



Microemboli as an Etiology of Acute Ischemic Stroke in Watershed zone

Thesis

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٢٠١٦

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ

صَدَقَ اللَّهُ الْعَظِيمُ



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List of Abbreviations

¹³³Xe	Xenon 133
A.C.A	Anterior Cerebral Artery
ACoA	Anterior Communicating Artery
ACZ	Acetazolamide
AEWSI	Anterior External Watershed Infarcts
ATP	Adenosine tri phosphate
BBB	Blood–brain barrier
BHI	Breath-holding Index
BOLD	Blood Oxygen Level-Dependent
BZ	Border Zone
CA	Cerebral Autoregulation
CBF	Cerebral Blood Flow
CBV	Cerebral Blood Volume
CO₂	Carbon dioxide
CPP	Cerebral Perfusion Pressure
CSO	Centrum semiovale
CT	Computed tomography
CVR	Cerebral Vasomotor Reactivity
CWS	Cortical watershed strokes
DM	Diabetes Mellitus
DWI	Diffusion Weighted Image
EEG	Electroencephalographic
EWS	External Water Shed
EWSI	External Watershed Infarction.
fMRI	Functional Magnetic Resonance Imaging

List of Abbreviations (cont.)

FV		Flow Velocity.
H⁺		Hydrogen
HDI		Hemodynamic Impairment
HDL		High Density Lipoprotein
HTN		Hypertension
ICA		Internal Carotid Artery
ICP		Intracranial pressures
IWS		Internal Watershed
IWSI		Internal Watershed Infarction.
LDL		low density lipoprotein
MAP		Mean Arterial blood Pressure
MCA		Middle cerebral artery
MES		Microembolic signals
MFV		Mean flow velocity
NIRS		Near-infrared spectroscopy
NO		Nitric oxide
NVU		Neurovascular unit
OEF		Oxygen extraction fraction
Paco₂		CO ₂ partial pressure
PCA		Posterior cerebral artery
PCoA		Posterior communicating artery
PET		Positron emission tomography
PEWSI		Posterior External Watershed Infarcts
SPECT		Single Photon Emission Computed
TCD		Transcranial Doppler
TEE		Trans-esophageal echocardiography

List of Abbreviations (cont.)

TIA	Transient Ischemic Attack
	Tomography
TTE	Trans Thoracic Echo
VBH	Velocity Breath Holding
WHO	World health organization
WS	Watershed
WSI	Water Shed Infarction

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Introduction

Stroke is a worldwide health problem. It makes an important contribution to the morbidity, mortality and the disability in the developed as well as the developing countries. A WHO collaborative study, which was done in 12 countries, showed that the incidence rates of stroke were 0.2 – 2.5 per 1000 population per year. It is the leading cause of adult disability and the second most common cause of death worldwide. It accounts for 10 – 12% of the total deaths in the developed countries (*Park et al, 2005*).

Disturbances in the cerebral function in stroke are caused by three morphological abnormalities, which include stenosis, occlusion or rupture of arteries, leading to ischemia, infarction and cerebral hemorrhage respectively (*Bladin et al, 1993*).

Watershed strokes are named because they affect the distal watershed areas of the brain. The original terminology came from the German literature, which used the analogy of an irrigation system. The German scholars compared the blood flow in distal arterial territories of the brain to the last field on a farm, which was the area with the least supply of water and therefore most vulnerable to any reduction in flow. In a medical context, the term “watershed” refers to those areas of the brain that receive dual blood supply from the branching ends of two large arteries (*Bladin et al, 1993*).

These events are localized to two primary regions of the brain:

1. Cortical watershed strokes (CWS), or outer brain infarcts, are located between the cortical territories of the anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral artery (PCA).
2. Internal watershed strokes (IWS), or sub cortical brain infarcts, is located in the white matter along and slightly above the lateral ventricle, between the superficial systems of the MCA and ACA, or between the deep and the superficial arterial systems of the MCA (*Momjian et al, 2005*).

The conventional theory implicates hemodynamic compromise produced by repeated episodes of hypotension in the presence of a severe arterial stenosis or occlusion. The lower perfusion pressure found within the border zone areas in this setting confers an increased susceptibility to ischemia, which can lead to infarction. This causal role of severe arterial hypotension has been well described and confirmed by the results of experimental studies in animals (*Howard et al, 1966*).

The typical clinical manifestations of syncope, hypotension, and episodic fluctuating or progressive weakness of the hands are also supportive of this theory of hemodynamic failure (*Bogousslavsky et al, 1993*).

Radiologic studies also support the hypothesis that border zone infarcts distal to internal carotid artery disease are more likely to occur in the presence of a non-competent circle of Willis (*Masuda et al, 1994*).

In sharp contrast with this widely prevalent interpretation, several pathologic investigations have emphasized an association between border zone infarction and micro emboli, and embolic material has been found within areas of border zone infarction in autopsy series (*Masuda et al, 1994*).

Preferential propagation of emboli in the border zone regions also has been found in experimental studies. Border zone infarction may be better explained by invoking a combination of two often interrelated processes: hypo perfusion and embolization (*Caplan et al, 1998*).

Hypoperfusion, or decreased blood flow, is likely to impede the clearance (washout) of emboli. Because perfusion is most likely to be impaired in border zone regions, clearance of emboli will be most impaired in these regions of least blood flow. Severe occlusive disease of the internal carotid artery causes both embolization and decreased perfusion. Similarly, cardiac disease is often associated with microembolization from the heart and aorta with periods of diminished systemic and brain perfusion. This theory, although it seems reasonable, remains unproved and has been challenged on many accounts (*Caplan et al, 1998*).