Available online at www.sciencedirect.com
ScienceDirect
The Surgeon, Journal of the Royal Colleges of Surgeons of Edinburgh and Ireland
www.thesurgeon.net

Treatment options for symptomatic carotid stenosis: Timing and approach

*Ashley K. Vavra, Mark K. Eskandari**

Division of Vascular Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

ARTICLE INFO

Article history:
Received 14 February 2014
Received in revised form
4 August 2014
Accepted 2 September 2014
Available online xxx

Keywords:
Carotid endarterectomy
Carotid stenting
Stroke

ABSTRACT

Stroke is a major cause of morbidity and mortality and up to 15–20% of ischemic strokes can be attributed to atherosclerotic internal carotid artery disease. The treatment of carotid artery disease has been the subject of a wealth of literature in the past twenty years since the publication of the landmark randomized controlled trials, the North American Symptomatic Carotid Endarterectomy Trial and the European Carotid Surgery Trial, in the early 1990s. Although these landmark trials have helped establish the current guidelines for treatment of patients with symptomatic carotid artery disease, there have since been major advancements in the medical treatment of cardiovascular disease and there still remains a great deal of controversy regarding the timing and technical approach to carotid revascularization. In particular, there has been a wealth of literature to determine whether carotid endarterectomy or carotid stenting should be used for revascularization and when this revascularization should occur following onset of symptoms. This update offers an overview of the standards for diagnosis and medical treatment of patients with symptomatic carotid artery disease, the indications for surgical revascularization and a review of the most pertinent literature as it pertains to the more controversial issues of technical approach and timing of surgical revascularization following onset of symptoms in patients with carotid artery disease.

Introduction

Symptomatic carotid disease can manifest as either a transient ischemic attack (TIA) or stroke (CVA). Although patients may present with either, it is important to note that TIA can be a harbinger of CVA. The exact incidence of TIA prior to CVA can be difficult to determine since symptoms may not always be recognized or reported by patients, but it is estimated that approximately 15% of CVA are preceded by TIA.[1] In fact, a population study of 1707 patients evaluated for TIA in the emergency room in northern California found that 5% of these patients subsequently had a CVA within 2 days and an additional 11% had a CVA within 90 days.[2] CVA is then associated with a dramatic increase in morbidity and mortality. Stroke is not only the 4th leading cause of death in the US but it is a major cause of serious long-term disability.[3] Between 2007 and 2010, 2.8% of Americans over the age of 20, or an

* *Corresponding author*. Division of Vascular Surgery, Northwestern University Feinberg School of Medicine, 676 N. St. Clair, Suite 650, Chicago, IL 60611, USA.
E-mail addresses: JGoldste@nmh.org, meskanda@nmh.org (M.K. Eskandari).
http://dx.doi.org/10.1016/j.surge.2014.09.001

Please cite this article in press as: Vavra AK, Eskandari MK, Treatment options for symptomatic carotid stenosis: Timing and approach, The Surgeon (2014), http://dx.doi.org/10.1016/j.surge.2014.09.001

estimated 6.8 million, had a stroke and an approximately 87% of these are ischemic.[3,4] Of the ischemic strokes, approximately 10–20% are secondary to underlying carotid artery disease with the vast majority secondary to atherosclerosis.

The diagnosis of symptomatic carotid stenosis entails a combination of imaging of the carotid arteries and the brain. When patients present with localizing neurologic findings in the distribution of the carotid artery, the first step involves imaging of the brain to confirm the diagnosis of ischemic CVA and rule out alternative etiologies, primarily intracranial hemorrhage. Once the diagnosis of TIA or CVA in the distribution of the carotid artery has been established, evaluation for significant carotid stenosis is a standard part of the tests used to determine underlying etiology. Traditionally, carotid angiography was the gold standard for the diagnosis of carotid stenosis. However, current first line investigation involves noninvasive modalities to determine the degree of carotid stenosis. Options include duplex ultrasonography, CT angiography (CTA) or MR angiography (MRA) of the neck. Each modality has advantages and disadvantages with regard to sensitivity and specificity for determining degree of stenosis and also whether additional diagnostic information can be ascertained to guide therapy.

