

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



## Carotid Endarterectomy

Mustafa Karacelik  
Izmir Tepecik Research and Training Hospital,  
Turkey

### 1. Introduction

Carotid endarterectomy (CEA) is still remain a good therapeutic modality for carotid artery disease in some medical centers if these centers do not have any endovascular surgical options. CEA may reduce the risk of possible neurological deficits, but has some surgical complications. Benefit in patients with stroke and to decline progressively in patients with cerebral TIA and retinal events in both the 50% to 69% and 70% to 99% stenosis groups, and also showed a trend towards greater benefit in patients with irregular plaque than a smooth plaque in both stenosis groups. This chapter summarises the CEA as a surgical therapy and its components.

### 2. Indications

In patients with 70% to 90% diameter reduction of an ipsilateral internal carotid artery measured on a conventional biplane angiogram, ipsilateral to either focal hemispheric symptoms (transient ischemic attack [TIA] or small stroke) or amaurosis fugax, surgically treated by CEA(1)

There have been five randomised controlled trials of endarterectomy in patients with a recent symptomatic carotid stenosis. CEA is of some benefit for 50% to 69% symptomatic stenosis and highly beneficial for 70% to 99% stenosis without near occlusion.(Fig.1) Benefit from endarterectomy depends not only on the degree of carotid stenosis, but also on several other factors, including the delay to surgery after the presenting event(2). For 70% stenosis (excluding near occlusion) absolute risk reduction (ARR) of 16% over 5 years (number needed to treat 6.3); 50% to 69% stenosis ARR of 4.6% over 5 years (number needed to treat 22); near occlusion, ARR of 5.6% over 2 years ( $p= 0.19$ ) but 1.7% over 5 years ( $p=0.9$ ); and CEA is not appropriate for symptomatic patients with 49% stenosis(13).

### 3. Diagnosis

Carotid angiogram is still “gold standard” for measuring the degree of carotid stenosis. Nowadays, *computed tomography angiography* (CTA) is more common used to visualize carotid arteries. Doppler ultrasonography is a helpful another noninvasive method, but it is not enough for decision making of operation.

