Carotid plaques and cerebral collateral circulation

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Internal carotid artery (ICA) atherosclerosis is one of the most frequent causes of stroke and transient ischaemic attack. Atherosclerosis is a degenerative disease of the arteries resulting in plaques consisting of necrotic cells, lipids, and cholesterol crystals. These plaques can result in symptoms of stenosis, embolism, and thrombosis. The aim of carotid imaging is to answer different questions about the cause of the cerebral event.
Carotid imaging makes it possible:
– To identify the obstructive pathology at the level of the epicranial vessels;
– To locate extra-/intra-cerebral vessel blockage;
– To quantify the degree of stenosis (occlusion).
To identify lesions other than atherosclerosis (congenital malformation, dissection, venous thrombosis).
Information from imaging studies (carotid duplex, CT scan, carotid magnetic resonance angiography, angiography) help us to choose among different therapeutic modalities (medical options with anti-coagulant or anti-platelet agents, thrombolysis, or carotid angioplasty + stenting and carotid endarterectomy) in an attempt to prevent future cerebral events.
In patients with acute cerebral ischaemia, neurovascular ultrasound with the combined use of carotid/vertebral duplex and transcranial colour coded Doppler (TCCD) allows the urgent detection, localisation, and severity grading of the arterial obstruction and study of the collateral circulation.
Using carotid ultrasound we can study the anatomical sites where blockages or narrowing of carotid arteries, which if present may increase the risk of having a stroke, are most frequently located.
The method shows a good level of accuracy; indeed, carotid duplex scanning is being used increasingly frequently as the only preoperative diagnostic imaging modality for patients eligible for carotid endarterectomy (1). It is estimated that as many as 80% of patients in the USA undergo carotid endarterectomy after Doppler ultrasonography as the only preoperative imaging study (1).
Carotid ultrasound enables us to study atherosclerotic plaques, in particular the degree of stenosis they cause and their morphostructural characteristics.
Numerous imaging and Doppler parameters are currently in use in various laboratories for the evaluation of ICA stenosis.
A panel of experts from a variety of medical specialties, convened under the auspices of the Society of Radiologists in Ultrasound, arrived at a consensus on the use of Doppler Ultrasonography in aiding diagnosis of ICA stenosis (2).
This consensus conference in 2003 recommended the following criteria for estimating stenosis:
- Normal: ICA PSV <125 cm/s and no plaque or intimal thickening is visible.
- <50% stenosis: ICA PSV <125 cm/s and plaque or intimal thickening is visible.
- 50-69% stenosis: ICA PSV is 125-230 cm/s and plaque is visible.
- >70% stenosis to near occlusion: ICA PSV >230 cm/s and plaque and lumen narrowing are visible.
- Near occlusion: A markedly narrowed lumen is seen on colour Doppler ultrasound.
- Total occlusion: No detectable patent lumen is seen on greyscale ultrasound, and no flow is seen on spectral, power, and colour Doppler ultrasound.

With stenosis over 90% (near occlusion), velocities may actually drop as mechanisms that maintain flow fail. Ratios may be particularly helpful in situations in which cardiovascular factors (e.g., poor ejection fraction) limit the increase in velocity. In such cases, ICA/CCA ratios above 3 may signify significant stenosis. With normal cardiovascular function and normal velocities, changes in ratios should be interpreted with cau-

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tion. To date, degree of stenosis has been the criterion most used to define stroke risk; recently, plaque morphology has emerged as an important contributory factor in stroke. Ultrasound studies have shown that hypo- or anechogenic plaques carry a higher risk of cerebrovascular events than echogenic ones. Similarly, heterogeneous plaques presenting a complex pattern of echogenicity in ultrasound examinations have also been more frequently associated with the occurrence of neurological symptoms than homogeneous lesions. Furthermore, most studies determining the surface characteristics in ultrasound have found that ulceration also predicted increased risk of subsequent stroke. These studies are, however, based on visual evaluation using different classification systems and presenting a high variability of intra- and interobserver agreement.

