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Chapter 8

Management of Atherosclerotic Carotid Artery Stenosis

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/57156

1. Introduction

Ischemic stroke is a leading cause of morbidity and mortality worldwide. Common etiologies of ischemic stroke include cardioembolic events, intracranial arterial stenosis, extracranial large vessel dissection (spontaneous and traumatic), genetic or familial causes such as Moya-Moya Disease and fibromuscular dysplasia, and carotid artery stenosis. The latter is responsible for a significant percentage of ischemic strokes due to carotid atherosclerotic disease and will be the focus of this chapter. Diagnosis is often made based on physical exam by the primary care physician and routine ultrasonic or radiographic screening. Detection of carotid artery stenosis typically results in the eventual referral to a general vascular surgeon or a cerebrovascular neurosurgeon when revascularization is indicated for intervention. Selecting candidates for medical treatment or revascularization is guided by data obtained from excellently performed trials including the *North American Symptomatic Carotid Endarterectomy Trial (NASCET)* and the *Asymtomatic Carotid Artery Stenosis (ACAS) Trial*. Treatment depends upon the severity of carotid stenosis and the absence or presence of stroke symptoms. Medical management, carotid endarterectomy, and carotid artery stenting with angioplasty, each have important roles in the appropriate treatment of carotid stenosis. It is the surgeon's responsibility to assess the patient's history, physical exam findings, imaging studies, and risk factors, to make appropriate recommendations on the best treatment for the patient at hand. The purpose of this chapter is to review the management of atherosclerotic carotid artery disease based on available data in the literature and to provide information useful in daily practice.

2. Epidemiology

Approximately 750,000 persons in the United States alone experience an ischemic stroke each year [1]. Stroke care expense for the United States healthcare system was 74 billion dollars

based on 2010 economic data and with the aging American population and higher incidence of obesity and diabetes in young adults, this cost to the American economy will increase [2]. An interesting analysis was published demonstrating that approximately 120 million neurons (equivalent to 714 kilometers or 444 miles of myelinated fibers) are lost each hour after a large arterial occlusion, thereby accelerating brain aging by 3.6 years per hour of ischemia time [3]. This neuronal loss often translates into permanent and devastating neurological sequelae.

It has been estimated that 20-30% of ischemic strokes result from extracranial carotid artery stenosis secondary to atherosclerotic disease [4,5]. Atherosclerosis is a chronic progressive process associated with modifiable risk factors that promote chronic inflammatory events within the arterial wall. Progression of atherosclerotic plaque formation causes ischemic stroke generally by one of two mechanisms: either a flow-limiting stenosis of the arterial lumen resulting in cerebral hypoperfusion typically in the watershed territories or more commonly, thromboembolic events from ruptured atherosclerotic plaque. Until one of these events causes a stroke, carotid stenosis remains asymptomatic and often goes undetected.

The prevalence of carotid stenosis can vary widely with geographic location due to cultural, genetic, and socioeconomic differences. The acquired nature of atherosclerotic disease implies that several of the risk factors that contribute to its development can be modified by individual changes in lifestyle, diet, and medical management.

3. Risk factors

Important modifiable risk factors for developing carotid atherosclerotic disease include smoking, hypertension, dyslipidemia and poor glycemic control in diabetic patients. Smoking is strongly associated with development of carotid atherosclerotic disease whereby comparing age-matched non-smokers, former smokers and current smokers, the prevalence of clinically significant carotid stenosis (>50%) was seen in 4.4%, 7.3% and 9.5% ($P<0.0001$), respectively. Treatment of hypertension has been associated with reduced risk of developing carotid stenosis and stroke. For every 20mmHg increase in systolic blood pressure the odds ratio of developing moderate carotid stenosis is 2.11. Additionally, every 10mg/dL increase in serum cholesterol level was associated with an odds ratio of 1.10 for developing hemodynamically significant carotid stenosis. Strict control of postprandial glucose levels in diabetic patients has been associated with a reduction of carotid intimal media thickness and may also help to reduce the incidence of stroke from carotid stenosis [6].

