REVIEW ARTICLE

A. Norbash MD.

Carotid Stenting; Clinical Perspectives and Overview of a Novel Developing Clinical Technology

Abstract: Carotid stenting is a technical procedure that can be easily performed, and this has exposes it to the concern of the technique being over-utilized or mis-utilized. There are controversies surrounding the actual technical performance of the procedure, in addition to the ideal patients who should benefit from the clinical procedure. These controversies, compounded by the ongoing evolution of the technical procedure in addition to the evolution of the clinical benefits, have fueled numerous debates between proponents and detractors for the procedure. Compounding the debates between proponents and detractors are the devastating potential complications of inappropriately performing or neglecting to appropriately perform carotid stenting. Such considerations accentuate the significance of judicious technology implementation and appropriate clinical deployment. This discussion will address background, technical considerations, potential complications, and applicability of carotid stenting in clinical practice.

Keywords: stenting, carotid, technique

Introduction

In the early 1990's sporadic cases of carotid stenting were initially reported in selective cases of patients with symptomatic carotid vascular disease including carotid dissection, and in patients with post-radiation fibrosis to the neck including secondary carotid vascular stenosis. Following initial successful demonstration of these proofs-of-principle, stent utilization broadened to also include close-term post-endarterectomy restenosis, ultimately leading to the implementation of carotid stenting as a direct competitor with carotid endarterectomy to primary atherosclerotic disease of the carotid.[1,2] As there has been increased utilization of carotid stenting, it has become clear that numerous and varied specific technical considerations related to carotid stenting could seriously impact on the success and complication profile of the procedure.[3,4] Many such considerations deal with not only preprocedure preparation, such as patient selection and workup, but also to specific intraprocedural choices, such as whether to perform angioplasty routinely pre or post stent placement and whether to use an intraprocedure protection device, and ultimately discussion controversies extend to the post-procedural management of the carotid stent patient. Complex post-procedural questions still remain controversial, such as questions applying to the duration and type of anticoagulation, and the appropriate method for imaging and clinical follow up.

When considering carotid stent placement, it is not only important to consider the short-term and periprocedural complications, it is also important to maintain a view of the longer-term complication profiles. Carotid stent placement can result not only in specific complications arising from embolic etiologies, additional non-thromboembolic complications additionally include stent misplacement, stent migration, reperfusion injury, upstream or downstream stenosis, and in-stent restenosis.

Department of Radiology
Boston University Medical Center
Room 2504
88 East Newton Street
Boston, MA 02118

These technical considerations should help clinically explain the procedure in terms of the cost-to-benefit ratio for each specific patient, in addition to the larger population basis for consideration of stent placement, especially when compared with competing conservative medical and surgical therapies.

As addition experience has been gained, many questions have similarly and specifically arisen regarding carotid protection procedures, although a clear conclusion regarding the cost-to-benefit ratio has yet to be achieved.

As the technology for stent placement has continued to improve, carotid stent trials have been organized, and are ongoing, with few large-scale or "definitive" trials having been statistically completed to date. Among carotid stent trials completed to date have been trials affording direct comparison of variations of carotid stent placement with historical endarterectomy cohorts, small-scale competitive trials comparing stenting and endarterectomy, and the numerous sequential comparisons to various trials with their closest competing prior trials.[1,3-5] This has been a rather disorganized process, and the largest scale direct-randomized trial permitting endovascular comparison against surgery is currently underway and far from being completed. Part of the ongoing carotid stenting technology assessment has resulted in a desire to accurately benchmark expected and reasonable carotid stent performance and risk rates, in order to understand what complication rates are acceptable for each group of patients, vis-à-vis traditional surgical endarterectomy and conservative medical therapy.

As the therapies continue to advance there is additional expansion of the carotid stent considerations beyond the current popularly debated indications, such as performing acute carotid stent placement at the time of stroke therapy in patients with carotid artery disease, and as the boundaries of the technical procedure are pushed into further challenging territories, considering intracranial stent placement for fixed atherosclerotic disease inaccessible to traditional extracranial carotid endarterectomy. As the evolution of cerebrovascular stenting has continued, among the more unexpected lateral developments has been the acceptance of using intracranial stenting as a scaffold for adjunctive coiling in treating ruptured and unruptured intracranial aneurysm patients.

Background

Stent-treatment of carotid vascular disease resulted as an increase in both stenting of other similar sized vessels in the body, and the increased acceptance for surgical therapy of carotid vascular disease when compared with conservative medical treatment.[3] Increased acceptance of surgical endarterectomy for the treatment of carotid disease for both symptomatic and asymptomatic patients with stenoses justifying treatment resulted from clinically significant trials included the ACAS and NASCET trials, which increased the confidence of referring physicians to surgical therapy for both their symptomatic and asymptomatic carotid stenosis patients. In the early 1990's, additional and dramatic development in stent technology permitted accurate placement of not only balloon mounted stents, but also self expanding stents in numerous locations within the body. Although many of these were off-label applications, nevertheless medium sized vessel stenting became not only feasible, but progressively safer.

Initially, balloon mounted stents were utilized for carotid stenting, although clear efforts were made to place these stents above the angle of the mandible, so that the stents could not be crushed post-procedurally by external soft-tissue manipulation or pressure. As self-expanding stents were placed on assemblies permitting cervical carotid placement from an inguinal Seldinger approach, these became the tools of choice, insofar as they allow the carotid to remain patent, while avoiding the crushability which disadvantaged balloon mounted stents by comparison.

Technical Consideration

Preprocedural considerations

Patients having radiation exposure to the neck for the treatment of cervical chain lymph nodes would occasionally present several years following their initial treatment with symptoms of carotid vascular disease. Unfortunately, the prior radiation made surgical exploration of the neck, and surgical exposure of the carotid, very challenging as a direct result of radiation having caused scarring and fibrosis of the soft tissues of the neck, which resulting in a "woody" neck, and posing considerable challenges where tissue plane dissection of the neck was attempted. This set of problems created a discrepant complication rates when compared with otherwise non-irradiated patients' surgical experiences. Therefore, these post-irradiation carotid disease patients became relatively easy treatment opportunities for carotid stenting. Similarly, in patients who presented with symptomatic carotid dissections, the complex and many-layered dissecting planes of these dissections in the carotid artery wall prevented simple surgical repair. Similarly, due to the challenges encountered with traditional surgical therapy, many of these patients were early candidates for endovascular stent treatment.