Once the diagnosis has been established, non-surgical modification of atherosclerotic risk factors for secondary prevention is standard. Modification of risk factors includes lifestyle changes such as smoking cessation and weight loss and control of hyperglycemia and hypertension, although strict blood pressure control in the setting of acute stroke may be contraindicated.[5] However, with regard to specific medications utilized for secondary prevention from stroke, perhaps the most benefit has been seen with antiplatelet therapy and statins. The risk reduction associated with antiplatelet therapy has been shown to be as high as 25% ($p < 0.001$)[6] and the current American Heart Association/American Stroke Associated (AHA/ASA) Stroke guidelines recommend the use of aspirin, clopidogrel monotherapy or combination of aspirin and dipyrimadole for secondary prevention of CVA.[7] There have also been multiple randomized control trials (RCTs) that have demonstrated the benefit of statins in reducing the risk of stroke.[8,9] The effects of statins are based on the reduction in LDL[10] as well as demonstrated stabilization and regression of carotid plaques.[11] The benefits of statins in reduction of general cardiovascular event risk is significant enough that the new American Heart Association/American College of Cardiologists joint recommendations for the treatment of blood cholesterol have expanded the criteria for use of statins to any patient with clinical evidence of cardiovascular disease, regardless of cholesterol level.[12] Risk reduction with current recommended best medical therapy (BMT) has improved significantly enough in the years since the major randomized controlled trials comparing BMT alone with BMT plus revascularization that some authors advocate medical therapy alone for symptomatic patients with carotid artery stenosis who are at relatively low risk for recurrent CVA.[13] At the very least, there is some evidence to support that institution of BMT significantly reduces the risk of recurrent stroke in the acute period.[14] Ultimately, what is important to recognize, however is that BMT as described in the original landmark trials comparing CEA plus BMT vs. BMT alone did not incorporate the most recent evidence based recommendations, including the wide use of statins. Therefore, there has been some debate regarding the threshold at which carotid revascularization should be utilized in symptomatic patients.

Data supporting carotid endarterectomy for symptomatic carotid stenosis

Most trials have used outcomes of stroke, MI and death to compare BMT alone with BMT plus carotid revascularization. The two landmark randomized controlled trials that compared BMT alone with BMT plus carotid endarterectomy (CEA) were the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST).[15–17] Both of these trials included patients with angiographic documentation of moderate (50–69%) to severe (70–99%) carotid stenosis and TIA or CVA within 6 months of enrollment and randomized them to BMT alone or BMT plus CEA. If the difference in methods for determining the degree of stenosis between the European and North American studies is normalized, then the conclusions of the two trials correlated. In patients with severe degree of stenosis (>70% NASCET/>80% ECST), there is a clear benefit of CEA in reduction of overall risk of stroke and death with an absolute risk reduction of 16.5% ($p < 0.001$) and 11.6% ($p = 0.001$) for NASCET and ECST, respectively.[15,16] However, some authors argue that the BMT used in these trials is outdated and doesn't reflect the true reduction in CVA risk seen with medical therapy alone. Factors such as the small proportion of lipid lowering medication used, the unavailability of medications such as statins and the use of goal SBP of <160 is inconsistent with current standard of medical care and resulted in a risk of CVA with medical therapy alone that is higher than that observed with todays BMT. The data from NASCET, ECST and subsequent trials have also shown that CEA may not be the best treatment option for symptomatic carotid stenosis in every patient, particularly in patients with moderate stenosis, women, and in patients who are high surgical risk.

In a follow-up evaluation of the NASCET trial data, the risk reduction of CEA was 6.5% ($p = 0.045$) compared to BMT alone in patients with moderate stenosis (50–69%) and there was no benefit in patients with <50% stenosis.[17] In women, because of the robust benefit of CEA in patients with >70% stenosis, CEA still conferred a benefit with an absolute risk reduction similar to that of men (15.1% vs. 17.3%); however, CEA did not significantly reduce CVA risk in women with moderate stenosis of 50–69% as compared to BMT alone. This observation has been substantiated in subsequent pooled analysis of NASCET and ECST data and a separate analysis of patients from both the NASCET and Aspirin and Carotid Endarterectomy trial.[18–20] In addition to gender, high surgical risk (e.g. patients with contralateral carotid occlusion and significant cardiac morbidity) may temper the benefit of CEA. Patients with angina or recent MI or uncontrolled risk factors such as hypertension or diabetes were specifically excluded from NASCET and ECST and some physicians have argued that the outcomes were skewed in favor of better operative candidates in these trials. As an alternative, carotid artery angioplasty

Please cite this article in press as: Vavra AK, Eskandari MK, Treatment options for symptomatic carotid stenosis: Timing and approach, The Surgeon (2014), http://dx.doi.org/10.1016/j.surge.2014.09.001