



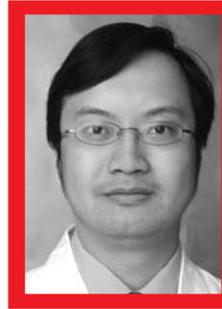
## Carotid Stenosis

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### Introduction

Carotid artery stenoses, particularly involving the origin of the internal carotid artery, are most commonly due to atherosclerosis. One of the common aetiological factors in Hong Kong is radiation therapy to the head and neck region, especially in nasopharyngeal carcinoma patients. Atherosclerosis is considered as an inflammatory disease. The process of atherogenesis consists of migration and proliferation of smooth muscle, arterial wall thickening, accumulation of foam cells, formation of fibrous plaque and fibrous cap and haemorrhage and thrombosis within the plaque. Endothelial dysfunction and platelet activation play a key role in the initiation of the process. Eventually, ulceration of plaque may occur and lead to thrombosis and distal embolism. The presence of an ulcerated plaque is associated with a stroke rate of 7.5% per year. The nature of the atherosclerotic plaque and the mechanisms by which it results in symptoms must be kept in mind when assessing the approach to carotid artery stenosis.

Stroke is the third leading cause of death in Hong Kong and accounts for more than 20 deaths per 100 000 population per year.<sup>1</sup> Carotid stenosis accounts for about 20% of ischaemic strokes and should be managed efficiently to minimise the incidence of stroke. Unfortunately, only about 15% of strokes are preceded by transient ischaemic attacks (TIAs).<sup>2,3</sup> Until recently, North American guidelines recommended that assessment and investigation be completed within one week of a TIA and British guidelines recommended assessment within 2 weeks.<sup>4,5</sup> A screening study carried out between 1995 to 1997 in Hong Kong showed that severe carotid stenosis was detected in 37.7% of patients with cerebrovascular disease, 24.5% of patients with peripheral vascular disease and 11.1% of patients with coronary artery disease.<sup>1</sup> Thus, the prevalence of carotid stenosis in Chinese population is not low in the patient group with atherosclerotic disease in other vascular beds. It had been suggested that screening of carotid stenosis might be considered in patients with ischaemic heart disease and irradiated nasopharyngeal carcinoma patients.

The prevalence of carotid artery stenosis in the general population is too low to justify widespread screening for this condition.<sup>6</sup> About 35% of patients with a carotid bruit have moderate or severe carotid stenosis. Patients found to have carotid bruit should be further evaluated.<sup>2</sup> However, unlike cardiac murmur, carotid bruit may be absent in patients with severe carotid

stenosis and thus all symptomatic patients should be investigated radiologically irrespective of the presence or absence of carotid bruit.

### Investigation

Symptoms of stroke or TIA referable to carotid territory include weakness or paralysis on the contralateral side, numbness or loss of sensation on the contralateral side, dysarthria, dysphasia, and amaurosis fugax on the ipsilateral side. If carotid stenosis is also present, it would be classified as symptomatic carotid stenosis. Patients presenting with motor weakness or speech deficit are at higher risk of subsequent strokes than patients presenting with sensory deficits or amaurosis fugax.

Carotid duplex ultrasound is the most frequent employed modality in the initial evaluation of patients with suspected carotid artery disease. Duplex ultrasound can provide an estimation of the degree of stenosis, structure and composition of plaque. With ultrasound finding of carotid stenosis of 60% or more, patient should undergo further diagnostic evaluation with non-invasive techniques such as contrast-enhanced MR angiography or CT angiography.

In terms of non-invasive investigation, a recent review suggested that contrast-enhanced MR angiography may be more sensitive (0.94, 95% CI 0.88-0.97) and specific (0.93, 95% CI 0.89-0.96) for 70-99% stenosis than Doppler ultrasound, MR angiography and CT angiography.<sup>7</sup> Intra-arterial angiography remains the gold standard when in doubt.

### Management of symptomatic carotid stenosis

Aggressive medical therapy had been shown to reduce atherosclerotic carotid artery stenosis and prevent symptoms.<sup>8</sup> Antiplatelet therapy had been shown to reduce risk of fatal strokes by 16% and non-fatal strokes by 28%.<sup>9</sup> Lipid lowering therapy reduce risk of strokes by 25%.<sup>10,11</sup> Angiotensin-converting enzyme inhibitors decrease stroke rates by 32% and were shown to have slowed progression of atherosclerosis in general.<sup>12,13,14,15</sup> Effective management of hypertension decreased stroke rates by 28% to 40%.<sup>16,17</sup> Smoking cessation had been shown to decrease women's risk of strokes by 48%.<sup>18,19</sup>