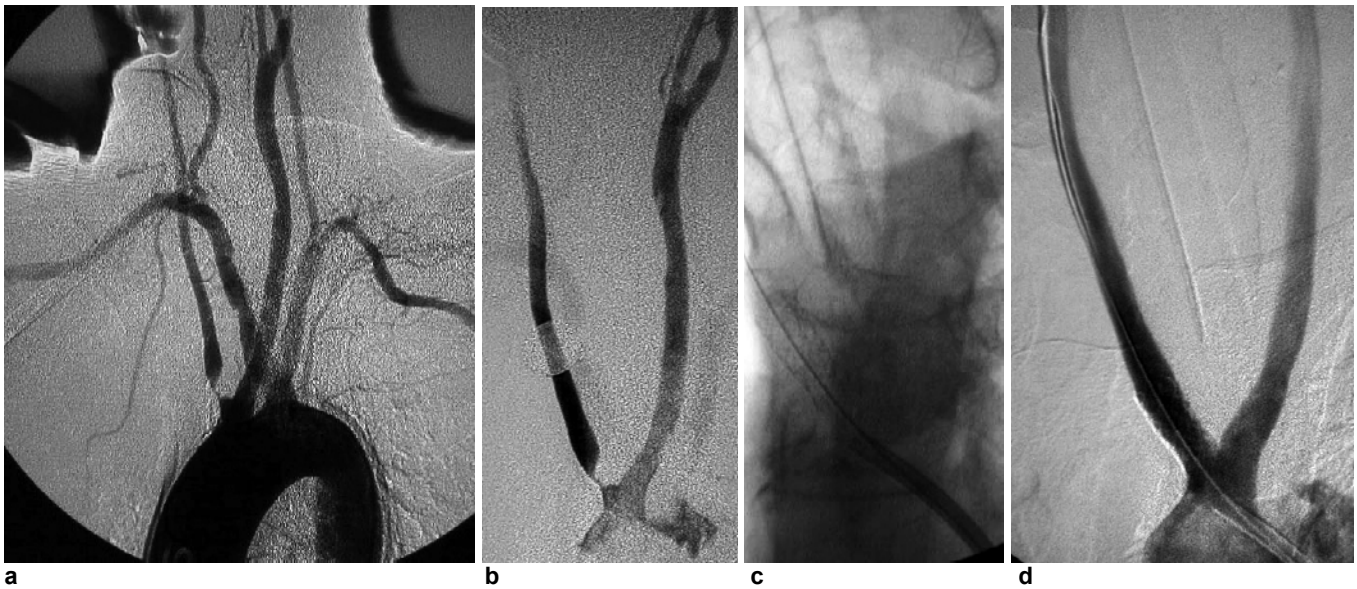

Figure 1:

a) In this patient with right hemispheric crescendo TIAs an arch aortogram demonstrates an unusual variant aortic arch, in which the right and left common carotid arteries arise from a single point of origin proximal to an unusual common origin of the bilateral subclavian arteries. There is a high grade stenosis of the right common carotid artery origin, directly above the shared common carotid artery origin site.

b) Magnified view of the shared common carotid artery origins more clearly demonstrates the high-grade stenosis of the caudal aspect of the right common carotid artery immediately at its origin. Incidental note is made of an approximately 50% right internal carotid artery stenosis seen at the top of the image.

c) An intraprocedural snapshot demonstrates a fluoroscopically expanded stent, guidewire, and stent placement assembly. Due to the low position of the guiding catheter, and the relatively large amount of respiratory motion preventing utilization of roadmapping for guidance, the stent was placed between puffs of manually injected contrast material which permitted visualization of the stenosis site, and placed with corroborating reference to superimposed radioopaque landmarks.

d) The post –procedure angiogram following stent placement demonstrates reduction of the high-grade common carotid artery stenosis to a normal baseline

As part of selecting the optimal patients, it became apparent that long-segment, and extremely irregular eccentric stenoses ran a significant risk of being dislodged during endovascular manipulations, resulting in such non-thrombic fragments being sent downstream as an embolic mass. Similarly, there should be concern when endovascularly manipulating a vessel which has diffuse atherosclerosis within it, as every manipulation of a guiding wire, catheter, protection device, carotid stent assembly, or angioplasty balloon runs the risk of dislodging and embolizing plaque. Therefore, in order to minimize the complication profile while gaining experience, smooth single-wall or concentric hourglass-shaped stenosis, are often considered ideal morphologic lesions for endovascular treatment.

Over time, there has been a considerable evolution in the work up and imaging preparation of patients who are candidates for carotid stenting. In the past, as part of the work up of these patients, initial efforts included identification of patency of the Circle of Willis, in addition to separate and pre with procedure arteriographic initial assessment. As the procedures have become more commonplace over the course of the past 10 years, patients are often considered candidates for endovascular therapy based on their endovascular preference, a screening ultrasound, with demonstration of a critical stenosis and/or relevant symptomatology.

When discrepant findings are identified on CT angiography, MR angiography, or ultrasound examination, catheter angiography clearly becomes the technological referee.

Preoperative work up includes a comprehensive history and physical examination, which often also serves as the anesthesiology clearance, since in some practices general anesthesia is often utilized for carotid stenting. If there are any unsuspected or abnormal neurologically based physical finding or post-TIA symptom, cross-sectional evaluation of the brain is urged to ascertain the absence of a large, bland infarct, which if missed runs the risk of potentially fatal hemorrhagic transformation. Arbitrarily, based on size criteria, many interventionalists are resistant to treat a carotid stenosis in a patient with a demonstrable ischemic infarct over 2cm in diameter, for fear that the improved inflow will cause a potentially life-threatening hematoma. Arbitrarily, once 6-8 weeks have elapsed since the patient's infarct, many proceduralists feel that the infarct has matured, and depending on the presentation it may be appropriate to proceed with stent placement.