4. Histopathology of atherosclerotic disease

It has been well established that carotid stenosis tends to occur at the bifurcation, which corresponds to vascular shear stresses as determined by *in vivo* measurements and *in vitro* flow models. The healthy artery is composed of three distinct layers, the tunica intima, tunica media and tunica adventitia, as seen from the lumen to the outer vessel wall. The tunica intima is

http://dx.doi.org/10.5772/57156

composed of a luminal endothelial layer consisting of an internal elastic lamina and a fibrocollagenous tissue layer, the latter two of which are thrombogenic. This tissue layer is covered externally by the tunica media consisting of smooth muscle cells followed by a fibrocollagenous layer composed of the external elastic lamina and an external fibrous serosa layer, which composes the tunica adventitia layer. Carotid stenosis is thought to form as a result of intimal endothelial injury by mechanical hemodynamic shear stresses and metabolic and inflammatory processes. The plaque material often contains macrophages, inflammatory cells, calcium, lipid and cholesterol deposits, thought to be formed as part of the healing process after endothelial injury [1].

After disruption of the arterial endothelial lining, expression of inflammatory cell adhesion markers such as VCAM-1, ICAM and other receptors are upregulated [1,7]. Additionally, platelets adhere to the disrupted endothelium after balloon angioplasty and they degranulate, thereby releasing various cytokines and growth factors including transforming growth factor beta (TGF-β), epidermal growth factor (EGF) and platelet derived growth factor (PDGF) [1,8]. These result in migration and proliferation of the vascular smooth muscle cells of the tunica media to form a neointimal layer in an attempt to heal the disrupted endothelium. This neointima becomes more permeable to inflammatory cells as degranulated platelets adhere and remodel the site of the injured intima [1,9,10]. T-cells, monocytes and lipid laden macrophages are seen in these plaques as they become more chronic, and calcium is often deposited during this process in an attempt to stabilize the plaque. Plaques with less calcification tend to be more vulnerable to rupture or thrombosis, indicating that the deposition of calcium appears to be protective and helps to stabilize the plaque by encasing the inflammatory materials, rather than leaving them exposed for further exacerbation of the inflammatory process [1,11].

The proliferation of smooth muscle cells is accompanied by an increase in matrix metalloproteinases (MMPs) such as MMP-2 and MMP-9, which help to remodel the vessel by dilating the stenotic segment, thereby initially compensating for the loss of intimal diameter by the early plaque. However, with progression of the plaque thickness, the vessel eventually can no longer dilate further to compensate once the plaque occupies about 40-50% of the luminal diameter, and the lumen becomes progressively more narrowed [1].

Vascular stenosis alone does not appear to correlate well with predicting which asymptomatic plaques will result in cerebrovascular symptoms, and therefore additional information about the plaque characteristics are important to assess the vulnerability of the plaque to progress and become symptomatic. Factors which appear to be important in identifying vulnerable plaques include echolucency of the plaque on high resolution B-mode ultrasound, absence of calcification, presence of intraplaque hemorrhage, surface irregularity, fibrous cap thickness, plaque volume and presence and location of a necrotic core [12].

5. Presentation and radiographic evaluation

The history alone can often give a great clue to the underlying cause of the carotid stenosis, once identified. Atherosclerotic disease is the most common cause of carotid stenosis, and is

more prevalent in older patients. In patients with a history of head and neck cancer and exposure to radiation therapy, intimal hyperplasia and other radiation changes would be the most likely underlying cause of the stenosis, and are typically more difficult to treat compared with atherosclerotic lesions [13]. Patients involved in a recent trauma or neck manipulation may have an arterial dissection that can lead to significant arterial stenosis or occlusion [14]. All of these causes could present with or without symptoms, and although the likelihood of symptoms may be more prevalent in higher degrees of stenosis, it is important to correlate the clinical history and presentation with the radiographic findings when evaluating carotid stenosis, as this will help to drive the decisions for conservative or invasive treatment of lesions identified. Currently, the US Preventive Services Task Force recommends against screening for carotid stenosis in the general asymptomatic population [15].

Several clinical trials have been performed to evaluate the patient populations who will benefit from various treatment options, including medical management, surgical intervention with carotid endarterectomy (CEA) or carotid angioplasty with or without stent placement (CAS), and also with or without distal embolic protection devices for endovascular treatments.

