2.2 Extracranial Carotid Artery Disease

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2.2.1 Introduction

Ischaemic stroke represents a major health problem and an important cause of morbidity and mortality in several western countries [12]. Mortality from stroke ranges between 10% and 30% [61] and its survivors remain at a high annual risk of recurrent ischaemic events and mortality both from myocardial infarct and repeated stroke [76]. Atherosclerosis from supra-aortic vessels, especially from the common carotid bifurcation, is the major single aetiology of ischaemic stroke in developed countries as opposed to intracranial occlusive disease and cardioembolization.

The association between internal carotid artery occlusion and severe ischaemic stroke was first credited to Savory [82], obtained from the autopsy of a woman with a history of monocular blindness and contralateral hemiplegia and occlusion of the left carotid artery associated with bilateral subclavian occlusions. Subsequent descriptions were reported [33, 87] and in 1914 Ramsey Hunt published an important paper, which correlated the presence of diminished cervical carotid pulsations with intermittent neurological symptoms and drew attention to the need for “careful examination of the neck vessels” in such patients [49]. With the introduction of angiography, Egas Moniz [62] provided the first demonstration in vivo of occlusion of the internal carotid and stroke (Fig. 2.2.1) and also described the correlation between transient strokes and carotid bifurcation stenosis [63]. His observations were confirmed in subsequent studies using angiography [18, 51], although the established arteriographic technique routinely practised often failed to visualize the extracranial vessels [13, 42].

Embolization from carotid bifurcation lesions was suggested by Miller Fisher [35, 36] to be the pathogenic mechanism of ischaemic brain symptoms associated with extracranial carotid disease and led to the possibility of preventing stroke by eventual surgical correction of the diseased arteries.

The most frequent lesion is stenosis at the common carotid bifurcation and origin of the internal carotid artery; however, atheroma of the aortic arch protruding into the ostia of the innominate and left common carotid arteries may cause severe flow-reducing stenosis and act as a source of cerebral embolization.

Reconstructive surgery for chronic arterial occlusive disease started in Lisbon in 1947, with the introduction of endarterectomy by João Cid dos Santos [19], a technique conceived to be used for the obliteration of limb occlusive disease ideally in short segmental obstructions.

The first carotid intervention was performed in Buenos Aires in 1951 by Carrea, Mollins and Murphy [17], consisting of resection of the proximal internal carotid segment and re-establishment of flow by anastomosing the external carotid to the distal internal carotid.

Fig. 2.2.1 First cerebral arteriogram performed by Egas Moniz
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DeBakey [24] described the first carotid disobliteration in 1953, in a patient with a complete occlusion, which succeeded in restoring flow. Eastcott, in 1954 [27], performed the first successful elective carotid operation on a patient with internal carotid stenosis and multiple transient ischaemic attacks (TIAs) in order to prevent stroke, resulting in the patient remaining asymptomatic for more than 30 years.

Successful endarterectomy of the innominate artery with a 2-year follow-up was described in 1956 [21], followed by several reports of correction of proximal and/or ostial lesions at the aortic arch through bypass procedures.

The development of arterial catheterization for arteriography [83] and its widespread use provided easier diagnosis of extracranial disease as a major cause of brain ischaemia and set the stage for the generalized use of carotid surgery, aiming to restore arterial perfusion to the brain and avoid distal atheroembolization to prevent severe ischaemic syndromes.

The 80 multicentre cooperative studies, in both Europe and the USA [29, 70], provided level 1 evidence for the benefit of carotid endarterectomy (CEA) in patients with transient neurological symptoms (TIAs) and reversible stroke; for carotid stenosis it was greater than 70%, contributing to a more appropriate and rational use of CEA.

Reduction of surgical risk and the need for specific accreditation of surgeons and institutions for the treatment of extracranial carotid disease were recognized [64] in order to ensure greater benefit from CEA. The selection of patients for surgical treatment, and the need to reduce overall morbidity and mortality in patient management, both for symptomatic and asymptomatic patients, must be considered; the impact of the new endovascular surgical procedures requires careful re-evaluation of established concepts, to offer the best available treatment for each patient, and to provide guidelines for institutions and individual practitioners dealing with extracranial carotid disease.

2.2.2 Pathogenesis of Brain Ischaemia

The mechanisms of neurological dysfunction in extracranial carotid disease are:

- **Atheroembolization** – from local thrombosis associated with unstable plaques [53, 88]

- **Haemodynamic** – with reduction of cerebral blood flow, associated with sudden occlusion of a carotid artery, severe bilateral disease and ostial stenosis in the aortic arch.

Local thrombosis in ulcerated plaques results from disruption of its endothelial surface and fibrous cap causing:

- Ulceration or subintimal haemorrhage
- Platelet and erythrocyte aggregation to the subendothelial layer
- Distal embolization of the thrombus and debris from the plaque contents

These events are associated with clinical symptoms and progression of the atheromatous plaque [5, 7, 37, 54].

High-definition ultrasonography [9, 72, 79] and magnetic resonance imaging [90, 91] allow in vivo visualization of carotid bifurcation lesions in patients with symptoms of brain ischaemia. It is possible to identify markers of plaque activity, such as:

- Echolucency
- Presence of heterogeneity in its echostructure
- Presence of echolucent areas near the arterial lumen
- Surface disruption and/or ulceration (Fig. 2.2.2), which correlates with the presence of ipsilateral appropriate neurological symptoms [72]
- Increased levels of elastin degradation products, cellularity and DNA contents of the plaque [39–41]

Stroke occurs when there is brain infarct due to local reduction of cerebral blood flow (CBF), which is maintained around 45–50 ml/100 g of tissue per min by the mechanisms of autoregulation, for systolic blood pressures between 60 and 130 mmHg [4, 23, 31, 38, 56, 60].

With flow reduction (CBF <16 ml/100 g tissue per min) there is cessation of electrical brain activity, flattening of the EEG and failure to synthesize biochemical neurotransmitters, but the neuron may still be viable. When CBF is <10 ml/100 g tissue per min, disruption of aerobic metabolism, reduction of depolarization of the cell membrane and cell necrosis occur, leading to infarct [38].

There is a central area of necrosis, surrounded by an area of impaired function but viable tissue known as the *ischaemic penumbra*, its extent depending upon the functional capability of the collateral circulation. The severity of the stroke is correlated with the location and extent of the brain infarct, and also with the dysfunction of the penumbra area, which may be recovered by re-establishment.