

Ain Shams University Faculty of Medicine. Neurology department

# "Carotid artery stenosis in cerebrovascular ischemic events: management and outcome"

Thesis Submitted for partial fulfillment of MD degree of neurology By:

#### Mohamed Khaled Ahmed Elewa Badr MCs of neuropsychiatry

Supervisors:

#### **Prof. Samia Ashour Mohamed Helal**

Professor of Neurology
Head of Neurology Unit
Faculty of Medicine - Ain Shams University

## Prof. Mahmoud Hemeda Mahmoud AL-Raqawy

Professor of Neurology Faculty of Medicine - Ain Shams University

#### Prof. Nahed Salah El-Din Ahmed

Professor of Neurology
Faculty of Medicine - Ain Shams University

### Dr. Hany Mahmoud Zaki El-Dine

Assistant professor of Neurology
Faculty of Medicine - Ain Shams University
2010

## **LIST OF CONTENTS**

Acknowledgement	P 2
List of tables	P 3
List of figures	P 6
List of abbreviations	P 8
1-Introduction and aim of the work	P 12
2-Review of literature	P 15
A- Extracranial carotid atherosclerotic stenosis fundamentals	. P 15
B- Screening for carotid stenosis	. P 23
C- Investigations	. P 30
D- Management	P 42
-Medical management	P 42
-Carotid endarterectomy	P 53
-Carotid artery stenting	P 62
3-Subjects and method	P 81
4-Results	. Р96
5-Discussion	P 132
6-Summary and conclusion	P 153
7-Recommendations	P 156
8-References	P 157
9-Appendix 1 (selected cases demonstration)	P 193
10- Appendix 2 (modified Rankin Scale)	P 211
الملخص العرب - 11	

#### **ACKNOWLEGEMENT**

First of all, I wish to express my sincere thanks to **GOD** for his care and generosity throughout my life.

No words will be sufficient to describe my faithful gratitude to my *Professor Samia Ashour* for her continuous support, wise helpful guidance and patience.

Special thanks to *Professor Mahmoud Hemeda* who had generously helped me and supported me a lot in doing this work.

Also, I would like to thank *Professor Nahed Salah El-Din* for her warm encouragement and kind support.

I should thank Assistant Professor Hany Zaki El-Dine for his continuous advice and guidance. I can't forget that he had taught me the principles of per catheter neuro-intervention.

Also I can't forget *Professor Francis Turjman* professor of radiology, Claud Bernard University, Lyon, France for his expertise teaching and advice.

Finally I should thank *my parents*; I owe them all success I had in my life.

# **LIST OF TABLES**

Table 1: TOAST classification	P 16
Table 2: OCSP classification	P 18
Table 3: consensus panel of gray-scale and Doppler ultrase	ound
criteria for diagnosis of ICA stenosis	
Table 4: Risk factors modification treatment goals	P 46
Table 5: Randomized trials of CEA versus medical therapy	y for
carotid artery stenosis	P 57
Table 6: High-risk criteria for CEA	P 60
Table 7: Potential complications of CEA	P 61
Table 8: SAPPHIRE criteria for high risk	P 68
Table 9: Indications and contraindications for carotid angiop	lasty
and stenting Definitions	P 73
Table 10: Comparison of Proximal and Distal EPD	P 75
Table 11: the mean follow up periods	P 96
Table 12: distribution of risk factors	P 98
Table 13: stratification of risk factors	P 98
Table 14: mode of presentation	P 99
Table 15: mRS score assessment at presentation F	' 100
Table 16: brain imaging findings F	101
Table 17: carotid duplex findings P	' 101
Table 18: distribution of degree of stenosis F	' 102
Table 19a: intracranial vascular assessment P	102
Table 19b: distribution of intracranial stenosis and occlusion. F	<sup>2</sup> 103
Table 20: comparison between Medical conservative group	(DAP
group & OAC group) and CAS group as regard the	main
determinants (in the 1st decisionP	107

Table 21: comparison between primary decisions according to
outcomeP 108
Table 22: comparison between types of conservative treatment
(DAP and OAC) according to outcomeP 109
Table 23: comparison between types of conservative treatment
(DAP and OAC) according to outcomeP 110
Table 24: comparison between patients who developed new
vascular event and other patients who didn't develop new vascular
event on conservative medical management as regard mean follow
up period and the ageP 112
Table 25: comparison between patients who developed new
ipsilateral vascular event and other patient who didn't develop
new ipsilateral vascular event on conservative medical
management as regard risk factors P 115
Table 26: comparison between patients who developed new
ipsilateral vascular event and other patients who didn't develop
new ipsilateral vascular event on conservative medical
management as regard stratification of risk factors P 116
Table 27: comparison between patients who developed new
ipsilateral vascular event and other patients who didn't develop
new ipsilateral vascular event on conservative medical
management as regard (patients who have >4 risk factors and
others with ≤4 risk factors) P 117
Table 28: comparison between patients who developed new
ipsilateral vascular event and other patient who didn't develop
new ipsilateral vascular event on conservative medical
management as regard clinical presentation P 119

