

Occlusive extracranial cerebrovascular disease: diagnosis and current management concepts

This is a common problem in everyday practice.

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The following article aims at a basic overview and is not intended to be a specialist-orientated scientific review.

Anatomical considerations

In order to fully understand the clinical presentation and concepts of management of occlusive extracranial cerebrovascular disease, a working knowledge of the relevant anatomy is helpful.

There are four major vessels supplying the brain – two internal carotids and two vertebrals. This constitutes the anterior and posterior circulation. The first branch of the internal carotid is the ophthalmic which supplies the eye via its retinal branch. The internal carotid then continues on to the temporoparietal region of the brain as the middle cerebral artery. The temporoparietal lobe provides motor and sensory function to the opposite side of the body. The dominant hemisphere, which is usually the left in right-handed people, and *vice versa*, contains the speech centre, known as Broca's area.

The anterior branch of the internal carotid inside the skull is the frontal artery which supplies the frontal lobes, responsible for memory and personality. This is the so-called silent area of the brain.

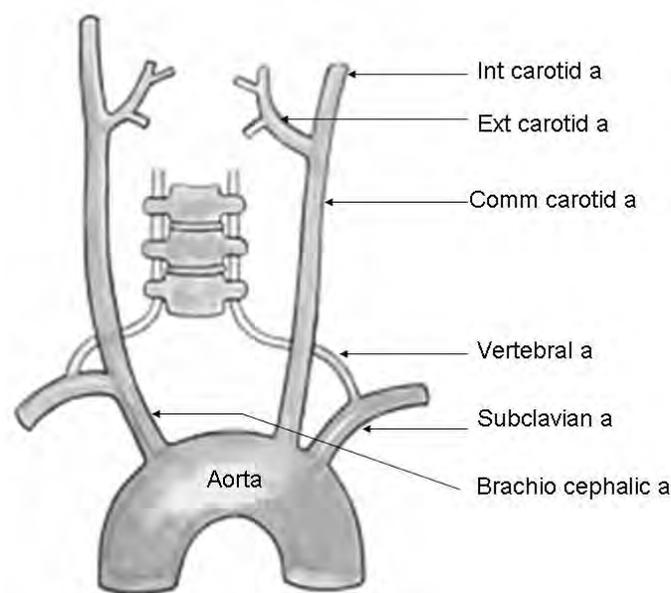


Fig. 1. Anatomy of the extracranial arterial system.

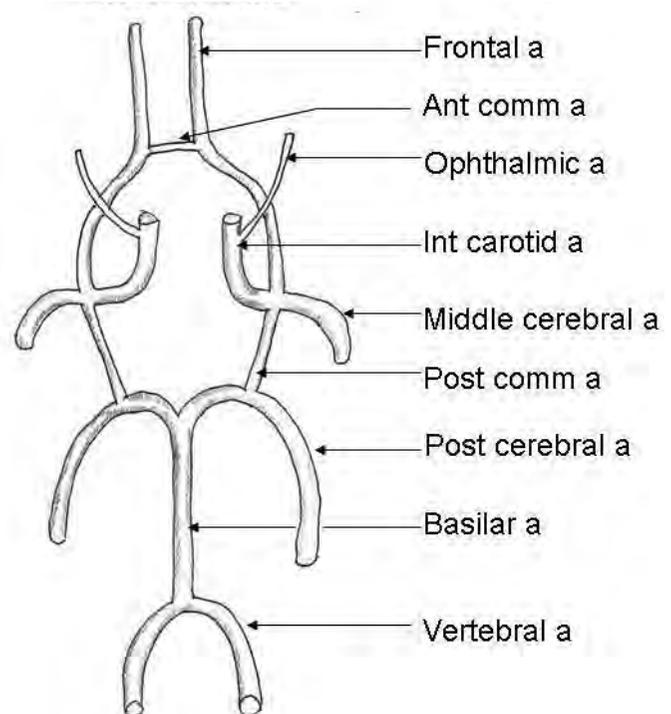


Fig. 2. Anatomy of the circle of Willis on the base of the brain.

The left and right vertebral arteries arise from the subclavian arteries. When they reach the base of the skull following their course through the neck they join together to form the basilar artery which then divides into the posterior cerebral arteries that supply the occipital lobes of the brain. These are responsible for central appreciation of vision. The basilar artery also gives small branches which supply the cerebellum, pons and mid-brain. In general this is largely responsible for co-ordination. On the base of the brain the carotid and vertebrobasilar systems anastomose by means of communicating branches to form the circle of Willis. This collateral circle is very efficient but the arteries beyond this level on the brain itself are of very small calibre and hence develop poor collaterals and behave as 'end arteries'. In other words, if the vessels are occluded in the neck compensation occurs through the circle of Willis, but if the occlusion occurs distal to the circle of Willis the collateralisation is extremely poor. The functional anatomy is illustrated in Figs 1 and 2.