One publication from the Netherlands reviewed four major population based studies for a meta-analysis to determine the prevalence of moderate (50-70%) and severe (>70%) carotid stenosis in men and women at various ages [16]. The investigators determined that the prevalence of asymptomatic moderate carotid stenosis ranged from 0.2% (95% CI, 0.0% to 0.4%) in men aged <50 years to 7.5% (5.2% to 10.5%) in men aged ≥80 years, and severe carotid stenosis ranged from 0.1% (0.0% to 0.3%) in men aged <50 years to 3.1% (1.7% to 5.3%) in men aged ≥80 years. For women, the prevalence of asymptomatic moderate carotid stenosis ranged from 0% (0% to 0.2%) in those aged<50 years to 5.0% (3.1% to 7.5%) in women aged ≥80 years, while severe asymptomatic carotid stenosis for women ranged from 0% (0.0% to 0.2%) to 0.9% (0.3% to 2.4%), between these age groups. Although this data helps to understand the prevalence of this condition, it can only be applied to this particular population that was studied.

Traditionally, patients who presented with stroke or TIA symptoms would undergo diagnostic catheter angiography for the diagnosis of carotid stenosis. With the advent of current non-invasive vascular imaging since the 1980's such as carotid duplex ultrasound, MRA and CTA, the most common presentation of carotid stenosis is an incidental finding of asymptomatic stenosis noted on one of these imaging studies which could be performed for a variety of reasons other than for stroke or TIA, including screening imaging studies performed to follow up clinical exam findings such as auscultation of a carotid bruit. The sensitivity and specificity of auscultation of a carotid bruit when used to evaluate for carotid stenosis are extremely poor. One study compared the sensitivity and specificity of detecting carotid or vertebral stenosis with duplex ultrasound evaluation compared with the gold standard catheter angiogram and also reviewed the presence or absence of a cervical bruit on examination. This study showed that the location and estimated degree of stenosis was accurately identified in 97% of carotid and 90% of vertebral stenosis cases with duplex ultrasound compared with catheter angiography, but the presence of a bruit on exam would only correctly diagnose 27.6% of patients with confirmed hemodynamically significant stenosis, and was falsely positive in 22.6% of

http://dx.doi.org/10.5772/57156

patients with confirmed normal vasculature, making the positive and negative predictive correlation of a cervical bruit auscultated on physical exam extremely unreliable [17].

CTA and MRA imaging modalities can often have a greater than 95% sensitivity and specificity for detecting hemodynamically significant vascular stenosis when compared with diagnostic catheter angiography as the gold standard imaging modality [18]. These non-invasive imaging studies have shown to be of benefit in screening for and following stability or progression of vascular stenosis, but it should be noted that in evaluating the accuracy of each of these imaging modalities and comparing with that of digital subtraction angiography (DSA) using an *in vitro* stenosis model, Smith et al found that the CTA and MRA studies tended to underestimate the stenosis whereas the DSA tended to overestimate the stenosis when evaluating the >70% stenosis model, while there was no significant difference between these imaging studies in the estimated stenosis when evaluating the <70% stenosis model [19].

6. Treatment options

The medical management of carotid stenosis has revolved around anti-inflammatory and anti-platelet agents as the drugs of choice. Marquardt et al studied the UK population and documented the frequency of ipsilateral ischemic stroke in the setting of asymptomatic carotid stenosis ≥50% [20]. It was reported that with adequate medical management, the risk was 0.34% for any ipsilateral non-disabling stroke, 0.0% for severe disabling stroke, and 1.78% for ipsilateral TIA. These results would support best medical management for all asymptomatic carotid stenosis, irrespective of the degree of stenosis. Aspirin is known to have anti-inflammatory properties by irreversible blockade of the cyclooxygenase (COX)-1 and COX-2 pathways of arachidonic acid metabolism. Carotid fibrous plaque formation and remodeling are influenced by several factors including MMPs secreted by leukocytes in the intima which remodel the extracellular matrix, and this results in thrombosis with vulnerable plaques in which the fibrous cap has become significantly thinned and embolic events resulting in TIA and stroke may ensue [1]. The Clopidogrel and Aspirin for the Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial evaluated the use of aspirin alone vs aspirin with clopidogrel in symptomatic carotid stenosis >50% and found that combination therapy reduced the frequency of asymptomatic microembolization as detected by transcranial doppler ultrasound more effectively than aspirin alone [21].

