Serum Level of Homocystiene in Patients with Extracranial versus Intracranial Arterial stenosis

A Thesis

Submitted for Fulfillment of Master Degree in Neurology & psychiatry

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Amal Ahmad Hussien

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List of Abbreviations

Abb.	Full term
ACA	Anterior cerebral arteries
AICA	Anterior inferior cerebellar artery
BBB	Blood brain barrier
CAC	Carotid artery calcification
CAS	Carotid artery stenosis
CE–MRA	Contrast-enhanced MRA
CHOL	Total cholesterol
CIMT	Carotid intima-medial thickness
CNS	Central nervous system
CRP	C-reactive protein
CSF	Cerebrospinal fluid
CT	Computerized tomography
CTA	Computed tomography angiography
Cys	Cysteine
DM	Diabetes milltus
DSA	Digital Subtraction Angiography
DUS	Doppler ultrasound
ECST	European Carotid Surgery Trial
ELISA	Enzyme-linked immunosorbent assay
ESRD	End-stage renal disease
FC	Fibrous Cap
FDG	Fluorodeoxyglucose
HBA1C	Glycosylated Hemoglobin A1c
Hcy	Homocysteine
HDL	High density lipoprotein
hHcy	Hyperhomocysteinemia
HTN	Hypertension
ICA	Internal carotid artery
IMT	Intima media thickness
IPH	Intraplaque Hemorrhage
LDL	Low density lipoprotein
MCA	Middle cerebral arteries
MFV	Mean flow velocity

List of Abbreviations cont…

Abb.	Full term
MRA	*Magnetic Resonance Angiography*
MRI	*Magnetic resonance imaging*
NASCET	*North American Symptomatic Carotid Endarterectomy Trial*
NECT	*Noncontrast-enhanced CT*
NIDDM	*Non-insulin dependent diabetes millitus*
NMDA	*N-methyl-D-aspartate receptor*
PARP	*Poly-ADP-ribose polymerase*
PCA	*Posterior cerebral arteries*
PICA	*Posterior inferior cerebellar artery*
PSV	*Peak systolic velocity*
ROS	*Reactive oxygen species*
SAM	*S-adenosylmethionine*
T2DM	*Type 2 diabetes mellitus*
TCD	*Transcranial Doppler*
TG	*Triglycerides*
tHcy	*Total homocysteine serum level*
TIA	*Transient ischemic attack*
TOF–MRA	*Time-of-flight MRA*
US	*Ultrasound*
WASID	*Warfarin-Aspirin Symptomatic Intracranial Disease*
WBC	*White blood cell*

Introduction

A cerebrovascular accident more commonly known as a stroke or brain attack is the term used to describe the sudden death of brain cells in a localized area due to inadequate blood flow, A stroke causes loss of function, sometimes permanently, in the part of the body that is controlled by the damaged part of the brain, nowadays the burden of chronic non-communicable diseases in developing countries has risen sharply in recent years and the rate of increase is set to accelerate ***(Sherlock et al., 2009).***

Stroke is the second most common cause of death worldwide and one of the major causes of long–term disability, carotid artery stenosis is an independent risk factor for ischemic stroke and for related forms of atherosclerotic vascular disease, raised levels of homocysteine (Hcy) have been previously described as an independent risk factor of coronary artery disease and stroke and there has been already reported particular association between high Hcy levels and ischemic stroke due to large artery atherosclerosis ***(Kenina et al., 2010; Streifler et al., 2001).***

Hcy is a naturally occurring metabolite of methionine, a compound essential for intracellular metabolism. Hcy reduces nitric oxide bioavailability by stimulating the formation of reactive oxygen species. In addition, Hcy increases matrix metalloproteinase activity, resulting in both an alteration of the vascular elastin/collagen ratio and reduced compliance of arterial walls. Hcy eventually causes a reduction of vessel radius by thickening the arterial wall. Experimental evidence suggests that the atherogenic propensity associated with hyperhomocysteinemia (hHcy) results from endothelial dysfunction and injury followed by platelet activation and thrombus formation ***(Streifler et al., 2001; Jeong et al., 2008).***

There is an independent association between increasing Hcy level and ischemic stroke, which appears to be as strong as all other conventional vascular risk factors, but it also confirms the hypothesis that there is a significant and strong association between increasing Hcy and large-artery disease (9-fold increased risk with high Hcy level) and less with small-artery disease (2-fold increased risk with high Hcy level) with no association with cardioembolic and other etiologic subtypes of ischemic stroke ***(Eikelboom et al., 2000).***

A study provided by ***Somay & his colleagues*** showed that Hcy level in the patient group was found to be significantly high compared to the control subjects. Negative correlation has been found between Hcy and vitamin B12. The correlation between the elevated Hcy levels and the serum lipid level has not been considered significant, however, it was found to be associated with intima-media thickness in the extracranial carotid arteries and moderate to severe carotid artery stenosis ***(Somay et al., 2005)***.

Aim of the Work

This study aims to

1) Assess serum level of homocystiene (Hcy) as a risk factor in patients with ischemic stroke whether extracranial or intracranial arterial stenosis.
2) To compare serum level of Hcy in patients with extracranial arterial stenosis against intracranial arterial stenosis.