Pathophysiology

In a review focusing on the causes of stroke Mackay and Naylor¹ found that 80% of strokes were ischaemic and 20% haemorrhagic in origin. Of the ischaemic strokes 80% were in the carotid territory of which 50% followed thromboembolism arising from the carotid bifurcation. The majority of these were from atherosclerotic plaques which ulcerate, exposing loose surface debris and providing a nidus for the formation of platelet thrombi. Stenosis results in turbulence which dislodges the material, causing distal emboli. Stenosis of 70 - 79% has a risk of stroke of 12%, rising to 26% when the stenosis exceeds 90%. This information is based on a 2-year follow-up. Other sources of emboli are the heart in 15% of patients, with non-atheromatous lesions such as kinks and coils, fibromuscular dysplasia, arteritis and aneurysms responsible in only 5% of patients.

Only 2% of strokes can be attributed mainly to haemodynamic reasons.

Another important cause of ischaemic stroke is intracerebral thrombosis due to small-vessel disease or haematological disorders.

Only 2% of strokes can be attributed mainly to haemodynamic reasons. This is a consequence of stenosis and occlusion involving all four vessels, with or without poor cardiac output. It stands to reason that most published studies relating to carotid disease pertain to atheromatous disease.

Patients may develop transient ischaemic attacks (TIA), a neurological deficit from which they can recover completely within 24 hours. A step beyond that is a reversible ischaemic neurological deficit (RIND) which resolves within a week. TIA and RIND have no cerebral infarction. A fixed deficit or a stroke may range from mild with minimal residual deficit to major disability with a dense deficit. Stroke by definition manifests with a CT-apparent infarct. One presumes that temporary deficits result from small emboli which fragment and dissipate while permanent deficits result from larger fragments which impact, resulting in thrombosis.

Symptom complexes

The neurological episodes present according to the areas of the brain affected, resulting in TIA, RIND or stroke.

Middle cerebral artery territory

These patients will manifest with a motor deficit on the opposite side of the body usually affecting the upper limb and in many cases associated with an ipsilateral visual disturbance, either complete blindness (amaurosis) or a scotoma, i.e. an area of blindness. If the dominant hemisphere is involved there may be an associated speech deficit.

Vertebrobasilar territory

This is characterised by episodes of ataxia, vertigo and visual dimming like a 'curtain being pulled across the eye'. These patients also often have nausea and vomiting associated with the attacks and there may be loss of consciousness.

Global ischaemia

Characteristically these manifest as syncope attacks due to episodes of low cerebral perfusion. Chronic cerebral ischaemia may result in light-headedness and diminished mentation (progressive loss of higher mental function). The differential diagnosis for episodes of global ischaemia includes cardiac arrhythmias, episodes of hypoglycaemia or epileptic activity.

It must be kept in perspective that severe stenosis of the carotid artery may be totally asymptomatic and the problem is to assess stroke risk in these patients according to the degree of the stenosis.

Investigation

The basic essential investigation in all patients presenting with temporary neurological deficits or stroke is a Duplex-Doppler scan of the carotids. If more detail is required, a computerised tomographic angiogram (CTA) is recommended which should include intracerebral views.

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Computed tomography (CT) or MRI of the brain is also helpful to exclude or define areas of infarction. In atypical cases one should also exclude other intracerebral pathology such as tumours.

Arch angiography via catheter is required if the previous investigations yield uncertain

results in the face of a strong clinical history.

In all patients full cardiac assessment should be performed and on occasion cerebral perfusion studies will be required in order to fully evaluate the haemodynamic-type presentations.

It must be emphasised that all patients presenting with a neurological deficit, temporary or permanent, should be investigated for a remediable cause. Fig. 3 is an arch angiogram showing typical stenosing plaque.

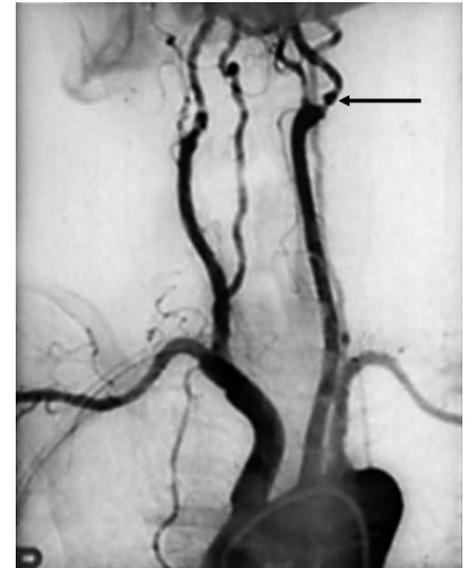


Fig. 3. Angiogram showing stenosing plaque at the origin of the left internal carotid artery (arrowed). This patient presented with left amaurosis and right upper limb monoparesis lasting for 2 hours – a classic middle cerebral artery territory TIA.