Classifications of carotid plaque morphology by visual analysis

There are three main parameters constituting the basis of plaque morphology classification: plaque echogenicity, texture and surface.
Several classifications of plaque echogenicity have been reported in the literature.
In 1988, Gray-Weale (3) described four different plaque types: Type 1 (anechogenic with echogenic fibrous cap), Type 2 (predominantly anechogenic but with echogenic areas representing less than 25% of the plaque), Type 3 (predominantly hyperechogenic but with anechogenic areas representing less than 25% of the plaque) and Type 4 (echogenic and homogeneous plaque).
In 1990, Widder et al. used a reverse classification, the most anechogenic plaques being assigned to Type IV and the most echogenic to Type I.
Finally, Geroulakos et al. (4) introduced a modified version of Gray-Weale's classification including a 5th category of unclassified calcified plaques which may have zones of acoustic shadowing which obscure the deeper part of the arterial wall as well as the vessel lumen. According to a recent consensus meeting on plaque characterisation, echogenicity should be standandised against three reference structures: flowing blood for anechogenicity, sternocleidomastoid muscle for isoechogenicity, and the adjacent transverse apophysis of the cervical vertebrae for hyperechogenicity.
This classification is very important because it tells us that behind different echogenic characteristics there lies a different stroke risk.
We know that echolucency of carotid atherosclerotic plaques on ultrasound B-mode images (5) has been associated with high incidence of brain infarcts as evaluated on CT scans. Plaques that appear echolucent on B-mode ultrasound are lipid rich.
In a study including patients with neurological symptoms and carotid artery stenosis, increased plasma levels of triglyceride-rich lipoproteins predict echolucency of carotid plaques, which is associated with increased plaque lipid content.
Other studies indicate that low levels of HDL cholesterol are associated with an increased risk of having echolucent, rupture-prone atherosclerotic plaques; a high level of HDL cholesterol stabilises plaques and counteracts their growth by reducing their lipid content and inflammation (6).
The inverse relationship between ischaemic stroke and the concentration of HDL cholesterol was recently confirmed by the Manhattan Stroke Study (patients with HDL <35 mg/dl -1.94 mmol/l- have a double risk having a stroke, than patients with HDL> 35 mg/dl -1.94 mmol/l-) (7).

Statins and stroke

In this context, it is right consider the use of the statins in cerebrovascular diseases. Many studies (placebo vs randomised and accurate controls) have shown that the statins, as primary and secondary prevention, considerably reduce vascular events in patients who suffer from cardiovascular pathology. A great number of these trials defined TIA and stroke as primary and secondary events. Although hypercholesterolaemia shows a less clear relationship with cerebrovascular accidents than with cardiovascular disease, the administration of statins reduces from 25% to 30% the possibility of having a stroke.
The SPARCL and HPS studies recently considered the efficaciousness of high-dose atorvastatin (80 mg-4.4 mmol/l) in patients who have had a previous stroke (8).
They confirmed that statins are able to influence positively the clinical prognosis of these patients, even those with previous cerebrovascular diseases.
In short, cholesterol has been always considered a poor predictor of the risk of having a stroke, but:
– high levels of cholesterol have been associated with a higher risk of ischaemic stroke;

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– statins have reduced the risk of ischaemic stroke;
– the use of statins may not be related to a higher risk of haemorrhagic stroke. The efficaciousness of the medicine seems to be independent of cholesterol levels.

In addition to the echogenic characteristics of carotid atherosclerotic plaques, we can evaluate carotid plaque surface irregularity and fibrous cup thickness (9-14).

These elements contribute to plaque vulnerability and can be used to select patients likely to obtain the most benefit from carotid endarterectomy.

TCCD makes it possible to establish whether the extracranial obstruction extends to the origin of the middle cerebral artery and/or anterior artery and whether the intracranial perfusion is preserved by intracranial activation of collateral compensatory pathways in patients affected by carotid stenosis or occlusion.

Compensatory haemodynamic mechanisms depend on individual anatomical and functional characteristics. Considerable variability exists in the anatomy of the circle of Willis, which is frequently asymmetrical and shows an ideal configuration in only a minority of cases (15-17).

The arterial anatomy of the collateral circulation includes extracranial sources of cerebral blood flow and intracranial routes of ancillary perfusion that are commonly divided into primary or secondary collateral pathways.

Primary collaterals include the arterial segments of the circle of Willis, whereas the ophthalmic artery and leptomeningeal vessels constitute secondary collaterals.

Interhemispheric blood flow across the anterior communicating artery (AcoA) and reversal of flow in the proximal anterior cerebral artery provide collateral support in the anterior portion of the circle of Willis.

The posterior communicating arteries (PcoAs) may supply collateral blood flow in either direction between the anterior and posterior circulations.

Reversal of blood within the ophthalmic artery may provide secondary collateral support (18,19).

Leptomeningeal anastomoses between distal segments of the major cerebral arteries also contribute to ancillary collateral blood flow (20).

The collateral ability of a vessel is ultimately determined by its luminal calibre.

The process of collateral recruitment depends on the calibre and patency of primary pathways, which may rapidly compensate for decreased blood flow, and the adequacy of secondary collateral routes.

AcoA diameter strongly modulates the effects of ICA lesions on cerebral haemodynamics. The AcoA is commonly recognised as the most important collateral pathway in the event of severe ICA stenosis or occlusion (21).

The importance of a functional PcoA in ICA obstructive disease is not yet clear, although a hypoplastic PcoA might increase the risk of developing cerebral ischaemia in patients with ICA occlusion (22,23).

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