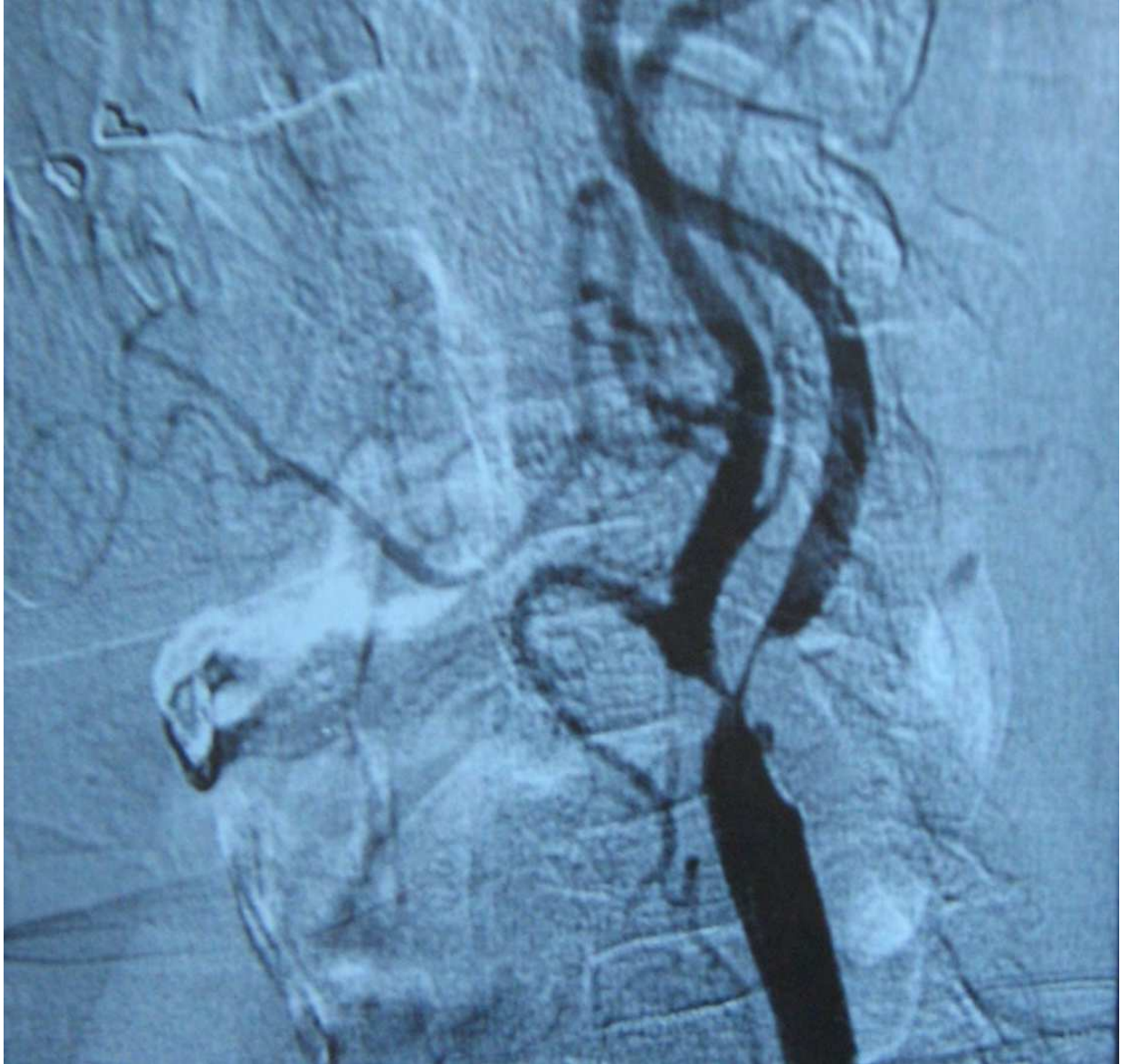


Fig. 1. Digital subtraction Angiography of the carotid arteries

#### **4. Techniques for Carotid Endarterectomy**

##### **4.1 The choice of anaesthetic**

CEA may be performed under local or general anaesthesia. Meta-analysis of the randomised studies showed that there was no evidence of a reduction in the odds of operative stroke or death (odds ratio (OR) 0.85, 95% confidence interval (CI) 0.63 to 1.16). Patients and surgeons can choose either anaesthetic technique, depending on the clinical situation and their own preferences. Local anaesthesia reduces need for intraoperative shunting and as a result a reduction in hospital stay occurs<sup>(3)</sup>(Fig.2).



Fig. 2. Local anaesthesia application

#### 4.2 Patch or no patch?

Choosing the method of closure of arteriotomy depends on diameter of the internal carotid artery (ICA). Small diameter (less than 5mm) of ICA should be closed by a native or nonnative tissue patch. The main issue regarding patch angioplasty is patching increases clamp time and infection risk. **Rerkasem** mentioned that a significant reduction in perioperative and long-term risks of ipsilateral stroke and of perioperative carotid occlusion and later restenosis associated with the use of patching. A policy of selective patching of only those arteries thought to require a patch at the time of operation compared with no patching has not been tested in randomized, controlled trials. These researchers support a policy of routine patching, but most included trials were small and some had methodological shortcomings(4). There is no evidence that patch type influences stroke rate, mortality or arterial restenosis in any way at all(5). There is some evidence that other synthetic (e.g. PTFE) patches may be superior to collagen impregnated Dacron grafts in terms of perioperative stroke rates and restenosis. Pseudoaneurysm formation may be more common after use of a vein patch compared with a synthetic patch(6).

### 4.3 Shunt decision

The main aim of shunting is to reduce the risk of perioperative stroke but it could possibly be associated with an increased risk of restenosis and late recurrent stroke. The data on the use of routine shunting from randomised controlled trials were limited. There were promising but non-significant trends favouring a reduction in both deaths and strokes within 30 days of surgery with routine shunting. The data available were too limited to either support or refute the use of routine or selective shunting in carotid endarterectomy. It was suggested that large scale randomised trials between routine shunting versus selective shunting were required. No one method of monitoring in selective shunting has been shown to produce better outcomes(7). The most recent trial used stump pressure measurement and patients with stump pressure < 50 mmHg required shunting(8).