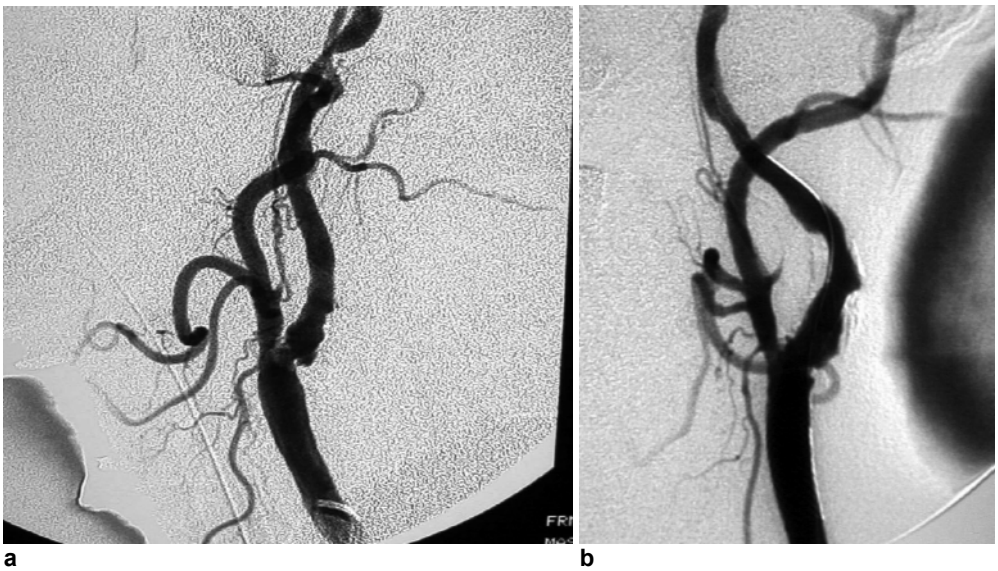

Figure 2: This patient is a 73 year old male presenting with monocular TIA's who has failed medical therapy. Typically, patients with this extensive type of atherosclerosis where there is one dominant lesion superimposed on a vessel with considerable diffuse disease would not be considered ideal candidates for endovascular manipulation and would be sent for endarterectomy. This patient has an isolated carotid circulation, and was referred for endovascular therapy following an unsuccessful endarterectomy attempt; the exposed carotid artery was so atherosclerotic at surgery, that a "soft-spot" could not be located which would permit cross-clamping of the carotid artery.

a **b**

a) Carotid angiography demonstrates an irregular stenosis at the origin of the internal carotid artery. In complex lesions such as this, the circumferential "shoulders" of the lesion can obscure the central channel, and suggest the increased value of three-dimensional angiography for assessing such lesions and patients.

b) Following stent placement and "touch-up" angioplasty, the control angiogram, demonstrates a reduction of the dominant stenosis to less than 15%, although the remainder of the atherosclerotic vessel remains unchanged in appearance.

As far as pharmacological preparation is concerned, many proceduralists place the patient on an anti-platelet agent between 48 and 72 hours prior to the procedure. It has been our practice to use a 300mg plavix load 48 hours prior to the procedure, with a 75mg daily plavix dose continued until the time of the procedure, and beyond the procedure for an approximately six-week period. Most proceduralists do not find it necessary to combine aspirin and plavix in the preprocedure stage, and many proceduralists utilize plavix until the six to eight-week postprocedure mark, at which time they switch the plavix to qDay adult aspirin.

Intraprocedural

There are a number of variables that can be considered under the category of intraprocedural techniques, such as the desire for general anesthesia or simple sedation, whether one should be concerned with hyper-reactive sinus syndrome and how to accommodate for that concern, and what specific types of stents and stent placement devices one chooses to utilize. Naturally, this discussion also extends to the potential or perceived added value of carotid protection devices.

It is often a challenging task for the proceduralist to identify a focal stenosis and treat it endovascularly. For the proceduralist to additionally layer on the responsibility for sedation is often more than can be wisely and appropriately managed. As such, it is often helpful to have an additional medical specialist available who is specifically responsible for the sedation of the patient, in the event that general anesthesia is not sought or in the event that an anesthesiologist is not present.

Similarly, where equipment is concerned, it is often valuable to have road mapping capability and a biplane neuroangiographic unit. In the event that these are available, if there is an unfortunate embolic complication which is clinically significant and angiographically visualized, additional emergent intervention such as thrombolysis becomes more straightforward and may be considered. Similarly, the ability to perform 3D catheter-angiography provides a dramatic difference in terms of morphologic analysis of the carotid artery.

Insofar as catheters and sheaths are concerned, long 7 French sheaths which have recently become popularized permit much smaller inguinal punctures that were previously possible with larger diameter short sheaths, and continue to allow ready access to the stenosis and superstenotic segments for protection and stenting.

A comprehensive diagnostic angiogram is ordinarily initially performed, with delineation of the bilateral cervical carotid arteries, and the carotid distribution intracranial supply. The intention is to demonstrate concordance of the angiographic findings with the underlying signs, symptoms, or history leading to the study, while simultaneously assessing the contralateral circulation. At this point, if there is determination of a sufficient level of stenosis to justify stent placement, systemic anticoagulation with heparin is performed and the formal stenting procedure is initiated.

