Imaging of acute stroke and therapy beyond the extracranial vessels

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Stroke is one of the leading causes of mortality and morbidity with great impact to the patients, their family members and the society at large. The World Health Organization made an estimated stroke death of 2.7 million in Asia in 2000 with more than half of the stroke deaths coming from China. The lifetime stroke risk estimated from the Framingham study in middle-aged adults is 1 in 6 or more. Women had higher risk because of their longer life expectancy. In year 2001, there were 3130 deaths caused by stroke, which accounted for 9.4% of the local mortality. Ischaemic stroke accounts for more than 70% in the local population.

The key point in imaging of acute stroke is to identify the area of umbra and penumbra. With the area of the umbra generally representing the infarcted tissue while the area of the penumbra representing the area of potential salvageable tissue.

Plain computed tomography (CT) remains the first line investigation for patients alleged to have a cerebrovascular event. This is because of the easy accessibility of CT. Functional imaging as CT perfusion and CT angiography can also be performed in the same setting. MR is currently not widely available for the imaging of acute stroke in the public sector. Besides, CT can pick up cerebral parenchymal, ventricular or subarachnoid haemorrhage quite readily. Other extra-axial haemorrhage, as acute on chronic subdural haemorrhage, which can mimic stroke clinically, can also be readily seen on CT.

Early CT signs of cerebral ischaemia include hyperdense middle cerebral artery sign, loss of gray white differentiation, insular ribbon sign, hypodense lentiform nucleus. These could be detected in 82% of patients with middle cerebral territory artery infarct within 6 hours of onset of symptoms. The hyperdense middle cerebral artery represents throbosis of the middle cerebral artery while other signs basically detect oedema of the cerebral tissue. Roughly for every 1% of increase in tissue water, there will be a 1.5HU drop in the CT number. In a systemic review of 15 studies involving CT in the detection of early sign of cerebral infarct, the prevalence of these signs is 61% ± 21% (standard deviation). The inter-observer agreement varied from 0.14-0.78. The mean sensitivity and specificity for detecting early infarct signs with CT were 66% (range 20-87%) and 87% (range 56-100%).

Diffusion-weighted imaging (DWI) is much more sensitive and specific in detecting acute infarct with reported sensitivities ranged from 88-100% and specificities 86-100%. The apparent diffusion coefficient (ADC) map needs to be generated to alleviate the T2 component of the diffusion-weighted imaging. True areas of restricted diffusion will show hyperintense signal on DWI images (Figure 1) and low signal intensity on ADC maps. Reduction in diffusion in ischaemic brain tissue could be observed as early as 30 minutes after arterial occlusion. The restricted diffusion persisted for about 100 hours before the relative ADC values started to increase.

CT perfusion (PCT) studies are basically cine scans over the brain after a bolus of 40ml of contrast injection. Our current scanner, Lightspeed 16 (General Electric Medical Systems, Milwaukee, Wisconsin) offers 2cm coverage. Functional maps of regional cerebral blood flow (rCBF), regional cerebral blood volume (rCBV) and mean transit time (MTT) could be generated (Figure 2). PCT can help to identify the ischaemic reversible penumbra and the irretrievable umbra. The latter will show low rCBF and rCBV whereas penumbra area shows an elevated rCBV despite a drop in rCBF because of cerebral vascular autoregulation attempting to compensate by a local vasodilatation.

Other methods of assessing cerebral perfusion include positron emission tomography (PET) and xenon CT imaging.

Intracranial stenosis accounts for 8-10% of all ischaemic stroke. Asian, African and Hispanic descents have higher incidence of intracranial stenosis.

Based on 114 consecutive post-mortem findings, Leung et al concluded that intracranial atherosclerotic disease was more common than extracranial atherosclerotic disease in local Chinese population. Distal branches of the intracranial arteries were commonly involved. Hypertension, diabetes mellitus and ischaemic heart disease were identified to be risk factors associated with intracranial atherosclerosis.

Transcranial Doppler and duplex Doppler studies of intracranial and extracranial carotid arteries within 7 days of stroke symptom in 716 patients had found arterial occlusive disease in 49% (n=345) of the patients in another local study. 37% had isolated intracranial disease, 10% had both intracranial together with extracranial disease and 2.3% had extracranial disease only. Patients were followed up for 6 months for any vascular events (including transient ischaemic attack, stroke and acute coronary symptom) and death. Number of vascular events and death was also shown to increase dramatically with the number of occluded intracranial vasculatures.
The WASID trial showed a comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis ranging from 50-99%. All the stenosis was angiographically proven. The primary end point was ischaemic stroke, brain haemorrhage or death from vascular causes other than stroke. Warfarin has shown no added benefit over aspirin and was associated with higher rates of death (p=0.02), major haemorrhage (p=0.01) and myocardial infarction or sudden death (p=0.02). The important message from this study was a 11-12% ischaemic stroke rate in the territory of the stenotic artery in these patients at 1-year follow-up. Further evaluation of the results showed the stroke risk at 1 year was related to the degree of stenosis. The probability of stroke in the territory of the stenotic artery was highest with severe stenosis >70% (P=0.0025).