Several major trials evaluating asymptomatic carotid stenosis include the Veterans Administration Trial (VA, 1993 [22]), the Asymptomatic Carotid Surgery Trial (ACST, 1994 [23]) and the Asymptomatic Carotid Artery Stenosis Trial (ACAS, 1995 [24]). The VA trial looked at medical management alone with aspirin 650mg po BID versus combined medical management with the same aspirin dose and with CEA for asymptomatic carotid stenosis of 50% or greater in 444 men in the VA medical system. This study failed to show any statistically significant differences in clinical outcome between these two groups [22]. The ACST group evaluated the timing of CEA for patients with asymptomatic carotid stenosis of 60% or greater. Patients were treated with best medical management and the treatment group received CEA as soon as

possible. The second group only received CEA if symptoms developed while on medical therapy. A total of 3120 patients were enrolled and this study failed to show any statistically significant differences in long term clinical outcome between groups [23]. In 1995, the ACAS trial was published which reviewed the results of 1662 asymptomatic patients with >60% carotid stenosis. Patients were randomized into two groups, the first consisting of medical therapy alone with aspirin 325mg daily and the second group treated with medical therapy and CEA within 2 weeks of randomization [24]. This trial found a reduced 5-year stroke risk from 11.0% in the medical arm to 5.1% in the surgical arm with a 3% perioperative morbidity and mortality.

Catheter based diagnostic cerebral angiography remains the gold standard imaging modality for diagnosing and measuring carotid stenosis. The risk of stroke for asymptomatic patients is 2-3% annually and 12% in symptomatic stroke patients [20,25]. Clinical trials have demonstrated measurable differences in the treatment strategy for symptomatic versus asymptomatic carotid stenosis. A majority of data advocates best medical management for asymptomatic carotid stenosis because of the very low incidence of ipsilateral stroke, regardless of the degree of stenosis. According to the ACAS and NASCET trial results, revascularization is recommended for symptomatic male patients with ≥50% ipsilateral cervical internal carotid artery stenosis, while revascularization is not recommended for symptomatic female patients until the severity of ipsilateral cervical carotid stenosis reaches ≥70% [26], however, this difference between men and women has remained somewhat controversial and these results have not been consistently reproduced [27]. Currently, carotid endarterectomy continues to be the gold standard for revascularization. If the patient has significant risk factors placing them at a high risk for endarterectomy, then revascularization via carotid angioplasty and stenting is an alternative therapy. Such risk factors typically include: previous ipsilateral carotid endarterectomy, recent myocardial infarction within previous thirty days, contralateral carotid occlusion, radiation to the neck, chronic obstructive pulmonary disease, and previous carotid stent.

Carotid stent placement is offered to patients who have no contraindications to long-term antiplatelet agent use and who are at a high risk for surgery. Distal embolic protection devices are generally used to lower the risk of embolic events from stent placement and balloon angioplasty, but recent recommendations vary; cases where there is a reasonably high potential for distal embolic events during the angioplasty procedure may benefit from distal protection devices [28–32]. Carotid angioplasty alone without stent placement is associated with a very high rate of re-stenosis. The CAVATAS trial examined the treatment of carotid stenosis with angioplasty alone (N=145) versus carotid angioplasty and stent placement (N=50) vs carotid endarterectomy (N=213). This trial showed that carotid endarterectomy resulted in significantly lower rates of carotid re-stenosis >70% 5 years after treatment compared with endovascular therapy (30.7% vs 10.5%). Additionally, in the endovascular treatment group, the patients treated with angioplasty alone had a higher rate of re-stenosis >70% compared with those treated with stent placement (36.2% vs 16.6%) [33]. With the placement of a stent, the in-stent re-stenosis rate has been reported to be as low as 5% after four years [34]. Risk factors that may increase the likelihood of recurrent stenosis after carotid angioplasty, stent or endarterectomy

http://dx.doi.org/10.5772/57156

have been examined and in a report from Skelly et al, these risk factors include prior stroke, transient ischemic attack, amaurosis fugax, and prior neck cancer [35].