Chapter 1

Arterial Blood Supply of Brain

The brain receives blood from two sources: the internal carotid arteries, which arise at the point in the neck where the common carotid arteries bifurcate, and the vertebral arteries. The internal carotid arteries branch to form two major cerebral arteries, the anterior cerebral arteries (ACA) and middle cerebral arteries (MCA). The right and left vertebral arteries come together at the level of the pons on the ventral surface of the brainstem to form the midline basilar artery. The basilar artery joins the blood supply from the internal carotids in an arterial ring at the base of the brain (the circle of Willis) (figure 1& 2). The posterior cerebral arteries (PCA) arise at this confluence, as do two small bridging arteries, the anterior and posterior communicating arteries. Conjoining the two major sources of cerebral vascular supply via the circle of Willis presumably improves the chances of any region of the brain continuing to receive blood if one of the major arteries becomes occluded ***(Purves et al., 2001).***

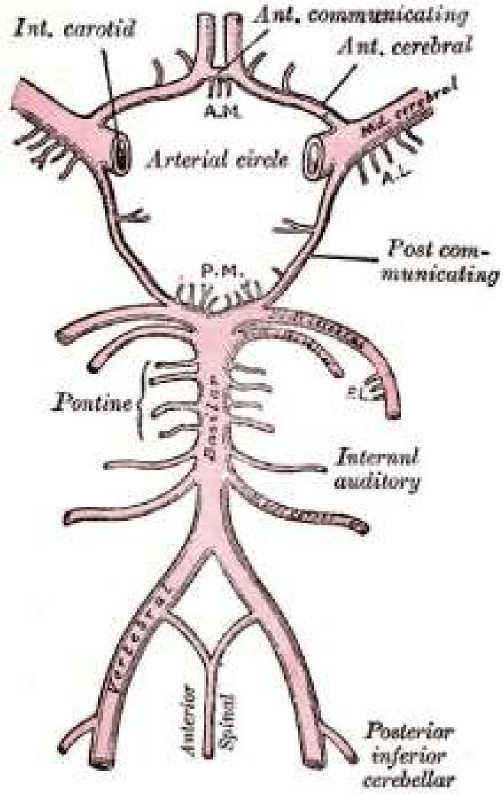

Figure (1): Arterial circulation at the base of the brain**.** ***(Gray's Anatomy of the Human Body., 20th U.S.)***.

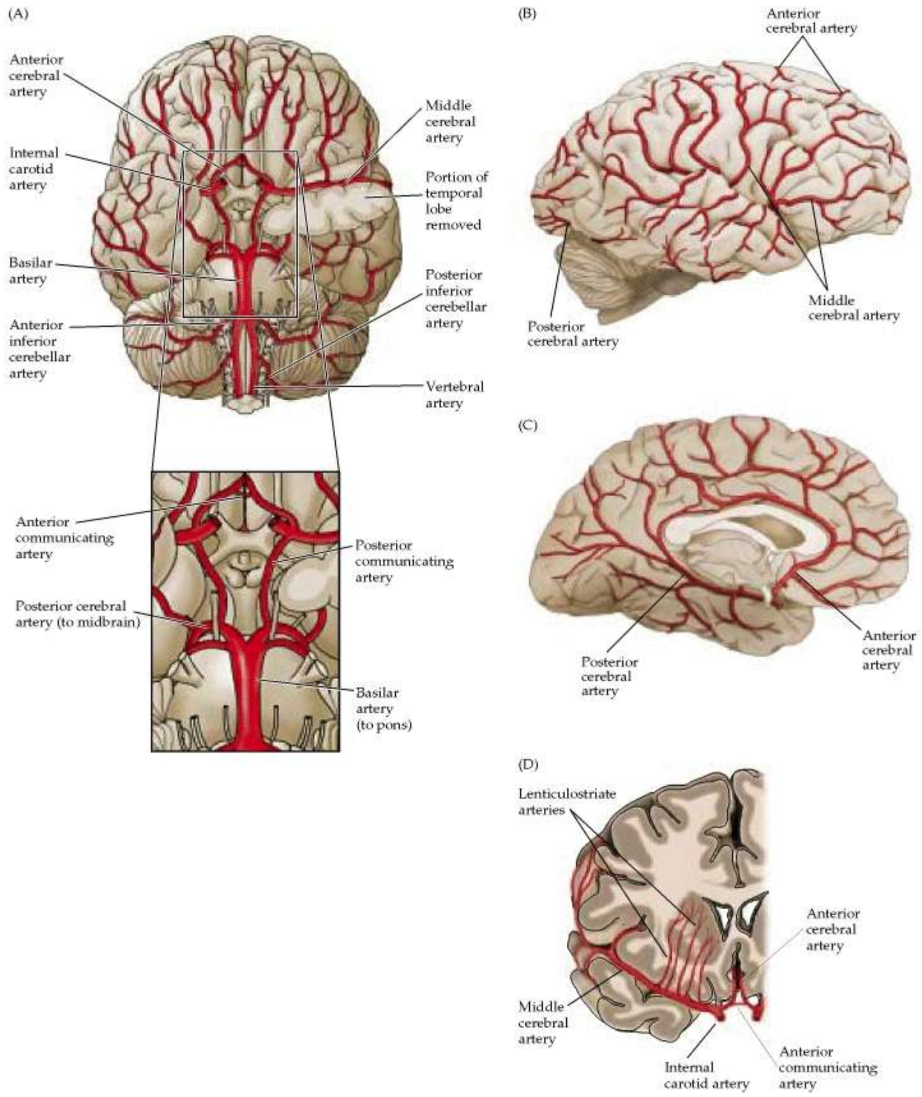

Figure (2): The major arteries of the brain. (A) Ventral view. The enlargement of the boxed area shows the circle of Willis. Lateral (B) and (C) midsagittal views showing anterior, middle, and posterior cerebral arteries. (D) Idealized frontal section showing course of middle cerebral artery. ***(Purves et al., 2001)***

The major branches arising from internal carotid artery (ACA & MCA) form the anterior circulation that supplies the forebrain. These arteries also from the circle of Willis. Each