effect of right hemisphere strokes on language is frequently observed after damage to the right inferior frontal sulcus, as this location contributes to linguistic and non-linguistic working memory capacity (executive function) that is needed for normal speech comprehension.[12]

Subcortical dementia is commonly associated with apathy, bradyphrenia, and impaired executive function.[13] This claim is supported by earlier meta-analyses that demonstrated a decline in executive function, measured by the Stroop and Trail-Making Test B, was more common in patients with subcortical vascular mild cognitive impairment (VaMCI) than in controls.[14] Complex cognitive functions that depend on the close integration of high order decisional neurons in the prefrontal cortex with primary and association

Table 4: Cognitive function in vascular dementia subtype

Vascular dementia subtype	MoCA-INA	Significance (p)
Subcortical	14.6 (SD ±6.1)[b,c]	0.001
Multiple/cortical	10.8 (SD ±5.5) [a,c]	
Mixed	9.1 (SD ±4.9) [a,b]	

a = compared with subcortical dementia; b = compared with multiple/cortical dementia; c= compared with mixed dementia

cortical areas are disrupted by small-vessel disease, which regularly breaks connections among prefrontal, sensory, motor, and limbic cortices.[14,15] Executive function impairment has been extensively documented in subcortical vascular cognitive impairment, leading to its inclusion in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), as one of the early cognitive alterations linked to vascular-related neurocognitive disorders.[14]

Compared to cortical and subcortical vascular dementia, mixed dementia showed the greatest cognitive deterioration, as vascular dementia and Alzheimer's disease are associated. For instance, white matter lesions and lacunae are typical vascular lesions in Alzheimer's disease, and vice versa. Older people with vascular dementia might also have neurofibrillary tangles and amyloid plaques. Concomitant brain disease is hypothesized to have the ability to collaborate to induce a more severe decrease in cognitive function.[16] Compared to subcortical injuries, cerebral cortex-related strokes typically result in more severe cognitive abnormalities. According to a study by Weaver *et al*, injuries affecting the left frontotemporal lobe and right parietal lobe were more common to cause post-stroke cognitive deterioration.[17]

The limitation of this study is that the sample size is small compared to previous studies. Analysis of the location and side of the infarct was also not carried out, so a correlation of the pattern of cognitive deficits with the strategic location of the infarct could not be done, indicating that further research in this field is still needed.

In conclusion, the cortical subtype, also known as multiple infarct dementia, is the most commonly observed subtype in VaD. While executive function is more dominantly damaged in the cortical subtype, language difficulties are more prevalent in multiple infarctions or cortical subtypes.

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DISCLOSURE

Ethics: This study received approval from the Institutional Review Board (IRB) of the Provincial General Hospital Prof. Dr. R. D. Kandou prior to its commencement (DP.04.03/D.XV/3038/2024). Informed consent was obtained from all participants of the study. The authors received no financial support for the research, authorship, and/or publication of this article, The authors have no potential conflicts of interests to disclose.

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Conflict of interest: None

Table 5: Pattern of cognitive deficit in vascular dementia subtype

Cognitive domain	Vascular dementia subtype (n)			Significance (p)
	Subcortical	Multiple/cortical infarct	Mixed	
Attention	23	31	10	0.10
Language	15	43	10	<0.001 [a,c]
Memory	35	45	11	0.21
Visuospatial	29	40	10	0.20
Executive function	39	27	11	<0.001[b,c]

a = compared with subcortical dementia; b = compared with multiple/cortical dementia; c= compared with mixed dementia

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