Large trials designed to evaluate surgical versus medical treatment for symptomatic carotid stenosis include the Veterans Administration 309 Trial (VA309, 1991 [36]), the European Carotid Surgery Trial (ECST, 1998 [37]), and the North American Symptomatic Carotid Endarterectomy Trial (NASCET, 1998 [26]). VA309 evaluated the results of treating 189 symptomatic patients with >50% carotid stenosis ipsilateral to the symptoms with best medical management or a combined approach of best medical management with CEA. The study found a statistically significant reduction in the stroke risk over 11.9 months for the surgical arm compared to the medical arm (7.7% vs 19.4%, P=0.11) [36]. In 1998, both ECST and NASCET were published. ECST evaluated 3024 patients with some degree of symptomatic carotid stenosis that was determined by varying modality and varying quality vascular imaging studies. The trial randomized 1811 patients to the surgical arm and 1213 patients to the medical arm, and the overall risk of surgery was determined to be about 7%, which did not vary with the degree of stenosis. For symptomatic carotid stenosis (as measured by the ECST method) of greater than 80%, the three-year major stroke or death rate was 14.9% for the surgical arm and 26.5% in the medical arm, revealing a statistically significant benefit for surgery in that group [37]. NASCET evaluated 1108 patients with symptomatic carotid stenosis in the CEA arm and 1118 demographically similar patients in the best medical management arm. The results showed no benefit for surgery below 50% stenosis, some benefit particularly in men with moderate stenosis (50-69%) and clear benefit for surgery with severe stenosis (>70%). The rate of any ipsilateral stroke over five-year follow up for moderate carotid stenosis (50-69%) was 15.7% in the surgical arm and 22.2% in the medical arm (P=0.045), with the immediate perioperative stroke or death risk being reported as 2% [26].

The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) evaluated 2502 symptomatic and asymptomatic carotid stenosis patients who were randomly assigned to CEA or CAS [38]. The study found no significant differences in combined stroke, myocardial infarction and death risk over 4 year follow up between these groups, however, there was a trend toward more myocardial infarctions in the surgical arm (6.8% vs 7.2%, CAS vs CEA, P=0.51) and a statistically significant higher rate of periprocedural stroke in the endovascular arm (6.4% vs 4.7%, CAS vs CEA, P=0.03). A study published in February 2013 evaluated the effect of these perioperative complications on long term survival. According to this trial, having a stroke within the first year resulted in a two-fold lower survival rate (HR=6.6; CI=3.7-12) than those patients who suffered a perioperative myocardial infarction two years after intervention (HR=3.6;CI=2-6.8), but this difference becomes negligible at 5 years (HR=2.7; CI=1.7-4.3 vs HR=2.8; CI=1.8-4.3) [39].

The Carotid and Vertebral Transluminal Angioplasty Study (CAVATAS) examined the treatment of carotid stenosis with carotid endarterectomy (N=213) vs endovascular treatment with angioplasty alone (N=145) or angioplasty and stent placement (N=50). The rate of recurrent stenosis >70% after endovascular therapy for all patients treated with or without stent placement was about 3 times higher than the restenosis rate after endarterectomy after 5 years of follow up (30.7% vs 10.5%, p=<0.0001). However, of the endovascular treated patients,

the occurrence of restenosis >70% in the angioplasty alone group compared to the stent group was more than twice as frequent (36.2% vs 16.6%, p=0.04). Of all patients with >70% restenosis in the first year after treatment with CEA or CAS compared to the patients with <70% restenosis in this same time period, there was a trend toward a higher ipsilateral stroke rate in the greater stenosis group, but this result did not reach clinical significance (9.7% vs 5.4%, p=0.4) [33]. These results suggest that CEA provides the greatest durability of treatment with fewer cases of hemodynamically significant recurrent stenosis compared with stent placement, although stent placement is significantly superior to angioplasty alone for long-term durability. Treated patients should be followed for recurrent stenosis, and although the greater stenosis group did not have a statistically significant increase in the number of ipsilateral stroke events, it would be wise to more closely monitor these patients, be more aggressive with medical management with anti-platelet agents, or even offer repeat treatment for those patients with progressively worsening stenosis during the follow up period.

7. Operative techniques for carotid endarterectomy

Patients with symptomatic carotid stenosis >50% or asymptomatic carotid stenosis >70%, or who had a stroke ipsilateral to the carotid stenosis while on best medical management should be offered a carotid revascularization procedure. CEA remains the gold standard of care for carotid stenosis. It should be considered for those patients who have a low medical risk for general anesthesia, have not had prior radical neck surgery or radiation to the neck and who have a surgically accessible carotid bifurcation.

