Correlation Between Plasma Fibrinogen Levels and Clinical Outcome in Patient with Acute Ischemic Stroke

Thesis Submitted for Partial Fulfillment of Master Degree of Neurology

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Dedication

To

The memory of my father,

To my mother, my two brothers and my sister

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List of Abbreviations

AAASPS	African American Antiplatelet Stroke Prevention Study
ATBC	Alph- tocoherol Beta carotene cancer prevention study
ACAS	Asymptomatic Carotid Atherosclerosis Study
ADA	American Diabetes Association
ADP	Adenosine diphosphate
AHA	American Heart Association
ASA	American Stroke Association
APCSC	Asia Pacific Cohort Study Collaboration
ATP	Adenosine triphosphate
ARIC	Atherosclerosis Risk In Communities
AF	Atrial Fibrillation
ACEIs	Angiotensin converting enzyme inhibitors
ARBs	Angiotensin Receptors Blockers
ACAS	Asymptomatic Carotid Artery Stenosis
ACST	Asymptomatic Carotid Surgery Trail
ALLHAT	Antihypertensive and lipid lowering treatment to prevent heart attack trail
ASCOT	the Anglo- scandinavian cardiac outcome trial
BBs	Beta Blockers
BI	Barthel index
BIP	bezafibrate infarction prevention
BMI	Body Mass Index
BP	Blood Pressure
CBF	Cerebral Blood Flow

CDC	Center of Disease Control
CEA	Carotid endarterectomy
CEE	Combined equine estrogens
CVD	Cardio Vascular Disease
DALYS	Disability- Adjusted life years
DIAS	Desmoteplase in acute stroke
DM	Diabetes Mellitus
DWI	Diffusion weighted imaging
EU	European Union
ECASS III	European Cooperative Acute Stroke Study
ESPS-2	The second European Stroke Prevention Study
FAD	Food and Drug Administration
GRACE	Greek – Atorvastatin and coronary heart disease evaluation
HRQOL	Health – Related Quality of Life
HRT	Hormonal Replacement Therapy
HTN	Hypertension
ICA	Internal carotid artery
ICAM	Intracellular adhesion molecule
ICH	Intracranial hemorrhage
IDH	Isolated Diastolic Hypertension
IIT	Intensive Insulin Therapy
ISH	Isolated Systolic Hypertension
KLIS	Kyushu lipid intervention study
LMW	Low molecular weight
MCA	Middle Cerebral artery
MPA	Medroxy progesterone acetate

MRFIT	Multiple Risk Factor Intervention Trial
NINDS	National Institute of Neurological Disorders and stroke
NMDA	N-methyl-D-aspartate
NOMAS	Northen Manhattan Study
NVAF	Non Valvular Atrial Fibrillation
OCs	Oral Contraceptives
PPAR-a	Peroxisome Proliferator Activator Receptor –a
PROSPER	Prospective Study of Pravastatin in Elderly at Risk Study
PROCAT	Prolyse in Acute Cerebral Thromboembolism
QOL	Quality of Life
RELP	Restriction Fragment Length Polymorphism
SAH	Subarachnoid haemorrhage
SDH	Systolic and Diastolic Hypertension
SHS	Strong Heart Study
SLSR	South London Stroke Register
SSCP	Single Strand Conformation Polymorphism
TASS	Ticlopidine Aspirin Stroke Study
TIA	Transient Ischemic attack
TF	Tissue Factor
WHI	Women Health Initiative
WHS	Women Health System

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INTRODUCTION

The World Health Organization has defined stroke as "rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin." By conventional clinical definitions, if the neurologic symptoms continue for more than 24 hours, a person is diagnosed with stroke **(Sacco, 2005).**

Mortality from stroke was the fourth leading cause of death in the United States, and stroke was a leading cause of long-term severe disability. Nearly half of older stroke survivors experience moderate to severe disability **(Miniño et al, 2011)**.

A stroke is caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue. The most common symptom of a stroke is sudden weakness or numbness of the face, arm or leg, most often on one side of the body (**WHO 2010**).

Other symptoms include: confusion, difficulty speaking or understanding speech; difficulty seeing with one or both eyes; difficulty walking, dizziness, loss of balance or coordination; severe headache with no known cause; fainting or unconsciousness **(Goldstein and Simel, 2005)**.

Although the association between plasma fibrinogen concentrations and risk of coronary heart disease is well described data on the association of plasma fibrinogen with risk of total stroke. Fibrinogen, a clotting factor, may accelerate the thrombotic process and could also act as a marker of inflammation. Three prospective studies of Caucasians showed that high plasma fibrinogen concentrations were associated with increased risk of total stroke **(Sato et al, 2000).**

The recommendations for primary prevention of ischemic stroke and myocardial infarction focus on cholesterol, hypertension, smoking habits and the development of fibrinogen related ischemic complications of atherosclerosis that can be easily identified and treated **(Scarabin et al, 2003).**

There is an association between an increase fibrinogen level in plasma and prognosis after acute ischemic stroke showing that patients with lower initial fibrinogen levels (4.5 g/L) had better functional outcomes even when corrected for age and initial stroke severity. They confirmed a relationship

between fibrinogen and prognosis independent of other cardiovascular risk factors and stroke severity. Because patients at risk for the development of fibrinogen-related ischemic complications of atherosclerosis can be easily identified and non-pharmacological treatment (cessation of smoking, diet, exercise) seems to lower raised fibrinogen levels together with several drugs (fibrates, pentoxifylline, defibrotide) clinically oriented secondary prevention recommendations should consider the role of fibrinogen in ischemic stroke**(Del Zoppo et al, 2009**).

The clinical use of fibrinogen measurement should be based on evidence regarding the ability of fibrinogen to predict ischemic stroke prognosis beyond that of current prognostic prediction methods or models, and evidence regarding the use of prognosis prediction to treatment of ischemic stroke. A large body of well-done studies demonstrates an association between fibrinogen levels and ischemic stroke prognosis .There are, however, uncertainties in the exact role that fibrinogen plays in the determining ischemic stroke prognosis and the reliability of fibrinogen assessment (**Woodward et al, 2005**).