

Cerebral Microbleeds and Cognition in Patients with Symptomatic Small Vessel Disease

Thesis

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Presented By

Kholoud Mahmoud Abdullah
M.B.B.CH

Under Supervision of

Prof. Dr. Hany Mahmoud Zakieldine
*Professor of Neurology and Psychiatry
Faculty of Medicine - Ain Shams University*

Dr. Iman Mohamed Bayomy
*Consultant of Neurology and Psychiatry
Faculty of Medicine - Ain Shams University*

Dr. Mona Mokhtar Wahideldin
*Lecturer of Neurology and Psychiatry
Faculty of Medicine - Ain Shams University*

Faculty of Medicine
Ain Shams University
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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببناك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Contents

Title	Page No.
List of Tables	i
List of Figures	iv
List of Abbreviations	vi
Introduction	1
Aim of the Study	3
 Classification of Cerebral Small Vessel Diseases	4
 Cerebral Microbleeds	16
Subjects and Methods	44
Results	49
Discussion	98
Summary and Conclusion	107
Recommendations	108
References	110
Appendix	138
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Aetiopathogenic classification of cerebral small vessel diseases.....	5
Table (2):	Standard criteria for CMBs identification on MRI and their rationale.....	18
Table (3):	Age differences in the study group.....	50
Table (4):	Sex and years of education differences in the two groups.....	51
Table (5):	Risk factors in both positive and negative groups.....	53
Table (6):	Risk factors regarding location of MBs	55
Table (7):	Classification of Microbleeds severity in CMB positive group	56
Table (8):	Distribution of microbleeds.....	58
Table (9):	Comparison between groups according to other MRI Parameters	59
Table (10):	Comparison between groups according to total score of MoCA test	60
Table (11):	MoCA test in CMB Positive group	61
Table (12):	MoCA test in CMB Negative Group.....	63
Table (13):	Demographic data differences between the CMB positive and CMB negative groups.....	64
Table (14):	Cerebrovascular risk factors differences in both study groups.....	67
Table (15):	Cerebrovascular risk factors according to deep and non-deep located CMBs	68
Table (16):	Antiplatelets intake differences between CMB positive and negative groups	70

List of Tables (Cont...)

Table No.	Title	Page No.
Table (17):	Antiplatelets count differences between CMB positive and negative groups	71
Table (18):	MRI parameters compared between CMB positive and negative groups	72
Table (19):	Relation between personal and clinical data and MoCA test	74
Table (20):	Comparison between groups according to MoCA test	75
Table (21):	Relation between occipital CMBs and MoCA test	77
Table (22):	Relation between Frontal CMBs and MoCA test	78
Table (23):	Relation between Temporal CMBs and MoCA test	80
Table (24):	Relation between Parietal CMBs and MoCA test	81
Table (25):	Relation between Basal ganglia CMBs and MoCA test	83
Table (26):	Relation between Thalamus CMBs and MoCA test	85
Table (27):	Relation between Cerebellum CMBs and MoCA test	86
Table (28):	Relation between Brain stem CMBs and MoCA test	87
Table (29):	Partial correlation between MoCA test cognitive indices	88

List of Tables (Cont...)

Table No.	Title	Page No.
Table (30):	Correlations between Frontal CMBs and cognitive indices after controlling different parameters.....	88
Table (31):	Correlations between Parietal CMBs and cognitive indices after controlling different parameters.....	89
Table (32):	Correlations between Basal ganglia CMBs and cognitive indices after controlling different parameters.....	90

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Pathogenesis of brain damage as a result of small vessel disease	8
Figure (2):	MRI manifestations of cerebral small vessel disease	10
Figure (3):	The topography of sporadic cerebral small vessel disease and its MRI features are shown in this schematic representation	23
Figure (4):	A proposed model of the pathophysiological pathways that can give rise to cerebral microbleeds.....	28
Figure (5):	Frequency of cerebral microbleeds in different populations and disease states.....	34
Figure (6):	Bar chart between groups according to age (years).....	50
Figure (7):	Bar chart between groups according to Metabolic risk factors and medications.....	53
Figure (8):	Pie chart level of microbleeds severity in CMB positive group.	56
Figure (9):	Sex differences between CMB positive and negative groups.....	65
Figure (10):	Hypertension differences between CMB positive and negative groups.	66
Figure (11):	Risk factors in deep and non-deep located MBs.	69
Figure (12):	Antiplatelets medication between CMB positive and negative groups.	70
Figure (13):	MRI parameters compared between CMB positive and negative groups	72