Because the surgery involves clamping the carotid artery temporarily, some surgeons will decide to place a silicone tubing to shunt the blood and allow continuous carotid flow throughout the operation, however, this can be associated with a higher rate of thromboembolic events and some surgeons will choose to place a shunt in only select cases [40,41]. If the surgeon chooses to selectively shunt only those patients who do not tolerate carotid clamping for the surgery, he or she can decide to perform this surgery either awake under local anesthesia allowing for intra-operative neurological exams or under general anesthesia with neuromonitoring to evaluate for changes in somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) while the carotid artery is clamped. If the surgeon chooses to shunt all carotids, then the routine use of neuromonitoring would not typically be required or justified. Some surgeons will measure stump pressures from the external carotid artery (ECA) after clamping to help determine if the patient will require selective placement of a carotid shunt, however, this has not been shown to be a good predictor of whether a patient will go on to have a stroke from the surgery. The authors here routinely use neuromonitoring for all patients under general anesthesia in order to choose the patients who will require selective shunting.

Pre-operative medical preparation is important, and patients undergoing CEA should be taking an anti-platelet such as aspirin daily. The use of clopidogrel, although not required, would not necessarily prevent the surgeon from performing the CEA, although there is a slightly higher risk of local hematoma for patients taking combination anti-platelet agents. A

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drain is often recommended in selected cases, particularly if the patient is taking both aspirin and clopidogrel at the time of the surgery, and if it is difficult to maintain a dry surgical field at the time of the operation.

The approach to the carotid sheath for the CEA begins with positioning the patient in the supine position on the operating table with the head turned slightly toward the contralateral side and the neck slightly extended for optimum exposure. The planned incision line should be marked with a skin marker along the anterior border of the sternocleidomastoid muscle, which would be approximately parallel to the expected course of the carotid artery, for optimum exposure. The neck should be prepped behind and below the ear from just above the mastoid down to the upper chest, just below the clavicle, and from midline out laterally to the anterolateral border of the trapezius muscle above the shoulder. After proper sterile technique for preparation and draping of the operative field, the skin is incised along the previously marked incision site. The platysma muscle is encountered and split parallel to the muscle fibers, which is also parallel to the incision. The omohyoid muscle is separated as needed for adequate exposure of the common carotid artery (CCA) and at least 2-3cm of the ECA and internal carotid artery (ICA). If additional exposure is required superiorly, the superior aspect of the planned incision should be extended superiorly and posteriorly just below the mastoid, and care should be taken to not injure the hypoglossal nerve at this level during the deeper dissection. Care should be taken to avoid injury to the recurrent laryngeal nerve or the esophagus during the dissection to the carotid sheath. The carotid artery typically resides medially in the carotid sheath, the internal jugular vein typically lies lateral to the carotid artery, and the vagus nerve typically lies deep to both of these structures and between them.

The systolic blood pressure (SBP) is raised prior to placing the clamp, typically to 140-160 mmHg for patients who are normotensive at baseline, to help promote perfusion through collateral circulation. Generally, raising the SBP by about 20% of the baseline should allow for adequate collateral circulation. The carotid artery is then clamped in the following order when the surgeon is ready to perform the endarterectomy, with the ICA being clamped first followed by the CCA (typically with a Fogarty carotid clamp or other atraumatic clamp device), followed by the ECA. If neuromonitoring is used, these signals are also monitored continuously, and changes in the SSEP and or MEP signals that would be consistent with ischemia changes should prompt the surgeon to selectively place a shunt into that carotid artery.

The arteriotomy is performed with a #11 scalpel blade until a pair of Potts scissors can be inserted into the true lumen and the incision can be extended from the CCA to the ICA full thickness through the plaque. Care must be taken to identify the superior thyroid artery origin, especially if there is back-bleeding after performing the arteriotomy, as this may arise very near the carotid bifurcation, unless a temporary clip is applied to this arterial branch. The plaque is then carefully but quickly teased from the endothelial layer of the carotid artery and the plaque is transected as far as possible with the exposure and the carotid artery wall is inspected for loose debris which is carefully removed and irrigated with heparinized saline. The carotid artery is then sutured with 6-0 prolene in simple running fashion, using a minimal full thickness stitch to reapproximate the incised vessel edges without causing additional

stenosis with the suturing. Multiple simple interrupted sutures can also be used, but this tends to be significantly more time consuming and is no more effective than the simple running suture. The use of heparinized saline throughout the procedure and back bleeding from the ECA to flush out any loose particles just prior to placing the last 6-0 prolene suture into the carotid artery is also recommended. The clamps are then removed in the reverse order that they were placed, with the ECA clamp removed first, followed by the CCA clamp, followed lastly by the ICA clamp. There are several standard techniques to close a cervical approach incision, which would typically include a subcutaneous layer of absorbable suture placed in inverted simple interrupted fashion followed by a cosmetic skin edge reapproximation with absorbable running subcuticular sutures, sterile adhesive strips or skin glue.