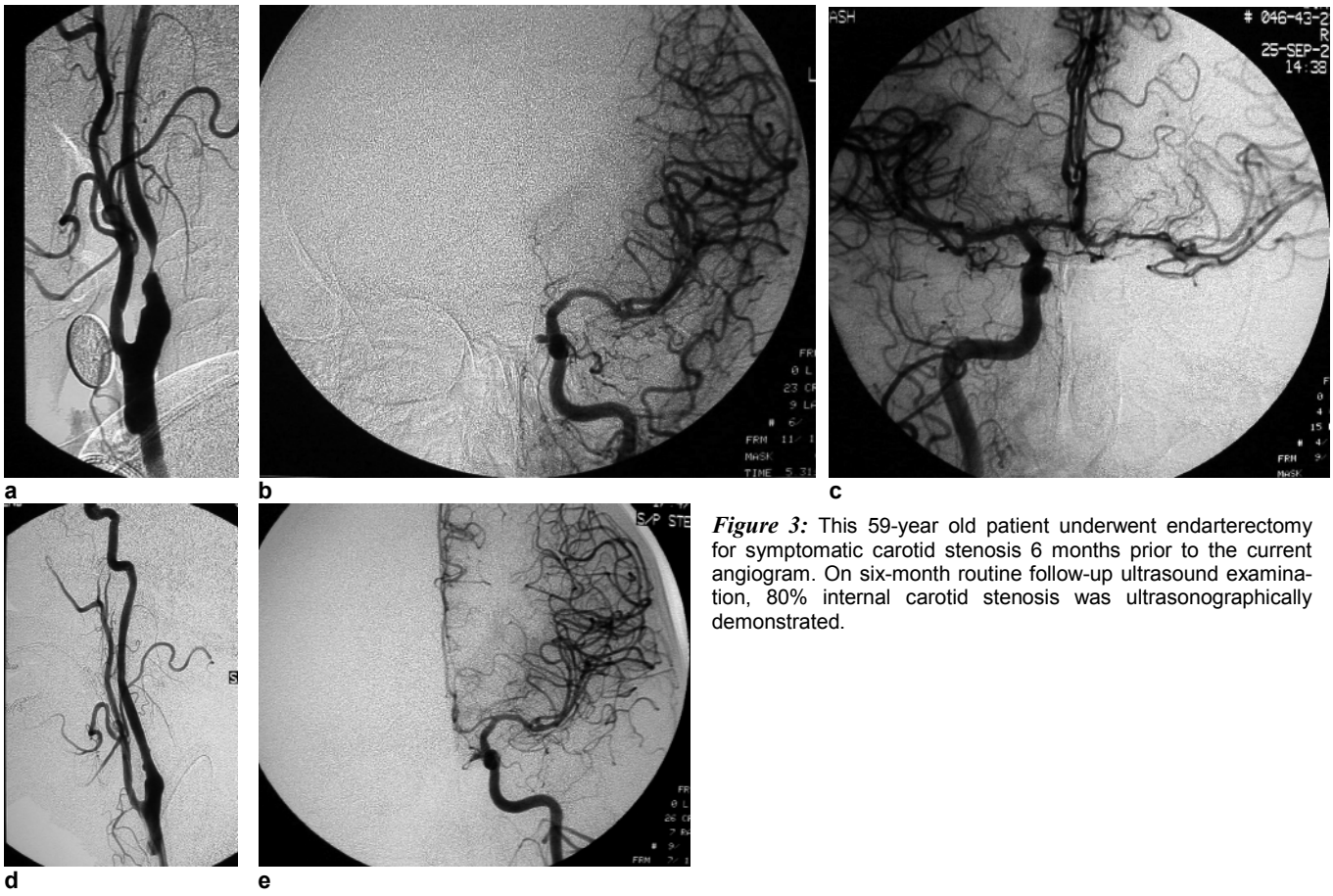

Figure 3: This 59-year old patient underwent endarterectomy for symptomatic carotid stenosis 6 months prior to the current angiogram. On six-month routine follow-up ultrasound examination, 80% internal carotid stenosis was ultrasonographically demonstrated.

a) Selective left common carotid angiography shows an endarterectomy defect with expansion of the angiographic lumen beyond the margins of the native vessel at the carotid bulb, in addition to a high grade stenosis superior to the endarterectomy defect. The actual site of the dominant stenosis may correspond with the site of cross clamping.

b) The cranial A-P image of the left common carotid injection demonstrates intracranial filling, with incidental note of a superior hypophyseal aneurysm (white arrow) and no antegrade opacification of the A1 segment.

c) Injection of the right common carotid circulation results in cross-filling of not only the left anterior cerebral artery circulation, but also filling of the left middle cerebral distribution of the anterior circulation, suggesting the lack of sufficient baseline inflow from the compromised left internal carotid circulation.

d) A carotid stent is now bridging the previously demonstrated stenosis, with less than 10% focal stenosis demonstrated at the site of stent placement, and subtle irregularities likely representing small subintimal collections of contrast material where the stenosis has been distracted.

e) Intracranial filling post carotid stent placement is now remarkable for antegrade opacification of the left anterior cerebral artery distribution, suggesting a change in the amount of available circulation from the left common carotid distribution. Such changes in circulatory filling may hypothetically expose the patient to an increased risk of "perfusion-breakthrough bleeding", although this has not been reliably documented or validated.

This determination is made to based on meticulous and specific measurements of the stenosis, the distal reference vessel beyond diseased carotid, and there should be careful, consistent, systematic, and documented application of measurement criteria in all patients undergoing carotid stenting.

There is technical controversy regarding the need for an initial angioplasty prior to stent placement, which is also known as a "preangioplasty." The controversy is centered on 2 different points of view; one point of view states that any manipulation of the plaque burden runs the risk of embolization, and therefore minimizing the number of interventions at the plaque, such as avoiding preangioplasty unless absolutely necessary to place the stent assembly, decreases the risk of downstream emboli. The second perspective states that preangioplasty is necessary to open the therapeutic channel, and to decrease the risk of plaque dislodgement with the stent assembly, which is a large diameter assembly. Neither these perspectives is supported by current directed examination; neither of these arguments have been substantiated in the literature.

Where stent sizing is concerned, significant problems are encountered if and when a stent is under sized, or when the selected stent is too short for the diseased segment of the carotid.