### 4.4 Surgical technique

Following intravenous heparinisation (5000units), vascular clamps are applied to the ICA, CCA and ECA respectively. A longitudinal arteriotomy is made from the CCA across the plaque and into the ICA beyond the stenosis. A shunt can be deployed at this stage if it is necessary.(Fig.3)

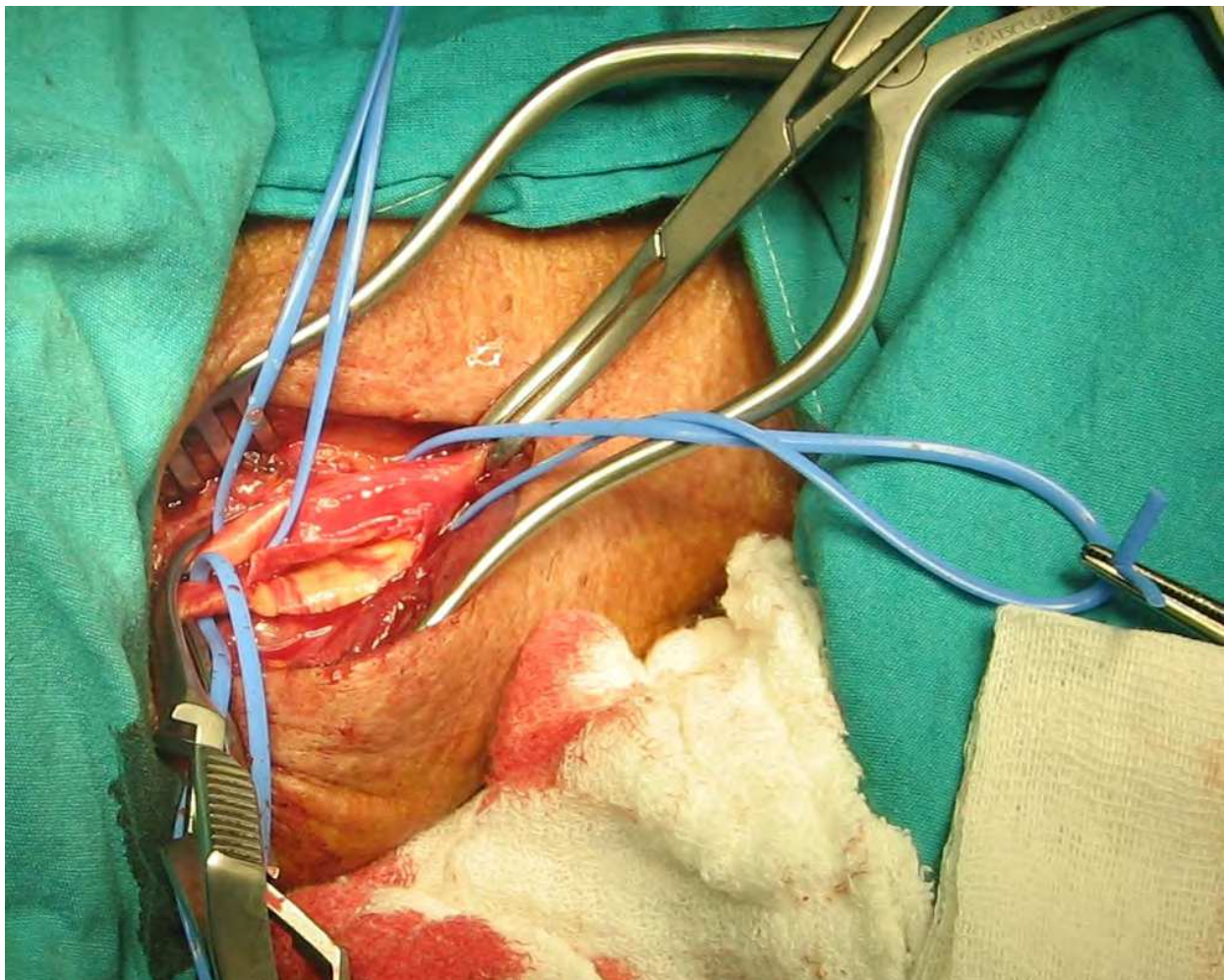


Fig. 3. Carotid endarterectomy

The endarterectomy plane is entered using a dissector or clamp and it is conventional to divide the plaque first at the CCA aspect and then carefully mobilise it free up into the ICA where it is cut transversely using micro scissors to avoid leaving a flap. Sometimes an additional 7,0 prolene sutures could be needed to restore without a flap in the vessel wall(5). The “eversion” endarterectomy is an alternative technique. The origin of the ICA is transected and re-implanted after eversion endarterectomy of the ICA and conventional endarterectomy of the CCA and ECA(8). In ACST-1 3000 patients were randomised between medical treatment only or medical treatment and immediate surgery. CEA involved a small (~3%) but definite peri-procedural risk of stroke or death, a substantial (~3% vs ~12%) reduction in the subsequent stroke rate over the next 5 years and hence a net reduction (~6% vs ~12%) in the overall 5-year risk of stroke or peri-procedural death. The 5-year findings of ACST-1 are already changing surgical practice, and long-term follow-up of stroke rates continues(9,10). Avoidance of patch-closure techniques particularly in thin arteries is an important advantage of carotid endarterectomy with anterior transverse arteriotomy(11).

#### 4.5 Difficult anatomy, make a decision for CEA or CAS?

**Schneider** and **Kasirajan** mentioned that anatomy influences decision-making in carotid disease management(12). Patients who have comorbidities, but complicated arterial anatomy, are best candidates for CEA.(Fig.4) Patients with a hostile neck are best suited to CAS. Patients with neck immobility, skin cancer at incision site, previous radical neck dissection, or a tracheostomy, can be treated with CAS. **Arya** et al. emphasized that CAS 30 day stroke and death/stroke rates are statistically significantly higher compared to CEA; however this superiority did not reach statistical significance when RPCTs were analyzed alone and those results did not justify the widespread use of CAS for treatment of suitable carotid bifurcation disease(13).



Fig. 4. An atherom plaque excised from carotid artery bifurcation