Management

Management comprises either intervention or best medical therapy. Intervention entails carotid endarterectomy (CEA) or carotid stent placement (CAS). It should however be emphasised that all intervention should be supported by best medical therapy in the long term.

Intervention

Once the presence of a lesion at the carotid bifurcation has been confirmed intervention should be considered.

Symptomatic patients

In patients who present with classic middle cerebral artery symptoms, two classic independent studies, the European Carotid Surgery Trial (ECST)² as well as the North American Symptomatic Carotid Endarterectomy Trial (NASCET)³ provide the guidelines for treatment. The same protocols in both studies addressed the benefits of carotid endarterectomy (CEA) against best medical treatment, which at that time comprised mainly aspirin together

Occlusive extracranial cerebrovascular disease

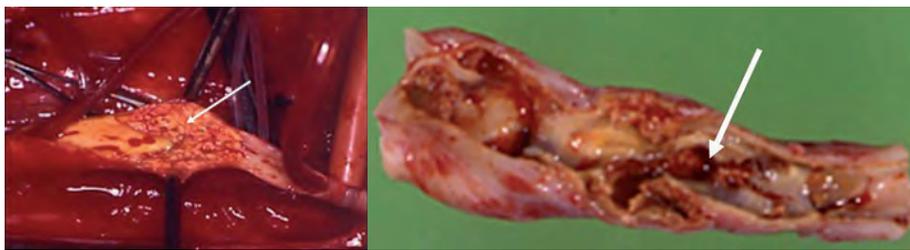


Fig. 4a and b. Endarterectomy specimens. Note luminal surface ulceration (arrowed).

with the control of medical risk factors such as ischaemic heart disease, hypertension, diabetes mellitus and smoking. There was however no hard protocol in the medical treatment arm. A total of more than 6 000 patients were studied and both studies came to similar conclusions although slightly different criteria were used in assessing the degree of stenosis on angiography. In both studies benefit was shown within 2 years of commencement. ECST showed benefit for 70 - 99% stenosis of stroke risk after surgery, which was 10.5% at 5 years. In the medical arm this figure was 19%.

Evidence for using statin therapy is convincing.

NASCET also showed that maximal stroke-free benefit for 70 - 99% stenosis at 5 years was 8.9% in the surgical group, as opposed to 28.3% in the medical group. Patients with 50 - 69% stenosis did benefit significantly but this benefit was much smaller. Women in this category showed minimal benefit,⁴ and the greatest benefit was in patients who were older than 75 years.⁵ There is little doubt that greater than 70% stenosis results in benefit from CEA, while 50%+ stenosis still entertains some debate. It is important to note that it is recommended that any centre embarking on carotid endarterectomy should have a proven stroke morbidity of less than 4% in symptomatic patients.

Asymptomatic disease

It is logical to assume that asymptomatic stenosis would present some stroke risk. The two best current trials compared CEA with best medical treatment for asymptomatic stenosis of greater than 60%, and concluded in favour of CEA.

The asymptomatic carotid atherosclerosis study (ACAS) randomised 1 662 patients and showed that the 5-year risk of ipsilateral stroke, perioperative stroke and death was reduced from 11% to 5.1%.⁶ The Asymptomatic Carotid Surgery Trial (ACST) comprised 3 120 patients and showed a difference of 11.8% versus 6.4% in favour of CEA.⁷ Both trials showed minimal benefit in women. The

major criticism revolves around the determination and standardisation of best medical therapy. This is currently being addressed by the Trans-Atlantic Carotid Intervention Trial (TACIT) study. The investigators intend to randomise 2 400 patients between standardised best medical therapy and intervention which entails carotid endarterectomy versus carotid artery stent. It must be pointed out that intervention should have a perioperative stroke rate of less than 3% in order to show benefit in asymptomatic patients.

What intervention?

Fig. 4 (a and b) shows typical ulcerating plaque removed at endarterectomy. The result of a carotid stent procedure is illustrated in Fig. 5 (a, b and c). CEA is a tried and tested therapy and is probably the best studied operation of all, while CAS is the relatively new alternative. Stenting is less invasive and certainly offers theoretical advantages to the patient in terms of periprocedural discomfort and morbidity.

There have been three major trials which address the issue of carotid endarterectomy versus carotid artery stent. The Sapphire Trial was a US-based study of high-risk patients, the majority of whom were asymptomatic.⁸ This study showed the non-inferiority of carotid artery stent versus CEA. CAS results were marginally better, and there was a 4.4% stroke and death rate after CAS compared with 9.9% after CEA, which did not reach statistical significance.