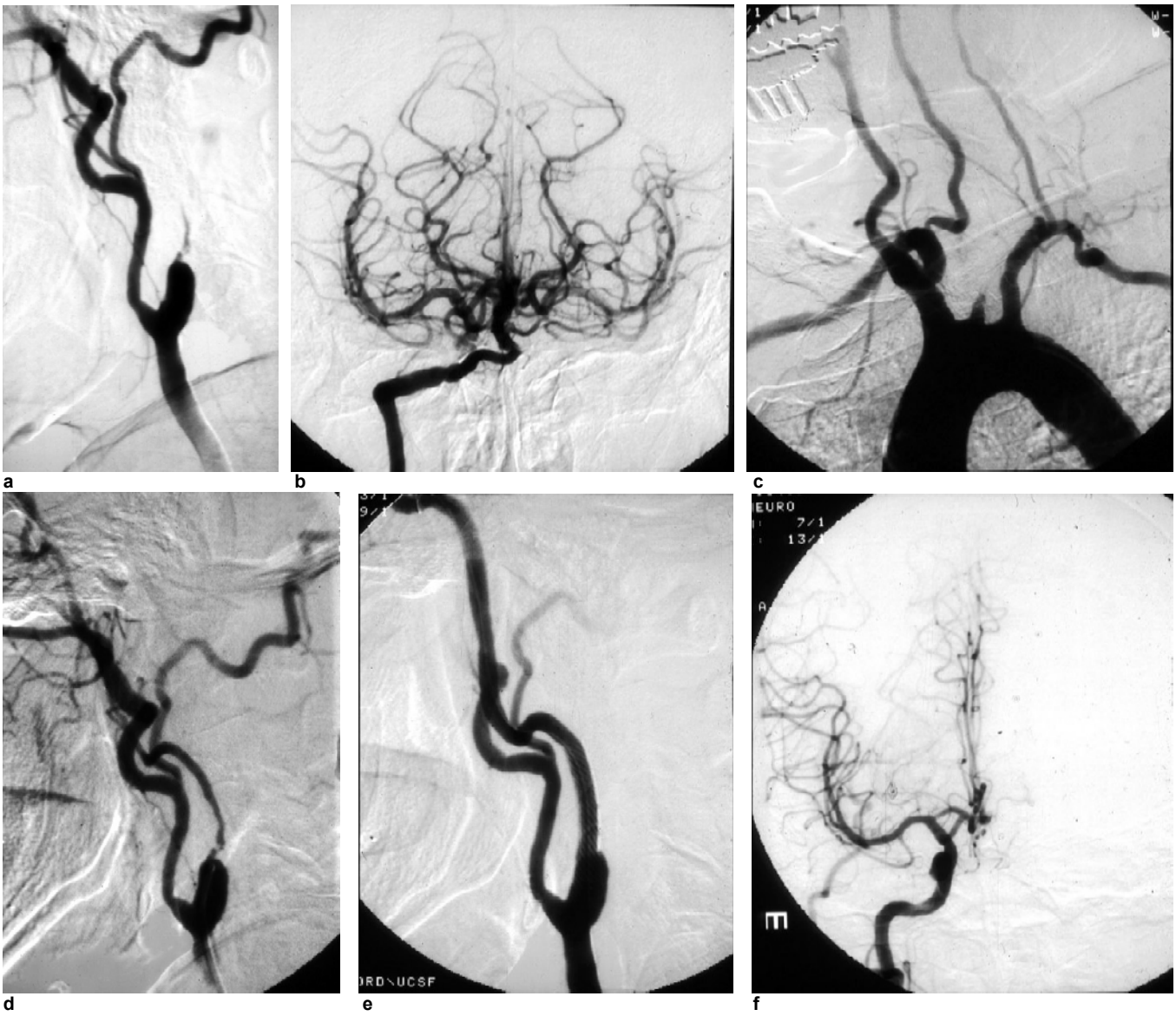

Figure 4: This 37 year old male presents with intermittent left sided weakness.
a) There is only slight filling of the right internal carotid artery above its origin, with an appearance of a residually filling narrowed channel superior to the dilated portion of the native internal carotid artery "stump" raising the possibility an acute occlusion.
b) Injection of the right vertebral artery demonstrates brisk opacification of bilateral anterior and posterior circulations, suggesting possible single artery supply to both distributions with a lack of any significant redundant circulation.
c) This projection of the aortic arch demonstrates occlusion of the left common carotid artery at the arch origin of the left common carotid artery.
d) Following gentle placement of a micro-catheter in the right internal carotid artery, there was demonstration of cranial-directed contrast filling with 0.2 cc of contrast material on a blank roadmap. This was done to ascertain that there was not a potential clot "torpedo" filling defect lying within the cervical carotid artery that could embolize intracranially with a more brisk or forceful injection. Once the lack of a filling defect was demonstrated, and the absence of an internal carotid clot was confidently demonstrated with a gentle micro-catheter hand injection. a brisk hand-injected contrast injection now demonstrates cervical internal carotid artery filling to the high-cervical level.
e) Control angiography demonstrates that a stent has now been placed in the high grade stenosis following pre and touch up angioplasties, with brisk opacification of the remaining cervical internal carotid artery.
f) There is new antegrade transcarotid intracranial filling in the right anterior distribution, without any distal secondary stenoses identified.

Therefore, it is suggested to most early practitioners that rather than attempt to place the shortest possible stent which is precisely sized to the vessel diameter, the selected stent should be utilized which is at least 2mm in diameter larger than the greatest diameter of the vessel being treated, and that the stent length be chosen to be at least 1.5 times as long as the segment of vessel which is intended for treatment. Once the stent is place, there is much controversy regarding whether a "touch-up angioplasty" is necessary. Similar to the preangioplasty controversy, practitioners believe that a "touch up angioplasty" permits a decrease in the stenotic percentage to the closest potential approximation of vascular diameter to the

normal baseline, with detractors stating that memory alloy materials, of which most stents are now composed, will permit gradual remodeling and this makes "touch up angioplasty" unnecessary. Even if there is general avoidance of "touch-up angioplasty," it should be considered if the residual stenosis, once the stent is placed, is greater than 50%.

Regarding hyperreactive sinus syndrome, some practitioners routinely administer atropine at the time of any carotid angioplasty or stent placement. Many practitioners avoid the administration of atropine, although they do have the appropriate dosage of atropine drawn up and ready for immediate injection. In addition to having atropine available for administration, many practitioners also use surface pacemaker pads applied to the patient's chest, so that in the event that there is profound bradycardia, the surface pacemaker can be utilized for temporary support until a more durable solution is formulated. Although transvenous temporary pacemakers in patients with persistent bradycardia are extremely helpful, prophylactic placement of these transvenous pacemakers is considered overly aggressive, since they do have a complication profile which may be unacceptable in these patients.[6]

In a patient who has not had antiplatelet therapy as a preparation for stent placement, most practitioners are cognizant of the concern over stent-generated distal emboli, and therefore will start the patients on a 2B-3A inhibitor such as integrilin, with initiation of plavix loading immediately post procedure. With this approach it is possible to taper the integrilin at 24-48 hours, and continue the plavix.