The long term follow up of case-series of symptomatic intracranial stenosis treated with balloon angioplasty alone showed a 3.4% annual stroke rate in the vascular territory of the treated vessel. Even if the residual stenosis is ≥50%, the annual stroke rate was 4.5%. The mean follow up period was 52.9 months.

Even better results with an annualised stroke rate of 1.8% in the treated vascular territory was reported by Wojak et al. with angioplasty alone performed in 60 consecutive symptomatic patients with intracranial stenosis ≥70%

Neurolink stenting of single target lesion with ≥50% stenosis of the intracranial arteries or extracranial vertebral arteries was shown to have high technical success (95%) with a 30D stroke rate of 6.6%. Follow-up at 6 months show stenosis of ≥50% in 32% intracranial stents and 42% extracranial vertebral stent. 39% of them were symptomatic with stroke or TIA.

Based on the SSYLVIA trial, the Food and Drug Administration had granted a Humanitarian Device Exemption designation for the NEUROLINK system.

To address the significant restenotic rate of the SSYLVIA, DES (drug-eluting stents) had been placed in the 8 patients with symptomatic intracranial stenosis (>70%) refractory to medical therapy. 4 Cypher (Cordis Corp) and 4 Taxus (Boston Scientific Inc) stents had been deployed. 1 patient had retinal embolism. The mean stenosis was reduced from 84.4% ± 10.2% to 2.5 ± 4.6%. The WingSpan trial combined balloon dilatation followed by deployment of a self-expanding stent in patient with ≥80% intracranial stenosis refractory to medical therapy. In 15 patients with a mean degree of stenosis of 72%, the stenosis was reduced to 54% after balloon angioplasty and further reduced to 38% after stent deployment. An update of the study had been presented in the American Society of Neuroradiology. There was 100% successful stent placement. Stroke or death rate was 4.4% at 30D and 7% at 6-months.

The current position statement of the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology and the American Society of Neuroradiology is as follows:

1. Balloon angioplasty with or without stenting may be considered for symptomatic patients with a ≥50% intracranial stenosis who have failed medical therapy.

2. Optimised medical therapy should be provided to patients with asymptomatic intracranial stenosis. This group of patients should have periodic non-invasive imaging at regular 6-12 month intervals and then by cerebral angiography if warranted. Magnetic resonance angiography or computed tomographic angiography would be the modalities of choice.

3. Further evaluation and advancement in both pharmacological and catheter-based therapies are needed to reduce the stroke caused by intracranial atherosclerosis.

Diagnostic cervicocerebral angiography remains the cornerstone or 'gold standard' even though there is a wide choice of non-invasive CT angiography, MR angiography or ultrasonography study of carotids and vertebrobasilar system. While the aim of stroke therapy is to salvage the devastating effect of ischaemia, we have to muster every single ounce of our effort to prevent stroke from happening. Diagnostic cervicocerebral angiography in expert hands should have a complication rate of less than 1%. Increased procedural and fluoroscopy time, increased number of catheter used and performing arch aortograms were all associated with higher procedural ischaemic complication. The 1.2% complication rate of diagnostic cerebral angiography in the Asymptomatic Carotid Atherosclerosis Study (ACAS) may be greater than the actual risk of stroke caused by the stenosis itself. Silent thromboembolism was seen in 25% of 66 patients after diagnostic angiography. Cognitive impairment has been demonstrated in patients with these subclinical infarcts after endarterectomy or carotid artery stenting.

Consensus and joint statement had been made by the American Academy of Neurology, American Association of Neurological Surgeons, American Society of Interventional and Therapeutic Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, AANS/CNS Cerebrovascular Section and Society of Interventional Radiology.

A summary of the consensus of the collaborating Neuroscience societies is as follows:

1. Patient safety is the paramount concern.

2. Formal training and experience in both cognitive and technical aspect of the neurosciences are important for the performance and interpretation of diagnostic and therapeutic cerebrovascular procedures. A minimum of 6 months of formal cognitive neuroscience training in an approved training programme in radiology, neuroradiology, neurosurgery, neurology and/or vascular neurology would be necessary before cervical carotid interventional procedures.

3. Limited credentialing for limited procedures eg. evaluation of carotid occlusive disease with limited training is unacceptable. Interpretative skills not conferred by casual training are needed for neurovascular conditions eg. vasculitis, identification of embolic complications, and identification of cerebral aneurysm. In other words, the one performing the cervicocerebral angiography should have the skills to interpret the other conditions that are shown on it.

4. Appropriately supervised cervicocerebral angiography training with an accumulated total of 100 diagnostic cervicocerebral angiograms is recommended before postgraduate training in...
cerebrocerebral interventional procedures.

5. The defined training pathway and quality assurance for carotid stent placement as described in "Quality Improvement Guidelines for the Performance of Carotid Angioplasty and Stent Placement" was espoused.

In conclusion, we have moved into the age where treatment of intracranial stenosis is no longer a bluff or a dream. Intracranial stenosis has a high prevalence in Chinese community. Exciting data are expected to come up from local trials and I look forward to seeing that in the near future.

References


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