## 5. General complications of Carotid Endarterectomy

As with all CEA's, acute coronary syndrome(ACS) is the main problem during and after CEA. In addition, even clinically "silent" myocardial injury detected by enzyme (troponin) leak has a negative effect on both perioperative and long-term survival. Postoperative hypertension is another major matter after CEA and affects 66% of patients. This phenomenon triggers the ACS easily and resolve spontaneously 48-72 hours postoperatively. The annual risk of MI or nonstroke vascular death after an ischemic stroke or TIA is 2%. A prospective study by **Kawahito** et al using Holter monitoring to detect myocardial ischemia identified a history of angina ( $p= 0.001$ ) and hypertension ( $p=0.020$ ) as being independently associated with perioperative myocardial ischemia in patients having CEA(14).

### 5.1 Neurological complications of Carotid Endarterectomy

Neurological complications may be as follows; mild deficits: visual disturbances, dysphagia, monoparesis, moderate deficits: severe deficits: hemiplegia. High-risk group for neurological complications are diffuse atherosclerotic disease and by the presence of a previous neurologic deficit. However, reoperation carries higher perioperative stroke and cranial nerve injury rates than primary CEA. Major causes of postoperative ischemia are perioperative thrombosis and embolism, and most strokes were within 24 hours of the procedure, whereas 3% after 24 hours of the operation. Manipulation of the carotid arteries causing stroke by embolization is avoided by prior mobilization of its branches. The risk of postoperative stroke can be determined by postoperative Transcranial Doppler measurement. In a study of Abbott et al., the risk of postoperative neurological deficit was 15 times higher in patients with clinically significant microembolism detected by TCD recording(15).

Other cause of postoperative ischemia is intracerebral hemorrhagic stroke which is resulted from a hyperperfusion syndrome is a rare complication after CEA with range of 0.2-0.75% and it is a fatal outcome. A strategy to prevent intracerebral hemorrhagic stroke consists in close blood pressure monitoring and control and reasonable handling of anticoagulant and antiplatelet agents. For example; Dextran 70 and 40 have been used to prevent thrombosis by decreasing platelet adhesiveness. If there is a large amount of using this product this may cause bleeding from operation side(16).