8. Interventional techniques for carotid angioplasty and stent

Patients who are not candidates for CEA due to high surgical risk factors are defined by Medicare guidelines, and include patients with recurrent stenosis after prior ipsilateral CEA, prior radiation therapy to the neck or previous ablative neck surgery such as radical neck dissection, surgically inaccessible cervical lesion above the C2 level, presence of a CCA lesion below the clavicle, contralateral vocal cord palsy, presence of a tracheostomy stoma, or patients with a contralateral ICA occlusion. Additionally, patients who are medically unstable and high risk for surgery, with COPD or other pulmonary condition which would make removal of the endotracheal tube at the end of the surgery difficult or dangerous for the patient, or recent acute myocardial infection within 30 days would also be considered high surgical risk, and a carotid artery stent procedure could be considered.

All patients receiving angioplasty of the carotid bulb should be prepared with cardiac defibrillator pads pre-procedurally, and atropine should be readily available for immediate injection in the event of severe bradycardia or asystole. Advanced cardiac life support (ACLS) materials should be readily available in the event of a potentially fatal cardiac arrhythmia that could occur as a result of the parasympathetic reflex from carotid bulb stretch during the angioplasty. The operator can choose whether to use distal embolic protection devices, however, there is no general recommendation available from the literature to support the use of distal embolic protection devices for all cases [28–32]. The authors here will routinely use a distal embolic protection filterwire device to allow continuous perfusion while providing a barrier to capture potentially large particulate matter during stent and angioplasty for carotid atherosclerotic disease when it is safe and feasible to place such a device. Additionally, Medicare requires that all carotid stent procedures be performed with distal embolic protection devices, whenever feasible.

The patient should be pre-medicated with anti-platelet agents such as aspirin and clopidogrel, and the authors here use 325mg aspirin and 75mg clopidogrel daily for 7 days prior to a scheduled elective stent placement, or a loading dose of 325mg aspirin and 300mg clopidogrel the day prior to a semi-urgent stent placement, or the day of an emergency stent placement with supplemental abciximab given as a bolus of 0.25mg/kg up to a maximum of 20mg bolus,

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followed by a continuous drip of 0.125mcg/kg/min to a maximum of 10mcg/min for 24h, and then followed by 325mg aspirin and 75mg clopidogrel daily for 3 months before the next follow up angiogram. At the time of the follow up angiogram, if there is no in-stent stenosis or other reason for additional procedures, then the clopidogrel can be stopped, and the patient is continued on low-dose aspirin 81mg daily indefinitely.

One potential complication with stent placement is thromboembolic events that have been found to occur in up to 10% of cases where the patient was found to not have adequate platelet inhibition with the standard anti-platelet therapy described above, and these individuals are described as "non-responders" [42]. It is now known that the incidence of non-responders to clopidogrel is potentially very high, ranging from 5-40% of treated patients, and appears to be more prevalent in the Asian population compared with the Caucasian or African populations. Clopidogrel is a pro-drug that is metabolized by the cytochrome P450 emzyme pathway in the liver into the active thiol metabolite. Factors such as platelet ADP receptor heterogeneity, poor drug absorption, drug-drug interactions, and differences in metabolism of the drug by the cytochrome P450 system, as well as patient non-compliance may all contribute to the variability of drug efficacy between individuals. Variant alleles of the CYP2C19 and CYP2C9 enzymes (CYP2C19 I331V, CYP2C9 R144C and CYP2C9 I359L) have been described to have a reduced conversion rate of the clopidogrel pro-drug into the active thiol metabolite [43]. Alternative anti-platelet agents such as prasugrel (Effient) may be used, as non-responders to clopidogrel typically will respond adequately to prasugrel. Other alternative anti-platelet agents should be evaluated with the most current pharmacological literature. A pharmacy consultation may be needed to find an effective alternative anti-platelet drug for patients who do not respond to a therapeutic level with these medications. It would be wise to test all patients who require elective pre-medication with aspirin and clopidogrel using a P2Y12 activity test before performing the procedure, whenever possible, in order to identify those patients who may be non-responders to the standard therapy.