Table 29: comparison between patients who developed new
vascular event and other patient who didn't develop new vascular
event on conservative medical management as regard brain
imaging findings P 120
Table 30: comparison between patients who developed new
vascular event and other patient who didn't develop new vascular
event on conservative medical management as regard cerebro-
vascular assessment [extra-cranial (carotid duplex) and intra-
cranial (MRA +/- CTA)] P 122
Table 31: secondary decision outcome P 125
Table 32: tertiary decision outcome P 126
Table 33: CAS data P 128
Table 34: CAS outcome in the three successive decisions P128
Table 35: distribution of risk factors among CAS patients P 129
Table 36: mode of presentation among CAS patients P 130
Table 37: CAS operative data P 131

# **LIST OF FIGURES**

Figure 1: comparison of NASCET and ECST angiographic
measurements of carotid stenosisP 32
Figure 2: carotid Doppler velocities and degree of stenosis.
Relationship between the mean peak systolic velocity (PSV) and the
percentage of stenosis measured angiographically P 33
Figure 3: Distal EPDs used in this study P 85
Figure 4: carotid stents P 86
Figure 5: MRA for a patient shows apparently occluded intra-
cranial Left ICA tandem to high grade stenosis (A). DSCA for the
same patient before any intervention shows that the apparently
occluded intra-cranial Left ICA is not true occlusion (B) P 104
<b>Figure 6</b> : 1 <sup>st</sup> decision chart P 105
Figure 7: outcome of DAP and OAC groups P 111
Figure 8: comparison between patients who developed new
vascular event and other patient who didn't develop new vascular
event on conservative medical management as regard follow up
duration P 113
Figure 9: comparison between patients who developed new
vascular event and other patient who didn't develop new vascular
event on conservative medical management as regard the
age P 114
Figure 10: comparison between patients who developed new
ipsilateral vascular event and other patient who didn't develop
new ipsilateral vascular event on conservative medical
management as regard (patients who have >4 risk factors and
others with ≤4 risk factors) P 118

Figure 11: 2 <sup>nd</sup> decision charts	P 1	24
Figure 12: 3 <sup>rd</sup> decision charts	P 1	26

#### LIST OF ABBREVIATIONS

A = Artery

A Com A= Anterior Communicating Artery

ACA = Anterior Cerebral Artery

ACAS = Asymptomatic Carotid Atherosclerotic Study

ACCF/SCAI/SVMB/SIR/ASITN = American College of Cardiology Foundation, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology and American Society of Interventional & Therapeutic Neuroradiology.

ACE = Angiotensin-Converting Enzyme inhibitors

ACST = Asymptomatic Carotid Surgery Trial

ARBs = Angiotensin Receptor Blockers

ARR = absolute risk reduction

ASA = aspirin

BMI = body mass index

BP= blood pressure

CABG = Coronary Artery Bypass Graft

CAD = coronary artery disease

CAPRIE = Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events

CAS = carotid artery stenting

CATS = Canadian-American Ticlopidine Study

CBF = Cerebral Blood Flow

CD = Carotid Duplex

CDUS = Carotid Duplex Ultrasonography

CEA = carotid endarterectomy

CHARISMA = Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization Management, and Avoidance