There is much controversy regarding carotid protection. There are 2 broad categories of carotid protection devices, these include umbrella or filter protection devices which capture emboli as they move downstream from the stent site, and balloon or redirecting protection devices, which arrest the flow of particular material distal to the stent for aspiration and export. [4,7-10] Either protection device necessitates the addition manipulation of the carotid artery, which tends not to be a healthy native carotid artery if it is undergoing treatment. Therefore, there are risks of plaque dislodgement and of carotid dissection related to the utilization of each of the two families of devices.

Although series have demonstrated comparable effectiveness of protected carotid stenting when compared to endarterectomy, direct comparison with and without carotid protection within a randomized trial has yet to be performed.[11,12] Therefore, although many practitioners intuitively, or based on limited numbers of patients, feel that the protected approach to carotid stenting allows safer performance of the carotid stent procedure, many proceduralists similarly feel that this is an unnecessary danger, and may actually expose the patient to much greater risk by dint of the additional manipulations which are necessitated in the diseased vessel. It is important to keep in mind that the added fractional complexity of protection system utilization has yet to be documented reliably, as has the added fractional protection "value" of protected stenting.

Post-Procedural

Following carotid stenting, the patient is converted to an antiplatelet agent pre-discharge. As previously mentioned, in the event that the patient presented without adequate antiplatelet administration preprocedurally, intravenous Integrilin is bolused following confident angiographic demonstration of the carotid lesion, is administered intravenously during the angiogram at least 15 minutes prior to stent placement, and is continuously administered for another 24-48 hours following stent placement. Once the stent procedure has been completed, oral plavix is initiated to overlap with integrilin or another 2B-3A inhibitor administration for 24-48 hours prior to discontinuation of the integrilin. Most of our carotid stent procedures are performed with percutaneous closure devices due to the high risk of continued bleeding postprocedurally once antiplatelet agents have been administered, and it is important to check the inguinal puncture site prior to discharge, in addition to doing a predischarge neurologic examination and comparison with baseline. At follow up, the patient is maintained on plavix 4 between 6 and 8 weeks, at which time a conversion is done to a full-dose adult aspirin. The aspirin is maintained on an ongoing basis in patients with carotid disease. Annual comparison studies are done utilizing ultrasound.

Complications

There are numerous cardiovascular, neurologic, and systemic complications that can be seen with carotid stenting, and it is important to understand the scenarios in which additional efforts may be beneficial to the patient, and when heroic or misdirected efforts may actually expose the patient to greater dangers.

One set of complications deal with the intra and periprocedural embolic neurologic complications. These may arise from the stent lattice if there has been inadequate anticoagulation and antiplatelet administration. The need for adequate antiplatelet therapy preprocedurally in elective patients cannot be emphasized too highly. As regards remote presentation of embolic complications following carotid manipulation, it is possible that during instrumentation of the carotid a dissection flap if

created which leads to emboli creation, and seeding, and which may present remote to the time of carotid stenting, and such a dissection spot may be in the immediate environment of the stent, or considerably inferior to or superior to the stent location depending on what manipulations took place within the treatment vessel. There are a number of serious intraprocedural technical complications which should be considered; include stent misplacement, among the most problematic of which is when a stent is dramatically undersized and travels within the carotid artery.