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (14):	Bar chart between groups according to MoCA test.	76
Figure (15):	Relation between Frontal CMBs and MoCA test	79
Figure (16):	Relation between Parietal CMBs and MoCA test.	82
Figure (17):	Relation between Basal ganglia CMBs and MoCA test.	84
Figure (18):	Scatter plot between total microbleeds and MoCA test irrespecting location in CMB positive group ($r = -0.898$; $p < 0.001$).	91
Figure (19):	MRI brain images of case (1).	92
Figure (20):	MoCA test of case (1).	94
Figure (21):	MRI brain images of case (2).	95
Figure (22):	MoCA test of case (2).	97

List of Abbreviations

Abb.	Full term
<i>AD</i>	<i>Alzheimer disease</i>
<i>ADC</i>	<i>Apparent diffusion coefficient</i>
<i>ApoE</i>	<i>Apolipoprotein E</i>
<i>Aβ</i>	<i>Amyloid β-peptide</i>
<i>BG</i>	<i>Basal Ganglion</i>
<i>CAA</i>	<i>Cerebral amyloid angiopathy</i>
<i>CADASIL</i>	<i>Cerebral autosomal dominant arteriopathy with subcortical ischemic strokes and leukoencephalopathy</i>
<i>CARASIL</i>	<i>Cerebral autosomal recessive arteriopathy with subcortical ischemic strokes and leukoencephalopathy</i>
<i>CMBs</i>	<i>Cerebral microbleeds</i>
<i>cSVD</i>	<i>Cerebral small vessel disease</i>
<i>CT</i>	<i>Computed tomography</i>
<i>DPWM</i>	<i>Deep / periventricular WM</i>
<i>ERPs</i>	<i>Event-related potentials</i>
<i>FLAIR</i>	<i>Fluid-attenuated inversion recovery</i>
<i>GRE T2 *</i>	<i>Gradient Echo T2*</i>
<i>HV</i>	<i>hypertensive vasculopathy</i>
<i>ICH</i>	<i>Intracerebral hemorrhage</i>
<i>MARS</i>	<i>Microbleed Anatomical Rating Scale</i>
<i>MCI</i>	<i>Mild cognitive impairment</i>
<i>MELAS</i>	<i>Mitochondrial encephalopathy with lactic acidosis and stroke-like episode</i>
<i>MMSE</i>	<i>Mini Mental State Examination</i>
<i>MoCA test</i>	<i>Montreal Cognitive Assessment tests</i>
<i>MRI</i>	<i>Magnetic Resonance Imaging</i>
<i>PET</i>	<i>positron emission tomography</i>
<i>PiB</i>	<i>Pittsburgh compound B</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>SVD</i>	<i>Small vessel disease</i>
<i>SWI</i>	<i>Susceptibility weighted imaging</i>
<i>TFNEs</i>	<i>Transient focal neurological episodes</i>
<i>TIA</i>	<i>Transient ischemic attack</i>
<i>VCI</i>	<i>Vascular cognitive impairment</i>
<i>VaD</i>	<i>Vascular Dementia</i>
<i>WMLs</i>	<i>White matter lesions</i>

ABSTRACT

Background: as life expectancy is increasing worldwide, cognitive impairment and dementia are becoming a major public health challenge facing all societies. Accumulating evidence is suggesting that cerebral small vessel disease (cSVD) is a leading cause for cognitive deterioration. Cerebral microbleeds (CMBs) are common in (cSVD) with less consistent results concerning their relation to cognition.