CI = confidence interval

CREST = Carotid Revascularization Endarterectomy vs. Stent Trial

CT = computed tomography

CTA = computed tomography angiography

CVA = Cerebro-Vascular Accident

CVS = Cerebro-Vascular Stroke

DM = diabetes mellitus

DSCA = Digital Subtraction Cerebral Angiography

ECST = European Carotid Surgery Trial

EPDs= emboli-protection devices

ERDP = extended release dipyridamole

ESPRIT = European/Australian Stroke Prevention in Reversible Ischemia Trial

ESPS = European Stroke Prevention Study

fps = frame per second

GP IIb/IIIa = Glyco-Protein IIb/IIIa

HDL-C = high-density lipoprotein cholesterol

**HOPE** = Heart Outcomes and Prevention Evaluation

HTN = hypertension

IBI = internal borderzone infarcts

ICA = Internal Carotid Artery

ICH = Intra Cranial Hemorrhage

IHD = ischemic heart disease

IMT=Intema Media Thickening

INR = international normalized ratio

LACS = lacunar syndrome

LDL-C= low-density lipoprotein cholesterol

LIFE = Losertan Intervention For Endpoint

LV = left ventricle

MATCH = Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance

MCA = Middle Cerebral Artery

MI = myocardial infarction

MRA = Magnetic Resonance Angiography

MRI= magnetic resonance imaging

N/A = Not available

NASCET = North American Symptomatic Carotid Endarterectomy Trial

NCEP = National Cholesterol Education Program

NICU = neurology intensive care unit

NIH = National Institutes of Health

NINDS = National Institute of Neurological Disorders and Stroke

NS = Non Significant

OCSP= Oxfordshire Community Stroke Project

OTW = Over the wire

PA = Posterior Anterior

PACS = partial anterior circulation syndrome

PAI = perforating artery infarcts

PCA = posterior cerebral artery

PET= Positron Emission Tomography

PO= oral

POCS = posterior circulation syndrome

PROGRESS = Perindopril Protection Against Recurrent Stroke Study

PTCA = percutaneous transluminal coronary angioplasty.

PVD = peripheral vascular disease

QD= Latin abbreviation means once per day

RHV = Rotating hemostatic valve

RRR =relative risk reduction

RX = Rapid exchange

SALT = Swedish Aspirin Low-Dose Trial

SAPPHIRE = Stenting and Angioplasty with Protection in Patients at High-Risk for Endarterectomy

SPARCL = Stroke Prevention with Aggressive Reduction of Cholesterol Levels trial

SUA = serum uric acid

TACS = total anterior circulation syndrome

TASS = Ticlopidine Aspirin Stroke Study

TCD= Transcranial Doppler

TIA =Transient Ischemic Attack

TMB = Transient Mono-ocular Blindness

TOAST = Trial of Org 10172 in Acute Stroke Treatment

UK = United Kingdom

VA = Veterans Affairs

VB = vertebro-basilar

WARSS = Warfarin Aspirin Recurrent Stroke Study

WASID = Warfarin Aspirin Symptomatic Intracranial Diseases

#### INTRODUTION

Stroke is the third leading cause of death (164,000 deaths/ year) in the U.S., behind heart disease and cancer. There are approximately 1 million stroke-related events each year, including 500,000 new strokes, 200,000 recurrent strokes, and 240,000 transient ischemic attacks (TIAs), (Kleindorfer, et al. 2005 and Thom, et al. 2006). Patients who suffered a transient ischemic attack had a 13-fold excess risk of stroke during the first year and a sevenfold excess risk over the first 7 years compared with people without transient ischemic attacks (Dennis, et al. 1990). The risk is higher in the first month and highest in patients with hemispheric TIA and carotid stenosis causing more than 70% luminal reduction (Streifler, et al. 1992). However, Carotid occlusive disease amenable to revascularization accounts for 5% to 12% of new strokes (Kleindorfer, et al. 2005 and Thom, et al. 2006). This clarifies the importance of prophylaxis and early interference.

The first balloon angioplasty for carotid stenosis was performed in 1979; reports in the early 1980s (Bockenheimer, et al. 1983), included a balloon occlusion system to reduce embolic complications (Theron, et al. 1990), then the first balloon-expandable stent was deployed in the carotid artery in 1989, these stents were prone to extrinsic compression, and major adverse events occurred in more than 10% of patients at 30 days (Marks, et al. 1994 and Diethrich, et al. 1996). Subsequently, issues about stent deformation were resolved by use of the self-expanding Wallstent (Roubin, et al. 2001), and later by self-expanding nitinol stents. However, risk of embolic stroke was the major concern that

limits early enthusiasm for endovascular treatment. Initial strategies focused on neurological rescue which was not always successful. Accordingly, treatment strategies shifted from neurological rescue to neurological protection, utilizing specialized emboli-protection devices (EPDs) to capture and remove embolic debris that were generated during the course of the interventional procedure.

With the evolution and maturation of carotid artery stenting (CAS) equipments and techniques, many nonrandomized and randomized (CAS) clinical trials had compared carotid stenting with the use οf an emboli-protection device with carotid endarterectomy (CEA) (American College of Cardiology Foundation, Society for Cardiovascular Angiography Interventions, Society for Vascular Medicine and Biology, Society Interventional Radiology and American Society Interventional & Therapeutic Neuroradiology Clinical Expert Consensus Document on Carotid Stenting. 2007) their results are summarized that; Currently, among patients with severe carotidartery stenosis (symptomatic stenosis greater than 50% and asymptomatic stenosis greater than 80%) and coexisting conditions, carotid stenting with the use of an emboli-protection device is not inferior to carotid endarterectomy (Jay, et al. 2004).

Although the large number of studies, unfortunately no available studies comparing medical treatment versus CAS in those patients with severe carotid artery stenosis. This emerges an important question, which is superior medical therapy or CAS?

## **AIM OF THE STUDY**

 To study the outcome of management of severe carotid artery stenosis by carotid artery stenting versus conservative medical treatment.