Clinical significance of Albumin in Acute Cardioembolic Strokes

Thesis

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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 Deoxyribonucliec 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-κB : 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***