Among patients with TIA or stroke and documented



carotid stenosis, a number of randomised trials have compared endarterectomy plus medical therapy with medical therapy alone. For patients with symptomatic atherosclerotic carotid stenosis greater than 70%, as defined by using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria, the value of carotid endarterectomy (CEA) has been clearly established from the results of 3 major prospective randomised trials: the NASCET, the European Carotid Surgery Trial (ECST), and the Veterans Affairs Cooperative Study Program.<sup>20,21,22,23,24</sup> Among symptomatic patients with TIAs or minor strokes and high-grade carotid stenosis, each trial showed impressive and absolute risk reductions for those randomised to surgery. For those with symptomatic carotid stenosis in the moderate category (50% to 69% stenosis), the result from NASCET and ECST demonstrated significant though less impressive benefits for CEA in this moderate group compared with medical therapy. For patients with carotid stenosis less than 50%, these trials showed that there was no significant benefit of surgery

Various comorbid features altered the benefit-to-risk ratio for CEA for moderate carotid stenosis. Benefits were greater among those with more severe stenosis, those more than 75 years of age, men, patients with recent stroke and patients with hemispheric symptoms.<sup>25</sup> Other radiographic features found to predict better outcomes after CEA included the presence of intracranial stenosis, the absence of leukoaraiosis, and the presence of collaterals.<sup>26,27</sup> Benefit from surgery was greatest within 2 weeks after last ischaemic event and fell with increasing delay.<sup>28</sup>

We had managed over 90 carotid endarterectomies in our unit since 1996.<sup>29</sup> In 2002, we started to use regional anesthesia when performing carotid endarterectomies unless the patients could not tolerate, in which cases, general anaesthesia will be used. Data suggest that regional anaesthesia might reduce the need of intraoperative shunting, duration of hospital stay, perioperative stroke and myocardial infarction.<sup>30</sup> We perform superficial cervical plexus block along the posterior border of the sternocleidomastoid muscle with a mixture of lignocaine and ropivacaine and supplemented by light sedation with dexmedetomidine infusion. Intraoperatively, we monitor the patients by (1) clinical neurological status, (2) measuring the middle cerebral artery flow velocity by transcranial Doppler, and (3) monitoring EEG with spectral edge frequency, particularly observing any significant change before and after vascular clamping.<sup>31</sup> We use a transverse skin incision with extension to the back of the jaw to have better cosmetic effect. After exposing the common carotid artery, internal carotid artery and external carotid artery, a trial cross clamping of the vessels will be performed. If there was no adverse effects as shown by the monitoring, intraarterial shunt is not used. An arteriotomy is then made and the atheroma is removed from the intima. We routinely repair the arteriotomy site with a vascular patch to enhance the diameter of the vessel. The median of days of hospital stay for patients having undergone carotid endarterectomy in our unit is 3 days. The stroke risk after CEA in our cohort was 2.2% over a mean follow-up period of five years. (Figure 1a and 1b)

Data on carotid balloon angioplasty and stenting (CAS)

for symptomatic patients with internal carotid artery stenosis in stroke prevention consists of a number of published case series and few randomised multicentre comparisons of CEA and CAS.<sup>32</sup> The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial randomised 334 patients to endarterectomy under general anaesthesia or stenting with the use of an embolic-protection device under local anaesthesia, testing the hypothesis that stenting was not inferior to endarterectomy.<sup>33</sup> Only 30% of the study population was symptomatic. Qualified CAS operators had a periprocedural stroke, death or myocardial infarction complication rate of 4%. The primary end point of the study (the cumulative incidence of death, stroke or myocardial infarction within 30 days after intervention, or death or ipsilateral stroke between 31 days and 1 year) occurred in 20 stent patients and 32 endarterectomy patients (30-day risk, 5.8% versus 12.6%;  $P=0.004$  for noninferiority). Most of the benefits was detected in the lower risk of myocardial infarction for the stent compared with the high-surgical risk general anaesthesia endarterectomy cases. At present, CAS has been used in selected patients instead of carotid endarterectomy in the presence of severe vascular or cardiac comorbidities or specific conditions. They may include contralateral laryngeal nerve palsy, radiation therapy to the neck, previous CEA with recurrent restenosis, high cervical internal carotid / below the clavicle common carotid lesions, severe tandem lesions, severe pulmonary disease, congestive heart failure (New York Heart Association class III/IV), known severe left ventricular dysfunction, recent myocardial infarction (>24 hours and < 4 weeks), unstable angina and contralateral occlusion. This definition, however, is not evidence based and is not universally shared.<sup>34</sup> Randomised trials comparing the efficacy of CAS versus CEA in preventing strokes are ongoing in United States, Europe and Australia and 2-year outcome data should come out in 1-2 years. 30-day strokes and mortality rates of the European trials did not support the hypothesis of non-inferiority as compared to carotid endarterectomy.