Aim of the Study: determine whether CMBs correlate with cognition in patients with symptomatic small vessel disease (SVD). If cognitive impairment is detected, determine whether this association remained after controlling for other MRI markers of SVD. Also to study the relation between different locations of CMBs and their effect on domains of cognition according to Montreal cognitive assessment (MoCA) test.

Subjects and Methods: this cross sectional study included eighty five Egyptian patients with symptomatic SVD, from the neuropsychiatry clinic of the Main Suez Hospital in Suez city, in the period between February 2017 and February 2018. Subjects were classified according to CMBs presence into CMB positive and negative groups .Both groups are assessed using MRI imaging and MoCA test for cognitive function.

Results: In our study, CMBs recorded a high prevalence rate of SVD patients. Subjects with MBs were mainly males and significantly older, with higher white matter lesion volume and more lacunar infarcts. MoCA test detected significant impairment in in visuospatial/ executive function, attention and total scores in CMB positive group. Both Frontal and Parietal MBs showed independent association with visuospatial/executive impairment. Deep MBs in Basal ganglia was proved to be independent risk factor for attention affection.

Conclusion: Presence and Location of MBs proved to be important in determining cognitive consequences. The relations with cognitive performance were mainly driven by frontal, parietal, and deep located MBs in basal ganglia. Memory affection in frontal MBs was dependent to severe white matter intensities and lacunes.

Keywords: *Cerebral Microbleeds – Cognition – Small Vessel Disease*

INTRODUCTION

Small vessel disease is a term used with various meanings and in different contexts (i.e., pathological, clinical, and neuroimaging aspects). These diseases are thought to be the most frequent pathological neurological processes and prevalent brain conditions that have a crucial role in at least three fields: stroke, dementia, and ageing (*Ding et al., 2017*). Cerebral small vessel disease (cSVD) is described as a predictor of cognitive decline and a major cause of vascular cognitive impairment (VCI) (*Lawrence et al., 2015; Pantoni, 2010; Romero et al., 2017*).

Unlike large vessels, small vessels cannot be currently visualised in vivo; therefore, the parenchyma lesions that are thought to be caused by these vessel changes have been adopted as a marker of small vessel disease.

Lacunar infarcts and white matter lesions (WMLs) have been recognized for years as characteristic MRI manifestations of SVD. In addition, cerebral microbleeds (CMBs) are recently recognized as an important new manifestation and diagnostic marker of small vessel pathology (*Charidimou & Werring, 2011*).

WMLs and lacunar infarcts have been well established through studies to be associated with cognitive impairment (*Yan et al., 2015*). However, CMBs clinical impact on cognition remains an active field of research (*Shoamanesh et al., 2018*).

CMBs are detected in about 5% of healthy individuals with no neurological disorder with a prevalence increasing with age to reach about 40% in those over 80 years old (*Vernooij et al. , 2008*). CMBs are commonly found in patients with cerebrovascular diseases, including ischaemic or haemorrhagic stroke, Alzheimer disease (AD) and vascular dementia (VaD) (*Cordonnier et al., 2007; Kester et al., 2014*).

Most studies were conducted on such groups of patients. They examined the association of CMBs with increased risk of stroke recurrence and intracerebral hemorrhage (*Imaizumi et al., 2015*), haemorrhagic transformation after ischaemic stroke and impairment of cognitive function (*Hashimoto et al., 2004*) (*Gregoire et al., 2013*). Investigation of their presence in relation to poorer microstructural integrity of brain white matter was conducted for explanation of such cognitive impairment (*Akoudad et al., 2013*).

There is a strong correlation between CMBs presence and the presence of other cerebral SVDs. Subjects with CMBs had significantly higher number of lacunar infarcts and more severe WMLs (*Chung et al., 2016*). This made the studying of CMBs relation with cognitive performance important in patients with SVD, which may give more explanations for different vascular pathology and mechanisms of cognitive impairment in SVDs.

AIM OF THE STUDY

Determine whether CMBs correlate with cognition in patients with symptomatic SVD. Also studying the relation between different locations of CMBs and their effect on various domains of cognition. Determine whether these associations were independent of coexisting WMLs and lacunar infarcts.