Postoperative evaluation of neurological outcome may be explained in a study Nouraei et al. following CEA, the distribution of saccades initiated by the cerebral hemisphere distal to the operated artery significantly changed in 25 patients. By contrast, there were 14 significant contralateral-hemisphere saccadic changes ( $P<.001$ ) significantly greater postoperative reduction was detected in early saccades generated by the ipsilateral hemisphere than by the contralateral hemisphere ( $P<.02$ ) CEA leads to significant hemisphere-specific subclinical changes in saccadic performance and, in particular, differentially affects the proportion of early saccades, a measure of the ability of the frontal cortex to successfully inhibit lower centers, generated by the 2 hemispheres. Saccadometry, a bedside test, provides data that can be statistically compared for individual and groups of patients. It could allow the neurological outcome of carotid surgery to be objectively quantified(17).

Navin et al. 12 randomized controlled trials (RCT) enrolling 6,973 patients were included in a meta-analysis. Carotid artery stenting was associated with a significantly greater odds of

periprocedural stroke (OR 1.72, 95% CI 1.20 to 2.47) and a significantly lower odds of periprocedural myocardial infarction (OR 0.47, 95% CI 0.29 to 0.78) and cranial neuropathy (OR 0.08, 95% CI, 0.04 to 0.16). The odds of periprocedural death (OR 1.11, 95% CI 0.56 to 2.18), target vessel restenosis (OR 1.95, 95% CI 0.63 to 6.06), and access-related hematoma were similar following either intervention (OR 0.60, 95% CI 0.30 to 1.21). In comparison with CEA, CAS was associated with a greater odds of stroke and a lower odds of myocardial infarction. While the results in this meta-analysis support the continued use of CEA as the standard of care in the treatment of carotid artery stenosis, CAS is a viable alternative in patients at elevated risk of cardiac complications(18).

Chronic tissue damage may occur in a subset of individuals with 70% ICA stenosis, globally exhibiting more extensive WMH. Overall, the median volumetric magnetic resonance (WMH) volume was greater in the hemisphere ipsilateral to the stenotic ICA ( $1.13 \pm 2.65$  vs.  $0.77 \pm 2.26$  cm<sup>3</sup>;  $p=0.005$ ), but there were no differences in hemispheric brain volumes between the stenotic and nonstenotic sides. In the subgroup of patients with moderate and severe WMH ( $n=41$ ), the hemispheric volume ipsilateral to the stenotic ICA was significantly smaller ( $543.46 \pm 22.17$  vs.  $548.66 \pm 26.7$  cm<sup>3</sup>;  $p=0.03$ ). Multivariate linear regression analysis revealed an independent effect of WMH grade on interhemispheric volume differences relative to the side of stenosis. (19).

**Goldberg** et al. evaluated the mechanisms of neurologic injury, the measurement of neurobehavioral outcomes, and use of neuroimaging to evaluate carotid revascularization outcomes. They found that neurologic injury after carotid revascularization results from three broad etiologies: atheroembolic, thrombotic, and hypo/hyperperfusion. Of the 47 studies examining the effect of carotid endarterectomy on neurobehavioral functioning, 25 found that some aspect of cognition improved, 12 revealed no change in cognition, and 10 revealed declines in some aspect of cognition. There is a wide variation in the measurement of neurologic outcomes in clinical registries and trials. Future efforts to correlate neuroimaging with cognitive outcomes may offer insight into methods to decrease neurologic injury after carotid revascularization. (20)

Chronic progressive tissue damage as another possible consequence of high-grade ICA stenosis, which can be detected using MRI volumetric methods for assessing volumetric magnetic resonance (WMH) lesion load and hemispheric brain volume differences to clarify if the morphologic changes observed are associated with neuropsychological deficits, and to investigate their relationship with regional cerebral perfusion measurements preferentially in a longitudinal manner(21)