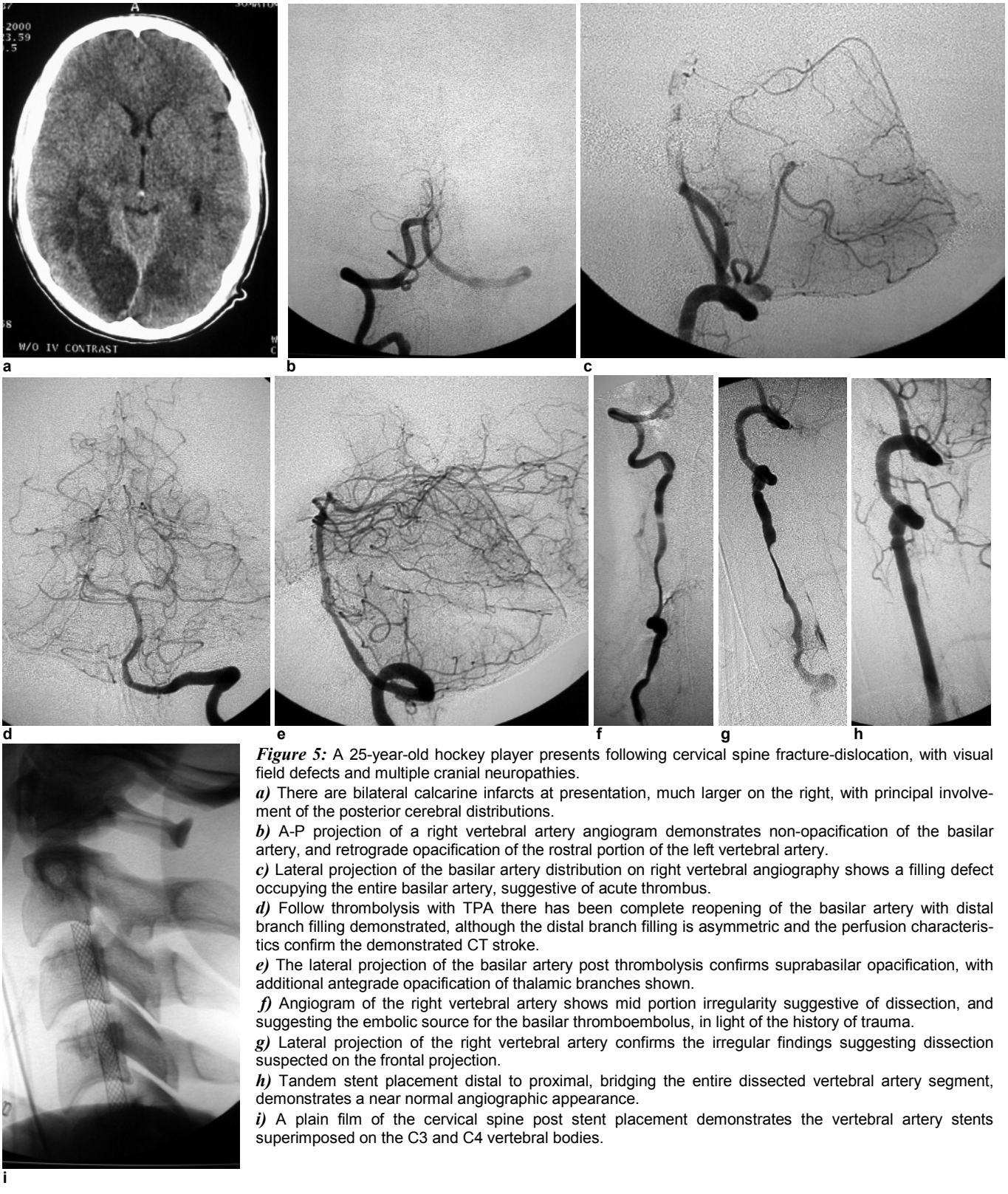

Figure 5: A 25-year-old hockey player presents following cervical spine fracture-dislocation, with visual field defects and multiple cranial neuropathies.

a) There are bilateral calcarine infarcts at presentation, much larger on the right, with principal involvement of the posterior cerebral distributions.

b) A-P projection of a right vertebral artery angiogram demonstrates non-opacification of the basilar artery, and retrograde opacification of the rostral portion of the left vertebral artery.

c) Lateral projection of the basilar artery distribution on right vertebral angiography shows a filling defect occupying the entire basilar artery, suggestive of acute thrombus.

d) Follow thrombolysis with TPA there has been complete reopening of the basilar artery with distal branch filling demonstrated, although the distal branch filling is asymmetric and the perfusion characteristics confirm the demonstrated CT stroke.

e) The lateral projection of the basilar artery post thrombolysis confirms suprabasilar opacification, with additional antegrade opacification of thalamic branches shown.

f) Angiogram of the right vertebral artery shows mid portion irregularity suggestive of dissection, and suggesting the embolic source for the basilar thromboembolus, in light of the history of trauma.

g) Lateral projection of the right vertebral artery confirms the irregular findings suggesting dissection suspected on the frontal projection.

h) Tandem stent placement distal to proximal, bridging the entire dissected vertebral artery segment, demonstrates a near normal angiographic appearance.

i) A plain film of the cervical spine post stent placement demonstrates the vertebral artery stents superimposed on the C3 and C4 vertebral bodies.

Stent migration has been described not only intraprocedurally, but also remote to the time of the procedure. As such, it is critically important to size the stent appropriately using sizing means at the disposal of the operator, based on angiographic equipment; many experienced practitioners will oversize a stent by 2 millimeters over the greatest diameter of the target vessel.

There are very few reported cases of embolic complications arising at the time of stent placement, which were prospectively or retrospectively considered as technically and clinically benefitted by directed intracranial thrombolytic therapy and by pursuing the clot intracranially for directed and aggressive microcatheter-based treatment. It may well be that many of the embolic complications are in fact atherosclerotic emboli, rather than thrombotic emboli. Additioally, it is not often that emboli lodge in the M1 segment, where subselective catheterization may afford a therapeutic benefit, and additionally it may be that rapid administration of a 2B-3A inhibitor is equally as beneficial as microcatheter-directed treatment of a far-distal embolus.

In addition to embolic complications, procedural complications also include reperfusion injury. In these patients, it may be that the chronic response to hypoperfusion has been maximal vasodilation through autoregulation, which has resulted in such a longstanding arteriolar and arterial-bed dilation that the counteracting ability to vasoconstrict has been blunted or temporarily lost in the hypoperfused circulation. The result is that this maximal and chronic vasodilatation may be extremely dangerous if the reflex protective vasoconstrictive reflex is blunted or temporarily absent. With the absence of the counteracting reflex, once the stenosis in the carotid is opened, this increases the pressure head to the carotid circulation, permitting leakage in the arterial and capillary bed, as a result of over-pressurization. Reperfusion may be a clinical concern in cases where there is aberrant or non-native physiologic inflow, such as a cerebral hemisphere supplied by a small posterior communicating artery, in whom there is to be re-establishment of a dominant flow from the native carotid circulation following treatment. Such examples include patients with unilateral occlusions with high-grade contralateral stenoses, where the stenotic vessel is supplying the majority of both hemispheres. In such patients, it may be beneficial to decrease the blood pressure immediately post stenting for a period of 24 to 48 hours although this is an empiric approach considered by some interventionalists, although it has yet to be reproducibly substantiated. Surprisingly, often reperfusion bleeding also occurs in patients in whom one would not necessarily suspect a reperfusion bleed, and another consideration is that it is also possible that many reperfusion bleeds in fact are hemorrhagic transformations of otherwise bland strokes which were not necessarily found on preprocedural screening.

Even though reperfusion bleeds are rare, they are high-profile events since the fatality rate and complication profile of reperfusion bleeding is extremely high, and therefore, any time a patient has accelerated onset of a headache or new development of advancing neurologic symptoms post carotid stenting, it is critical to perform a cross sectional evaluation of their brain at the earliest opportunity in the event that a reperfusion bleed can be identified and addressed.

As far as arterial post-stent restenosis is concerned, the inflammatory, atherosclerotic and scarring pathways ensuing from intervention may result in stenosis within a stent, also known as “in-stent” restenosis, although the procedural manipulations in addition to altered vascular compliance and physiology do raise the question of potential upstream and downstream stent-related stenoses. The in-stent restenosis rate in the carotids has not been reported to be any higher than that elsewhere in the body for similarly sized vessels. Similarly, upstream and downstream stenoses may not necessarily be a reflection of altered vascular physiology secondary to the stent placement, and may in fact represent a progression of the normal atherosclerotic pathophysiology in the host vessel. Regardless, treatment methods for in-stent restenosis include intravascular transient brachytherapy, in addition to in-stent restenting or telescopic stenting, balloon angioplasty, and the utilization of cutting balloons. Cutting balloons may be successful in coronary applications, although for natural reasons regarding the discrepant complications between an embolizing coronary or embolizing carotid iatrogenic-complication dissection there may be apprehension about using this technology in the carotid distribution. Similarly, intracarotid brachytherapy may be intellectually appealing, although most practitioners would likely recommend initial simple balloon angioplasty of in-stent restenosis, since for the time being it has demonstrated considerable success with renal in-stent restenoses, prior to embarking on more elaborate treatment schemes such as brachytherapy or cutting balloons.