The patient is placed in the supine position on the angiography table with the femoral artery access site prepared in the usual sterile fashion. Using the modified Seldinger technique, the femoral artery is accessed with a long access catheter typically with at least a 6F inner diameter (ID) to allow room for placement of a distal protection device and the stent device simultaneously, along with any additional 0.014 or 0.018 inch microwires, termed "buddy wires," which may be placed to improve the stability of the guide catheter in the CCA. The guide catheter is positioned in the CCA just proximal to the carotid bifurcation and appropriate digital subtraction angiography (DSA) is performed to optimally visualize the stenosis and the takeoff of the ICA. A 0.014 inch microwire is guided beyond the ICA stenosis using a road map. The distal protection device is deployed over the microwire into a straight segment of the ICA proximal to the petrous segment. Occasionally, the stenosis will be so severe that pre-dilation angioplasty of the stenosis with a balloon that has a low crossing profile, such as a 2.5mm x 30mm Maverick or Mini-Trek balloon, before the placement of the distal protection device or the stent may be required. Cardiovascular instability or arrhythmias are uncommon when inflating a small balloon such as this at the ICA origin. An appropriately sized stent is selected, which is typically about 30-40mm in length to cover the lesion completely and about 1-2mm

greater diameter than the widest measured carotid diameter into which the stent will be deployed, typically at the bifurcation [44]. Because the carotid artery bulb is typically significantly larger than the cervical segment of the ICA, some carotid stents are designed with a tapered diameter, such as 6mm diameter distally and 8mm diameter proximally, to accommodate for this and to prevent the stent from being significantly oversized distally for an appropriately selected diameter for the proximal ICA. The appropriately selected stent is then positioned across the ICA stenosis, taking care to avoid placement of the distal end of the stent at a curved segment of the ICA, as some patients may have a relatively tortuous ICA course. This will help to avoid kinking of the stent or occlusion or dissection of the ICA. After the stent is deployed across the lesion, a DSA run is performed to confirm the location of the stent and to evaluate for residual stenosis. An appropriately selected balloon is then chosen and positioned along the center of the greatest stenosis. At the time of balloon inflation, care should be taken to watch the heart rate and blood pressure, as stretching of the carotid bulb could result in significant bradycardia or asystole. The balloon should be inflated only a few seconds, and should not remain inflated for more than 10-20 seconds during the initial post-stent angioplasty. The balloon may be left inflated longer as long as the patient remains asymptomatic with the occlusion of carotid blood flow, but this should not be done for longer than 1-2 minutes at a time. The distal protection device is then recovered, taking care to avoid inadvertently snagging on the stent tines and potentially dislodging the position of the stent. The femoral arteriotomy access site is then closed and the patient should remain flat with the accessed leg straight for at least 1 hour after placement of an arterial closure device, or for 4-6 hours with a sandbag or clamp to hold pressure on the femoral arteriotomy site if no closure device is used.

9. Conclusions

The NASCET evidence supports the treatment of symptomatic hemodynamically significant carotid artery stenosis of ≥50% by NASCET criteria for men, and ≥70% for women. The only trial that advocates surgical intervention for asymptomatic carotid stenosis is the ACAS trial, and surgical intervention for asymptomatic carotid artery stenosis ≥60% was supported, but other trials would support best medical management because of the very low incidence of ipsilateral stroke from asymptomatic carotid stenosis, regardless of the degree of stenosis. Carotid endarterectomy remains the gold standard treatment for patients who are medically stable enough to tolerate the surgery. Carotid angioplasty without stent placement has a high rate of recurrence of stenosis, and therefore with current devices available, patients in whom endovascular treatment has been chosen for carotid stenosis should be treated with stent placement and should be pre-medicated with anti-platelet agents such as aspirin and clopidogrel, or alternative drugs such as prasugrel in clopidogrel non-responder patients. These medications should be continued for at least 3 months post-procedurally and the low dose (81mg) aspirin should be continued indefinitely.

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