Cerebral hyperperfusion after carotid endarterectomy (CEA) impairs cognitive function and is often detected on cerebral blood flow (CBF) imaging. In this study 158 patients with ipsilateral internal carotid artery stenosis ( $>$  or  $=$  70%) underwent CEA. Neuropsychological testing was performed preoperatively and at the 1st postoperative month. Cerebral blood flow was measured using single-photon emission computed tomography before, immediately after, and 3 days after surgery. Magnetic resonance imaging was performed before and 1 day after surgery. The incidence of postoperative cognitive impairment was significantly higher in patients with post-CEA hyperperfusion on CBF imaging (12 [75%] of 16 patients) than in those without (6 [4%] of 142 patients;  $p<0.0001$ ). Postoperative cognitive impairment developed in all 5 patients with cerebral hyperperfusion syndrome regardless



of the presence or absence of new lesions on MR images. Although cerebral hyperperfusion syndrome after CEA sometimes results in reversible brain edema visible on MR imaging, postoperative cerebral hyperperfusion often results in impaired cognitive function without structural brain damage on MR imaging(22).

Two groups (A and B) of 15 patients each, with internal carotid backpressure >30 mmHg were operated and they did not use a shunt in Group A during CEA and group B was operated upon with a shunt. They measured gradual increase of levels of IL-1b and TXB2 during cross-clamping and during reperfusion in group A ( $P<0.05$ ). The levels of TNF $\alpha$  increased only during reperfusion ( $P<0.05$ ). The concentration of IL-1b and TNF $\alpha$  remained almost stable in group B, whereas the concentration of TXB2 reduced but not significantly ( $P>0.05$ ). The levels of PGE2 remained stable in both groups. The increase of proinflammatory mediators during carotid cross-clamping when no shunt is used. The critical concentration of these mediators that threaten the brain's vitality is not yet detected. However, the clinical significance of this is unclear, since there were no perioperative strokes(23).

Reperfusion injury is a dangerous situation in the critical care unit and free radicals and lytics toxicity may play a role as well. Patients with critical stenosis with maximally dilated blood vessels at baseline (optimized cerebrovascular reserve) are also at risk for hyperperfusion injury. Presentation may include headache, seizure, status epilepticus, cerebral edema, ICH, or subarachnoid hemorrhage. There was no benefit from surgery in the near-occlusion group in ECST where the rate of endarterectomy in the medical group was lower than in NASCET. Prevention with tight blood pressure control during the periprocedural period is as critical as management of the injury itself (24).

A case series of Pappada et al. of 413 CEAs in 390 patients who suffered from the new onset of an ischaemic hemispheric deficit or the worsening of a pre-existing deficit within 72 h after surgery were included in this study. A major stroke after CEA is caused, in most of cases, by the acute ICA occlusion with or without intracerebral embolic occlusion. Reopening of the occluded ICA gives good results when intracerebral vessels are patent and when the occluded ICA is satisfactorily reopened(25).

Diffusion-weighted imaging (DWI) has indicated that CAS is associated with a significantly higher burden of microemboli. This prospective study analyzed the neuropsychologic outcomes after revascularization in 24 CAS and 31 CEA patients with severe carotid stenosis compared with a control group of 27 healthy individuals. The cognitive performance was similar between CEA and CAS patients at all points. The new brain lesions, as detected with DWI after CAS or CEA, do not affect cognitive performance in a manner that is long-lasting or clinically relevant. Despite the higher embolic load detected by DWI, CAS is not associated with a greater cognitive decline than CEA(26).

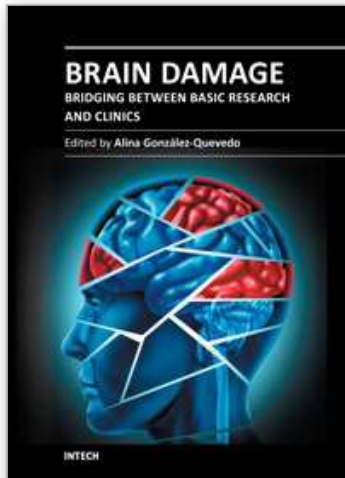
The North American Symptomatic Carotid Endarterectomy trial(NASCET), enrolled 2885 symptomatic patients had carotid stenosis were categorized as follows: 1) low, moderate stenosis (<50%), 2) moderate stenosis (50-69%), and 3) severe stenosis (70-99%). Patients were assigned to either CEA and best medical management or best medical management alone. Primary stenting for the treatment of post-CEA stroke is encouraging clinical result may be also explained by the fact that the interval between onset of neurological symptoms and stent implantation(27).