Technology Assessment

In order to focus on technology assessment, it is necessary to initially look at the complication rates that justified endarterectomy as a therapeutic alternative in the first place, when compared with conservative medical management. In the NASCET trial, the

surgical endarterectomy benefit included a 6.5% five year risk reduction in patients who underwent endarterectomy, when compared with those who underwent conservative treatment, in the event that their stenosis was greater than 70% in transverse diameter, and symptomatic. Specifically, the stroke rate was 15.7% in the operated patients vs. 22.2% in the medically treated patients, leading the authors to conclude that a durable benefit was gained in symptomatic individuals with a greater than 70% stenosis.

The asymptomatic carotid artery stenosis trial (ACAS) demonstrated that in patients with a greater than 60% stenosis in whom symptoms were absent, there was only a 5.8% reduction in stroke risk at 5 years. Therefore, it is important to consider the comparative decrease in the stroke rate, when assessing whether a certain treatment risk is justified; clearly the acceptable complication profile differs dramatically when comparing a low life-expectancy individual with multiple crescendo TIAs and comorbidities, with an otherwise healthy and a asymptomatic high life-expectancy patient with the same percentage stenosis. When examining endarterectomy trials, there are 3 particular end points which are commonly considered as significant; stroke rate, death rate, and rate of periprocedural myocardial infarction. In the Birmingham Alabama group of 415 carotid endarterectomies, the high-risk patients had a 7.1% risk rate, and the non high-risk patients had a 2.8% complication rate. In the Cleveland endarterectomy cohort of 3,061 patients, similarly in high-risk patients the risk of stroke, death, and MI was 7.4% and 2.9% for the non high-risk patients. When comparing existing carotid stent trial data with endarterectomy, the Sapphire trial was performed using the angio-guard carotid protection device and the precise stent, and resulted in a complication rate of 5.8%, which was less than half that of the endarterectomy cohort which had a 12.6% complication rate. The CAFE trial, comprising 212 patients who had percusurge carotid protection with stent placement, had a 6% stroke risk rate.

When comparing these figures, and keeping in mind the carotid endarterectomy success rate, it is important to consider targets of 8% an upper limit of acceptable risk rate in high-risk patients, and in non high-risk patients, the risk of carotid stenting should be no greater than 3% if the practitioner intends to compete with endarterectomy risk rates.

Current Developments

There are at least two sets of current development which exist independent of the ongoing materials, technology and delivery-device evolutions of the actual stents. These three current developments include the convoluted development of the various protection devices, and the advancement and application of stenting to newer areas such as combined thrombolytic therapy in patients with acute stroke, or further intracranial advancement as part of vascular "repaving."

Protection Devices

There are two families of "protection devices" which are used for carotid stenting that can be thought of as filter devices, and as redirecting devices. Redirecting devices are capturing devices, which can also be thought of as "filters" or "umbrella" devices and which are deployed downstream to the stent location in order to capture emboli before they reach the brain. Redirecting devices act to redirect the blood flow out of the internal carotid artery in order to create a safe location for the redirected emboli generated from the stent location. Examples of the filter devices include the Neuronet device, the Accunet, and the Filterwire. Examples of redirecting devices include the Percusurge device, and the Parodi device. To date, no controlled trials have been performed comparing protected and unprotected stenting, although there is data demonstrating the favorable complication profile for protected and unprotected stenting when compared with endarterectomy.

Combined Procedures

In patients who have generated thromboemboli from critical stenoses or dissections, or in vessels with coexisting significant atherosclerotic disease, it may be necessary to treat the carotid artery at the same sitting as performing emergency transarterial Thrombolysis in order to either treat the culprit lesion, or to allow passage of the Thrombolysis catheter. In these patients, it is critically important to address anticoagulation intraprocedurally with heparin and 2B-3A inhibitors, since few of these patients have been on a sufficient dose of antiplatelets to protect them from acute stent thrombosis. An important consideration in these patients deals with the inability to easily reverse platelet inhibition; as an example, if a patient has a large completed hemispheric infarct and has received robust antiplatelet therapy, in the event that there is a hemorrhagic transformation of the stroke it may be catastrophic. In patients with large and completed strokes, therefore, the recommendation is to consider simple carotid angioplasty rather than immediate stent placement, and in the event that the patient's condition stabilizes, delayed stent placement can then be considered.

Intracranial Stenting

Intracranial stenting is being explored in the setting of recurrent TIAs and thromboemblic propagation, which may be seen more commonly in the posterior circulation than in the anterior circulation. Due to the tortuosity of the intracranial circulation, and the lack of the outer elastic lamina, the complication profile from dissection is relatively high, and therefore these patients need to be especially considered as regards their therapeutic options. Much additional experience with intracranial stenting has been gained recently with intracranial stenting for stent-assisted intracranial aneurysm coiling, although the direct translation to the treatment of atherosclerotic disease is limited, since the aneurysm-treating stents have very low diametric pressure when compared with atherosclerosis-treating stents, which are designed to exert greater radial pressure, on average. Due to the low relative number of fixed similarly-located intracranial stenoses, it may be challenging to compile sufficient trial-based information to understand the fractional advantages of primary stent treatment of intracranial fixed stenoses when compared with balloon angioplasty, or with aggressive medical treatment.

Conclusions

Carotid stenting is easy to perform technically, and although the complication profile includes stroke and death, the incidence of complications tends to be sufficiently low to encourage over-utilization and mis-utilization of the technology by both experienced and novice physicians. The dramatic growth and controversial implementation of carotid stenting in treatment pathways belies the poorly managed strategy for implementation by organized medicine, and even by individual physician practices in many instances. In order to responsibly deploy the technology it is necessary to not only understand the optimal triage, intraprocedural, and post-procedure techniques, it is also important to understand what the permissible range of complications can be for the particular population of patients treated. In spite of the controversies surrounding carotid stenting, the ease and economy of the procedure, in the context of the rapidly expanding pool of treated patients and the dramatic development pathway, suggest that carotid stenting will be a primary, if not the dominant, treatment method for high-grade carotid stenoses for the foreseeable future.

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