There are still many challenges related to therapy of occlusive extracranial cerebrovascular disease.

Symptomatic patients were addressed by the SPACE Trial which was performed in several European centres but mainly in Germany.⁹ This showed a combined stroke and death rate of approximately 6% in both groups. They also concluded that CAS was not

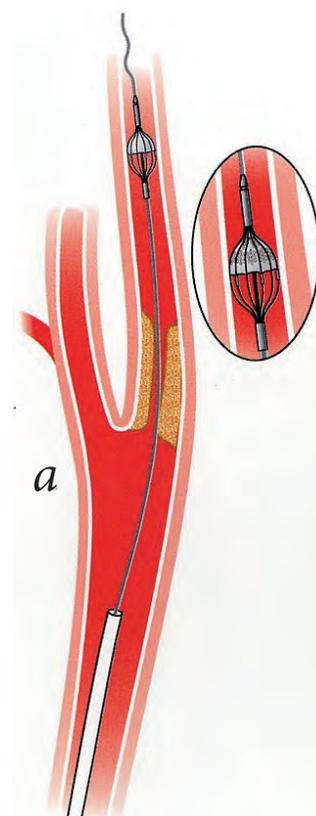


Fig. 5a. Carotid stent procedure. Embolic protection device. Fig. 5b. Stenosis before stent insertion. Fig. 5c. Post stent insertion.

inferior. Multiple French centres conducted the EVA 3S which also addressed symptomatic patients and showed that CEA was significantly better than CAS, with a stroke and death rate after CEA of 3.9% versus 9.6% after CAS.¹⁰

Local work in Durban shows mortality and morbidity after carotid artery stent to be 2.3% versus 1.9% after CEA, which compares favourably with the previously reported studies, and in selected patients results are equivalent.

The choice of therapy still requires investigation and more studies related to the nature and morphology of the carotid plaque are required. It must be re-emphasised that either modality must be carried out in high-volume centres and there is no place for 'casual' operators.

Best medical therapy

There have been considerable advances in the concept of best medical therapy since the initial trials. It goes without saying that best medical therapy should provide the platform in all patients at risk of cerebrovascular events and should be given to all patients with carotid artery disease, whether they are being managed conservatively or by interventional means. Detailed discussion of evidence for best medical therapy is beyond the scope of this paper.

The guidelines of the European Stroke Initiative defined modern best medical therapy in stroke prevention as follows:¹¹

Level 1 evidence

- Maintain blood pressure at or less than 140/90 (130/80 in diabetics)
- Statin therapy
- Reduce heavy alcohol consumption
- Antiplatelet therapy
- Avoid hormone replacement therapy in women.

Level 2 and 3 evidence

- Stop smoking
- Tight glycaemic control
- Lose weight if the BMI is elevated
- Regular exercise
- Diet that is low in salt and saturated fat and high in vegetables, fruit and fibre.

Evidence for using statin therapy is convincing. This results in the lowering of cholesterol and LDL levels, which reduces the risk of stroke. There is also evidence

that statin therapy stabilises the plaque and reduces plaque progression by reduction of inflammatory cell activity as well as resorption of the soft lipid core.

Antiplatelet therapy is now recommended by the American Heart Association, and they feel that dual therapy should be given using aspirin and dipyridamole.¹²

Conclusion

It would appear that any future studies will have to include a comparative arm in which best medical therapy is standardised as outlined above. There are still many challenges related to therapy of occlusive extracranial cerebrovascular disease.

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In a nutshell

- Surgically remediable neurological episodes are usually embolic in nature and related most commonly to atherosclerotic plaques situated at the carotid bifurcation.
- The likelihood of embolisation is related to the degree of stenosis causing turbulent flow which dislodges loose surface material on the plaque.
- Symptoms may be temporary (TIA, RIND or fixed) stroke. The clinical presentation depends on the anatomical area affected by transient or permanent ischaemia.
- All deficits, temporary or fixed, should be investigated, initially with Duplex-Doppler and when indicated CT angiography. A CT scan of the brain is essential if symptoms are atypical or if a fixed deficit is found.

Indications for intervention

- Symptomatic stenosis more than 70%. There is some evidence that patients with more than 50% stenosis will benefit if the perioperative neurological morbidity is less than 4%. This issue remains debatable.
- Asymptomatic points towards more than 60% stenosis but the provisory is that there is a less than 3% peri-procedural neurological morbidity.
- Carotid endarterectomy remains the gold standard for treatment. Stent placement should be shown to be equivalent in certain circumstances but is not the routine standard of care. Selection criteria remain to be clearly defined.
- Best medical therapy in terms of lipid control antiplatelet therapy and general medical care has evolved and any therapy should be measured against this.