## 6. References

- [1] Haimovici H. (1996) *Haimovici's Vascular Surgery Principles and Techniques*, Blackwell Science, USA
- [2] Rerkasem K, Rothwell PM. Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane Database of Systematic Reviews* 2011, Issue 4.
- [3] Rerkasem K, Rothwell PM. Local versus general anaesthesia for carotid endarterectomy. *Cochrane Database of Systematic Reviews* 2008, Issue 4.
- [4] Rerkasem K, Rothwell P.M. Systematic Review of Randomized Controlled Trials of Patch Angioplasty Versus Primary Closure During Carotid Endarterectomy *Stroke* 2010;41:e55-e56
- [5] Beard J.D, Gaines P.A.(1998) *Vascular and Endovascular Surgery*, W.B. Saunders Company Ltd, UK
- [6] Rerkasem K, Rothwell PM. Patches of different types for carotid patch angioplasty. *Cochrane Database of Systematic Reviews* 2010, Issue 3.
- [7] Rerkasem K, Rothwell PM. Routine or selective carotid artery shunting for carotid endarterectomy (and different methods of monitoring in selective shunting). *Cochrane Database of Systematic Reviews* 2009, Issue 4.
- [8] Palombo D, Lucertini G, Mambrini S, Zettin M. Subtle cerebral damage after shunting vs non shunting during carotid endarterectomy. *European Journal of Vascular and Endovascular Surgery* 2007;34:546-51.
- [9] Kasprzak P, Raithel D. Eversion carotid endarterectomy: technique and early results. *J Cardiovasc Surg* 1989, 30: 49.
- [10] Halliday A. The Asymptomatic Carotid Surgery Trial has changed clinical practice. Pages 56-60 in: *Vascular and Endovascular Controversies*. Biba Publishing, 2006.
- [11] Çinar B, Göksel O, Aydoğan H, Filizcan U, Çetemen S, Eren E. Early and mid-term results of carotid endarterectomy with anterior transverse arteriotomy. *Türk Göğüs Kalp Damar Cer Derg* 2005;13(3):255-259
- [12] Schneider PA, Kasirajan K. Difficult Anatomy: What Characteristics Are Critical to Good Outcomes of Either CEA or CAS? *Semin Vasc Surg* 2007, 20:216-225
- [13] Arya S, Garg N, Johanning JM, Longo GM, Lynch TG, Pipinos II. Carotid Endarterectomy and Stenting: A Meta-analysis of Current Literature. *j.jss*.2007,12, 610
- [14] Ritesh Maharaj. A Review of Recent Developments in the Management of Carotid Artery Stenosis. *Journal of Cardiothoracic and Vascular Anesthesia*, Vol 22, No 2 (April), 2008: pp 277-289
- [15] Abbott AL, Levi CR, Stork JL, Donnan GA, Chambers BR Timing of clinically significant microembolism after carotid endarterectomy. *Cerebrovasc Dis* 2007; 23: 362-367.
- [16] Wilson PV, Ammar AD: The incidence of ischemic stroke versus intracerebral hemorrhage after carotid endarterectomy: a review of 2,452 cases. *Ann Vasc Surg* 2005; 19: 1-4.
- [17] Nouraei SA, Roos, J; Walsh SR, Ober, JK, Gaunt, ME; Carpenter, RH. Objective Assessment of the Hemisphere-Specific Neurological Outcome of Carotid Endarterectomy: A Quantitative Saccadometric Analysis. *Neurosurgery* 2010: 67;6, 1534-1541