Our protocol for carotid angioplasty and stenting is described as below. With respect to preprocedural therapy, adequately dosed dual antiplatelet therapy is essential. Patients would receive a combination of clopidogrel 75 mg and aspirin 160 mg for 5 days before CAS. The procedure is carried out under local anaesthesia. Continuous monitoring of pulse oximetry, blood pressure and heart rhythm is essential. Usually, the procedure is performed through a 7F or 8F right femoral arterial sheath. The role of initial diagnostic angiography is limited to the lesion side as determined by preprocedural noninvasive imaging. We obtain angiographic runs with an evaluation of lesion severity, carotid bifurcation, anatomy of common carotid artery and ipsilateral intracranial anatomy. The diagnostic catheter would then be exchanged for a guiding catheter. The tip of the guiding catheter is positioned in the distal common carotid artery. Heparin bolus of 4000 units will be administered after guiding catheter placement. Next the lesion is crossed with a 0.014-inch guidewire, usually that of an embolic protection device. The embolic protection device is deployed in the distal cervical internal carotid artery. Intravenous atropine 0.5 mg may be applied before stenting and balloon angioplasty, especially in elderly patients with heavily calcified

plaque. With the rapid exchange monorail system, stents such as Wallstent would be positioned to cover the lesion with adequate anchorage and deployed. Subsequent balloon angioplasty would be performed for optimal stent expansion. Femoral sheath would be removed when the activated clotting time has fallen below 150 seconds. Patient will be discharged with instruction to take clopidogrel 75mg daily for 4 to 6 weeks, except for patients treated for lesions related to prior neck irradiation, in whom clopidogrel treatment may be extended to 1 year. In the absence of contraindication, aspirin 160mg daily is prescribed indefinitely. We would arrange early computed tomographic angiography and ultrasound duplex study as a reference for later follow up evaluation. We had carried out 10 CAS in the last year and there was no post-procedural ipsilateral stroke or mortality. (Figure 2a and 2b)

### Management of asymptomatic carotid stenosis

Patients with asymptomatic carotid stenosis treated medically only have a small risk of future stroke of about 2% per annum. If CEA can be performed safely with a perioperative stroke and death rate of no more than 3%, randomised trials showed a significant benefit of surgery over 5 year follow-up, with an overall reduction in the risk of stroke from about 11% over 5 years down to 6%.<sup>35,36</sup> An alternative paradigm was employed in our unit. The workup in our unit for asymptomatic carotid stenosis would include tests for cerebrovascular reactivity (which indicates cerebrovascular reserve). Patients with poor cerebrovascular reactivity would be of higher risk of subsequent stroke and would be offered carotid intervention.<sup>37</sup> Upon a mean follow up of 67 months, none of the 16 patients with asymptomatic carotid stenosis and normal cerebrovascular reactivity developed stroke.

A variety of different imaging techniques have been developed for the indirect or non-invasive assessment of cerebral haemodynamics in patients with carotid artery disease. One method would be to measure flow velocity in the middle cerebral artery (MCA) by transcranial Doppler ultrasound (TCD).<sup>38</sup> It has been demonstrated that during carbon dioxide inhalation there is little change in MCA diameter and therefore any change is directly proportional to the change in flow. Both carbon dioxide and acetazolamide have been used to measure the vasodilatory reserve.<sup>39,40</sup> TCD-based techniques are cheap and simple and are tolerated by almost all patients. Impaired reactivity determined using this method correlated with evidence of ischaemia on magnetic resonance spectroscopy, as determined by the presence of lactate and a reduction in the neuronal marker N-acetyl aspartate.<sup>41</sup> It also correlated with vasodilatation, detected as an increased CBV (cerebral blood volume) to CBF (cerebral blood flow) ratio, estimated by PET.<sup>42</sup> Other options include stable Xenon-CT (also employed in our unit), SPECT, PET, MRI to have quantitative or relative measurement of CBF and CBV.<sup>43</sup>

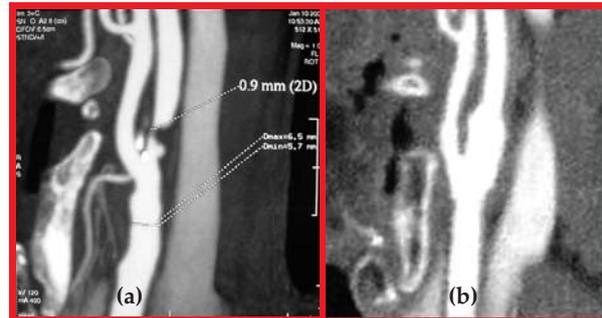


Figure 1 (a) CT angiogram showed typical proximal severe internal carotid stenosis; (b) CT angiogram showed satisfactory revascularisation after CEA.

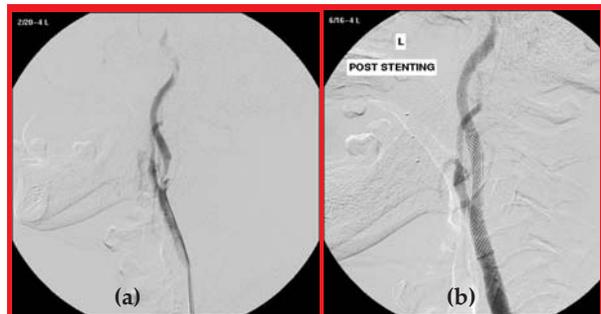


Figure 2 (a) DSA showed typical severe internal carotid stenosis with ulcerated plaque; (b) Post-CAS DSA showed satisfactory revascularisation.

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