LARGE ARTERY ATHEROSCLEROSIS: CAROTID STENOSIS, VERTEBRAL ARTERY DISEASE AND INTRACRANIAL ATHEROSCLEROSIS.

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Atherosclerosis of the large arteries is responsible for about 15 % of all ischemic strokes. Within the last decade, there has been significant progress in the medical management of atherosclerosis. Blood pressure lowering and control of dyslipidemia have improved, resulting in enhanced secondary stroke prevention. Even with the availability of surgical and endovascular therapies for some large artery atherosclerotic lesions, specifically carotid disease, the importance of intensive medical management cannot be overemphasized. In this presentation, I shall discuss contemporary management principles of two conditions: Cervical carotid atherosclerosis and intracranial atherosclerosis.

Cervical Carotid Atherosclerosis

Carotid atherosclerosis accounts for about 7% of ischemic strokes. In the Framingham Heart study, the degree of stenosis was predicted by common baseline atherosclerotic risk factors such as older age, cigarette smoking, systolic blood pressure and total cholesterol. In studies from the pre-statin era, patients with an asymptomatic carotid stenosis less than 75% had an annual stroke risk of 1.3%; and with a stenosis greater than 75% the annual risk of stroke was 2-2.5%. On the other hand, using 1990's medical therapy, symptomatic carotid stenosis over 70% carries an annual stroke risk of 10-15%. Intensive medical therapy and carotid revascularization procedures reduce these risks.

An important study in recent years is the Carotid Revascularization Endarterectomy versus Stenting trial (CREST). The trial originally focused only on symptomatic carotid stenosis patients. In 2005, recruitment was extended to asymptomatic patients in order to reflect the real-world scenario, where the majority of revascularization procedures are performed among asymptomatic patients. The primary outcome was stroke, myocardial infarction (MI) or death during the periprocedural period or any ipsilateral stroke within 4 years.

After 4 years of follow-up, the primary outcome occurred in 7.2% of the 1262 patients in the CAS group and 6.8% of the 1240 CEA patients, p=0.51. There was no difference in the primary outcome between the procedures throughout the duration of follow-up. However, upon review of the individual components of the outcome, important differences emerged. In comparison to the CEA group, patients in the CAS group had significantly higher perioperative strokes (4.1% CAS versus 2.3% CEA, p=0.01) and perioperative minor ipsilateral strokes (2.9% CAS versus 1.4% CEA, p= 0.009). Perioperative MI was significantly higher among the CEA patients (1.1% CAS versus 2.3% CEA, p= 0.03). The significant increase in strokes among the CAS patients was noted up to 4 years (6.2% CAS versus 4.7% CEA, p= 0.049).

The traditionally accepted endpoint of stroke and death in the perioperative period, and stroke up to 4 years of follow-up (excluding MI) was significantly higher in the CAS arm (6.4% with CAS and 4.7% with CEA, p= 0.03). A noteworthy feature about the assessment of outcomes in CREST was the regular screening for MIs with EKGs and cardiac enzymes before and after the procedure. Some critics question the inclusion of MI within the primary outcome while evaluating procedures intended for stroke prevention. As outcomes go, does a stroke or an MI have greater impact? The physical component of the SF 36 questionnaire for health related quality of life, was significantly worse at one year among stroke patients, but showed an uncertain effect among MI patients. The mental component was also significantly worse among stroke patients at one year. On the other hand, long-term mortality rates were higher among patients who suffered an MI in the perioperative period, even after adjustment

of baseline co-morbid factors. Whether the perioperative MI event is causally linked with later mortality or whether it is a marker of patients with a greater atherosclerotic disease burden is unclear.

The benefit of CEA was not uniform in the NASCET study. Some patient subgroups that experienced greater benefit include the following:

1. Men
2. Patients with ulcerated lesions
3. Patients with hemispheric TIA/stroke (compared to retinal events)

Details regarding these issues can be found in previous guidelines from the AAN and AHA/ASA.

Asymptomatic carotid stenosis

In previous trials from the 1990's, the annual risk of stroke with medical therapy was approximately 2.0-2.5% per year. With contemporary therapy, the risk has come down to about 1% per year or less. The improved results with medical therapy has led to a reappraisal of the role for CEA in asymptomatic stenosis. The CREST 2 study has been funded by NIH to compare CEA or CAS vs. contemporary, optimal medical therapy. Methods for risk stratification will be discussed during the presentation.

Intracranial atherosclerosis

Will review epidemiology and results of WASID and SAMMPRIS trials

See Table 2 regarding medical treatment protocol used in SAMMPRIS

Conclusion:

Large artery atherosclerosis is an important, medically treatable, cause of ischemic stroke. Strict control of atherosclerotic risk factors is essential. Surgical and endovascular options benefit patients with symptomatic, moderate to severe carotid stenosis, although the benefit is not as robust in women. Any future endovascular or surgical interventions for asymptomatic cervical carotid stenosis or intracranial atherosclerosis will be held to stringent safety standards, given the low stroke rates achieved by contemporary intensive medical therapy. Current clinical trials will examine the merits of carotid revascularization versus contemporary medical therapy in asymptomatic patients (CREST 2). Aggressive medical therapy is also beneficial for symptomatic intracranial atherosclerosis and will serve as a benchmark for any future comparisons of endovascular treatment.

Table 1: Patients at high surgical risk for Carotid Endarterectomy, where Carotid artery Stenting may be considered as an option.

Anatomical factors (surgically inaccessible carotid stenosis)*:*

Obesity

High carotid bifurcation

Severe cervical spine arthritis

Clinical factors:

Clinically significant cardiac disease (Congestive heart failure, abnormal stress test, need for open heart surgery)

Severe lung disease

Contralateral Carotid Occlusion

Contralateral laryngeal nerve palsy

Previous radical neck surgery

Previous radiation to the neck

Recurrent stenosis after carotid endarterectomy

Table 2: Intensive medical therapy for patients with Intracranial atherosclerosis, used in SAMMPRIS.

Aspirin 325 mg daily

Clopidogrel 75 mg daily for the first 90 days after enrolment

Management of primary risk factors:

1. Systolic blood pressure: target < 140 mmHg (< 130 mmHg if diabetic)
2. LDL cholesterol: target less than 70 mg/dl.
3.

Management of secondary risk factors:

1. Diabetes: target Hemoglobin A1C<7%
2. Non-HDL cholesterol: target < 100 mg/dl
3. Smoking cessation
4. Excess weight: body mass index (BMI) < 25 kg/m2 if the enrollment BMI is 25-27 kg/m2 or 10% weight loss if the enrollment BMI is > 27 kg/m2
5. Insufficient exercise: moderate intensity exercise at least 3 times per week for 30 minutes per session.

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