



Clinical significance of Albumin in Acute Cardioembolic Strokes

Thesis

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List of Abbreviations

ACC	: American College of Cardiology
AF	: Atrial fibrillation
AHA	: American heart association
ALT	: Aspartate aminotransferase
APOA2	: Apolipoprotein A-II
ASA	: American stroke association
AST	: Aspartate aminotransferase
BBB	: Blood brain barrier
BCCAO	: Bilateral common carotid artery occlusion
BNP	: Brain natriuretic peptide
CA-1	: Cornu amonis-1
CBC	: Complete blood count
CBF	: Cerebral blood flow
CCR5	: Chemokine receptor type 5
CCS	: Causative classification system for Ischemic stroke
CD40	: Cluster of differentiation 40
cDNA	: Complementary Deoxyribonucleic acid
CEA	: Carotid endarterectomy
CE	: Cardioembolic
CI	: Confidence interval
CNS	: Central nervous system

CRP	: C-reactive protein
CSF	: Cerebrospinal fluid
CT	: Computed topography
DWI	: Diffusion weighted imaging
ECG	: Electrocardiogram
ELISA	: Enzyme-linked immunosorbent assay
ESC	: European society of Cardiology
ESR	: Erythrocyte sedimentation rate
FLAIR	: Fluid attenuation inversion recovery
GABA A	: Gamma-aminobutyric acid A
GABA	: Gamma-Aminobutyric acid
GFAP	: Glial fibrillary acidic protein
GTP	: Guanosine-5'-triphosphate
GWA	: Genome-wide association
HDL	: High density lipoprotein
H-FABP	: Heart-type fatty acid binding protein
HK-2	: Human kidney-2
H-NMR	: Hydrogen nuclear magnetic resonance
HPLC	: High-performance liquid chromatography
HAS	: Human serum albumin
HS	: Hemorrhagic stroke
ICH	: Intracranial hemorrhage
IGFBP4	: Insulin-like growth factor binding protein 4

IL	: Interleukin
IMA	: Ischemia modified albumin
INR	: International normalized ratio
IS	: Ischemic stroke
KFT	: Kidney function test
LAA	: Large artery atherosclerosis
LAD	: Left atrial diameter
LA	: Left atrium
LCFA	: Long chain fatty acids
LC-MS	: Liquid chromatography–mass spectrometry
LDL	: Low density lipoprotein
LFT	: Liver function test
LMWH	: Low molecular weight heparin
LOC	: Level Of Consciousness
LVEF	: Left ventricular ejection fraction
LV	: Left ventricular
Lys	: Lysine
MAC	: Mitral annular calcification
MCA	: Middle cerebral artery
MCAO	: Middle cerebral artery occlusion
MI	: Myocardial infarction
miRNA	: Microribonucleic acid
MMP	: Matrix metalloproteinase

MRI	: Magnetic resonance imaging
mRNA	: Messenger ribonucleic acid
MRS	: Modified Rankin scale
MS	: Mass spectrometry
MVP	: Mitral valve prolapse
NDKA	: Nucleoside diphosphate kinase A
NF- κ B	: Nuclear factor Kappa Beta.
NIHSS	: National institute of health stroke scale
NMDA	: N-methyl D-Aspartate
NO	: Nitrous oxide
NOMAS	: Northern Manhattan study
NYHA	: New york heart association
OAC	: Oral anticoagulants
OR	: Odd's ratio
PDGFA	: Platelet-derived growth factor subunit A
PF4	: Platelet factor 4
PFO	: Patent foramen ovale
PGD2	: Prostaglandin D2
P-gp	: P-glycoprotein
PPBP	: 4-phenyl-1-(4-phenylbutyl) piperidine
PPIA	: Peptidyl-prolyl isomerizes
PUFA	: Poly unsaturated fatty acids

RA	: Right atrium
Rho A	: Ras homolog gene family, member A
RNA	: Ribonucleic acid
ROS	: Reactive oxygen species
rtPA	: Recombinant tissue plasminogen activator .
SAH	: Subarachnoid hemorrhage
SD	: Standard deviation
SNP	: Single Nucleotide Polymorphism
SSS	: Stroke scandinavian scale
SWMA	: Segmental wall motion abnormalities
TBI	: Traumatic brain injury
TC	: Total cholesterol
TEE	: Transesophageal Echocardiogram
TIA	: Transient Ischemic attacks
TLR4	: Toll like receptor 4
TNF	: Tumor necrosis factor
TOAST	: Trial of ORG 10172 in acute stroke treatment
TTE	: Transthoracic echocardiogram
UFD1	: Ubiquitin fusion degradation protein 1
VEDF	: Vascular endothelial derived factor
VWF	: Von Willebrand factor

Introduction

Stroke is a costly disease from human, family and societal perspectives. Starting from human costs, stroke is a leading cause of death and disability. As a consequence, stroke ranks as the second cause of death in the world population after ischemic heart disease (the third only if neoplastic diseases are considered as a group) (*Di Carlo et al., 2009*). Annually, about 16 million first ever strokes occur in world, causing a total of 5.7 million deaths (*Strong et al., 2007*)

About 85% of all stroke deaths are registered in low- and middle-income countries, which also account for 87% of total losses due to stroke in terms of disability-adjusted life years (DALYs), calculated worldwide, in 72 million per year (*Lopez AD et al., 2006*). Given the immense burden that ischemic stroke exerts, the need to develop more precise estimates of a stroke survivor's prognosis remains an important goal (*Kristian and Siesjo BK, 1998*). The prediction of outcome after ischemic stroke is important for clinicians, patients, and researchers (*Whiteley et al., 2009*)

Albumin is the most abundant plasma protein, accounting for 55-60% of the measured serum protein. It consists of a single polypeptide chain of 585 amino acids with a molecular weight of 66 500 Da (*Gosling et al.,1995*) Human serum albumin is a major component of plasma, cerebrospinal fluid, and interstitial fluid, and an important circulating carrier, which is synthesized mainly in the liver (*Preeti Sahota et al.,2011*)

The neuroprotective effects of human albumin have been demonstrated in models of acute cerebral ischemia, including transient and permanent middle cerebral artery occlusion models or global ischemia models (*Belayev et al.,2001*). It has also been shown to improve cerebral perfusion (*Liu Y. et al., 2001*), to normalize changes in diffusion-weighted magnetic resonance imaging (*Belayev et al., 1998*) to reverse post ischemic micro vascular stasis (*Belayev et al.,2002*) and to contribute to the systemic mobilization and supply of free fatty acids to the post ischemic brain (*Rodriguez de Turco et al.,2002*) These studies used albumin doses of 1.25 g/kg to 2.5 g/kg and found them to be markedly neuroprotective, with a therapeutic window of 4 to 5 hours (*Belayev et al.,2002*)

Albumin-neuroprotection is mediated via multiple mechanisms. Several specific albumin-binding sites are expressed by micro vascular endothelial cells on their surface (*Schnitzer et*