- [18] Yavin D, Roberts DJ, Tso M, Sutherland GR, Eliasziw M, Wong JH. Carotid Endarterectomy Versus Stenting: A Meta-Analysis of Randomized Trials. *The Canadian Journal of Neurological Sciences* 2011; 38, 2; 230 – 235
- [19] Enzinger C, Ropele S, Gatttringer T, Langkammer C, Schmidt R, Fazekas F. High-grade internal carotid artery stenosis and chronic brain damage: a volumetric magnetic resonance imaging study. *Cerebrovasc Dis.* 2010;30(6):540-6.
- [20] Goldberg JB, Goodney PP, Kumbhani SR, Roth SM, Powell RJ, Likosky DS. Brain Injury After Carotid Revascularization: Outcomes, Mechanisms, and Opportunities for Improvement. *Annals of Vascular Surgery* Volume 2011, 25, 2, 270-286
- [21] Enzinger C, Ropele S, Gatttringer T. High-Grade Internal Carotid Artery Stenosis and Chronic Brain Damage: A Volumetric Magnetic Resonance Imaging Study. *Cerebrovasc* 544 is 2010;30:540-546
- [22] Hirooka R, Ogasawara K, Sasaki M, Yamadate K, Kobayashi M, Suga Y, Yoshida K, Otawara Y, Inoue T, Ogawa A. Magnetic resonance imaging in patients with cerebral hyperperfusion and cognitive impairment after carotid endarterectomy. *J Neurosurg.* 2008 Jun;108(6):1178-83.
- [23] Tachtsi M, Pitoulis G, Kostoglou C, Papadimitriou D. The proinflammatory mediator's production from ischemic brain during carotid endarterectomy. *Int Angiol.* 2011 Oct;30(5):429-33.
- [24] Badruddin A, Taqi MA, Abraham MG, Dani D, Zaidat OO. Neurocritical Care of a Reperfused Brain. *Curr Neurol Neurosci Rep* (2011) 11:104-110
- [25] Pappadà G, Vergani F, Parolin M, Cesana C, Pirillo D, Pirovano M, Santoro P, Landi A, Ferrarese C. Early acute hemispheric stroke after carotid endarterectomy. Pathogenesis and management. *Acta Neurochir (Wien).* 2010;152(4):579-87.
- [26] Wasser K, Pilgram-Pastor SM, Schnaudigel S, Stojanovic T, Schmidt H, Knauf J, Gröschel K, Knauth M, Hildebrandt H, Kastrup A. New brain lesions after carotid revascularization are not associated with cognitive performance. *Journal of Vascular Surgery* 2011, 53, 1, 61-70.
- [27] Anzuini A, Briguori C, Roubin GS, Rosanio S, Airolidi F, Carlino M, Pagnotta P, Mario CD, Sheiban I, Magnani G, Jannello A, Melissano G, Chiesa R, Colombo A. Emergency Stenting to Treat Neurological Complications Occurring After Carotid Endarterectomy. *J Am Coll Cardiol* 2001;37:2074 -9

IntechOpen



## **Brain Damage - Bridging Between Basic Research and Clinics**

Edited by Dr. Alina Gonzalez-Quevedo

ISBN 978-953-51-0375-2

Hard cover, 282 pages

**Publisher** InTech

**Published online** 16, March, 2012

**Published in print edition** March, 2012

"Brain Damage - Bridging Between Basic Research and Clinics" represents a collection of papers in an attempt to provide an up-to-date approach to the fascinating topic of brain damage in different pathological situations, combining the authors' personal experiences with current knowledge in this field. In general, the necessary link between basic and clinical neurosciences is highlighted, as it is through this interaction that the theoretical understanding of the pathophysiological mechanisms can be successfully translated into better ways to diagnose, treat and prevent the catastrophic events that occur when the brain suffers from external or internal noxious events. The book spans different aspects of brain injury, starting from damage occurring in the fetal and child brain, followed by different neurodegenerative processes. Attention is also focused on the negative effects of drug addictions and sleep deprivation on the brain, as well as on the early assessment of brain injury for preventive strategies employing sensitive biomarkers.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Mustafa Karaçelik (2012). Carotid Endarterectomy, Brain Damage - Bridging Between Basic Research and Clinics, Dr. Alina Gonzalez-Quevedo (Ed.), ISBN: 978-953-51-0375-2, InTech, Available from: <http://www.intechopen.com/books/brain-damage-bridging-between-basic-research-and-clinics/carotid-endarterectomy>

**INTECH**  
open science | open minds

### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen