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# Angioplasty and stenting of the carotid artery

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**C**urrently, carotid angioplasty and stenting is useful in patients who are not good candidates for carotid endarterectomy because of anatomically inaccessible lesions, restenosis following previous endarterectomy, radiation-induced stenosis, and other high-risk conditions. The practice of carotid endarterectomy is supported by large prospective, randomized, controlled trials that demonstrate that it is an effective therapy for symptomatic carotid stenosis if the complication rate of the procedure is <6%, and that it is effective for asymptomatic stenosis if the complication rate is <3%. Because carotid endarterectomy is a relatively simple and low-risk surgical procedure, it will be difficult to prove that carotid artery angioplasty and stenting is as safe and effective as carotid endarterectomy. Recently published series of carotid angioplasty and stenting report stroke and death rates ranging from 2% to 8%.

## Justification for invasive treatment of carotid stenosis

It will not be easy for carotid angioplasty and stenting to supplant carotid endarterectomy. Carotid endarterectomy is a relatively simple surgical procedure and the artery is generally easily accessible. The complication rate is very low with experienced surgeons, and the procedure can be done under local anesthesia. The practice of carotid endarterectomy is supported by multiple prospective randomized controlled trials. In these multicenter trials, bias was minimized and end points were well defined. The results of these trials are published in the most important medical journals.

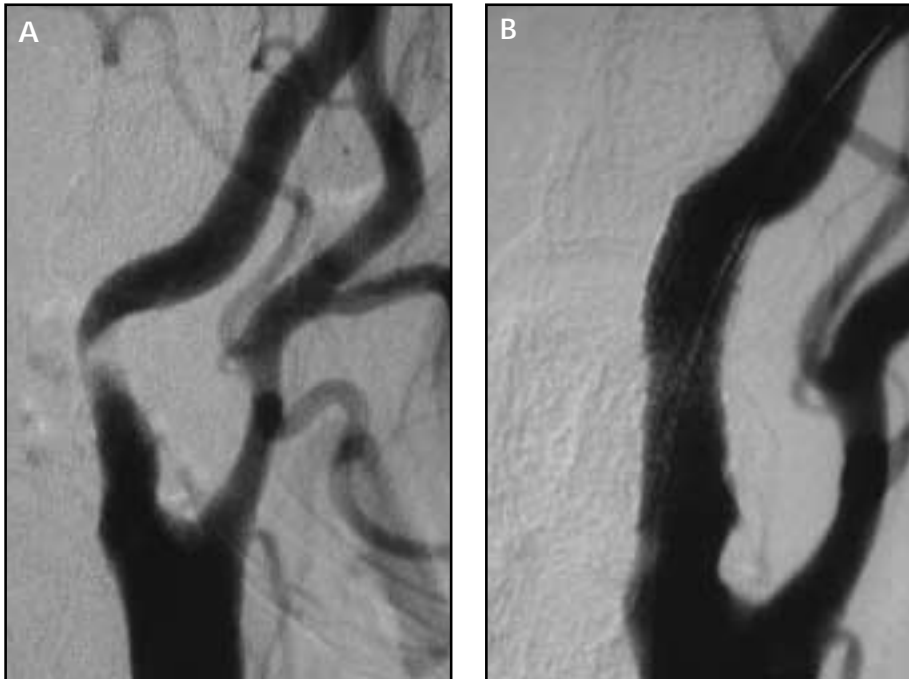
The North American Symptomatic Carotid Endarterectomy Trial (NASCET) study initially demonstrated a benefit with surgery for symptomatic patients with stenosis >70% and a 5.8% risk of perioperative stroke and death.<sup>1</sup> A moderate reduction of stroke risk was later shown by NASCET for endarterectomy in patients with stenosis of 50% to 69%.<sup>2</sup> The European Carotid Surgery Trial (ECST) demonstrated a benefit with

surgery for symptomatic patients with a stenosis >70% and if the complication rate is <7%.<sup>3</sup> The Asymptomatic Carotid Atherosclerosis Study (ACAS) trial reported a benefit for asymptomatic patients with >60% stenosis and a complication rate <3%.<sup>4</sup>

## Literature regarding carotid angioplasty and stenting

The data supporting the use of angioplasty and stenting of carotid artery stenosis is not nearly so compelling as that supporting carotid endarterectomy. No trials comparing carotid angioplasty and stenting with carotid endarterectomy have been published. A number of large case series of carotid angioplasty and stenting have been published. Theron et al<sup>5</sup> of France reported 69 cases complicated by 2 embolic events (3%) and no deaths. Diethrich et al<sup>6</sup> of the Arizona Heart Institute reported 110 cases with a 6.4% periprocedural stroke rate and a 2% periprocedural death rate. The University of Alabama group reported the results of 271 cases, with a 7% rate of neurological events (4% permanent) and 1 death

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**FIGURE 1.** (A) Symptomatic atherosclerotic stenosis of the internal carotid artery origin. (B) Successful stenting with Smart Stent (Cordis Endovascular, Miami Lakes, FL).

(retroperitoneal hemorrhage).<sup>7</sup> Wholey<sup>8</sup> has reported experience with carotid angioplasty and stenting in 315 cases with a 3.8% rate of perioperative stroke and death. Henry et al<sup>9</sup> subsequently reported the results of 315 carotid angioplasty and stent procedures with a 3.9% risk of stroke, including 1 death. The Washington Hospital Center reported their experience with 140 cases, which were complicated by a 6.4% periprocedural stroke rate and 1 death.<sup>10</sup>

There are problems with the published data regarding carotid angioplasty and stenting. The data comes from uncontrolled trials with variable patient selection; the data is often collected retrospectively; the collection of data is not blinded or otherwise unbiased; end-points are not well defined; and follow-up is incomplete. The data is published in subspecialty journals, obscure journals, or non-peer-reviewed journals.

Wholey et al<sup>11</sup> have reported the results of a survey of institutions throughout the world performing carotid artery angioplasty and stent-

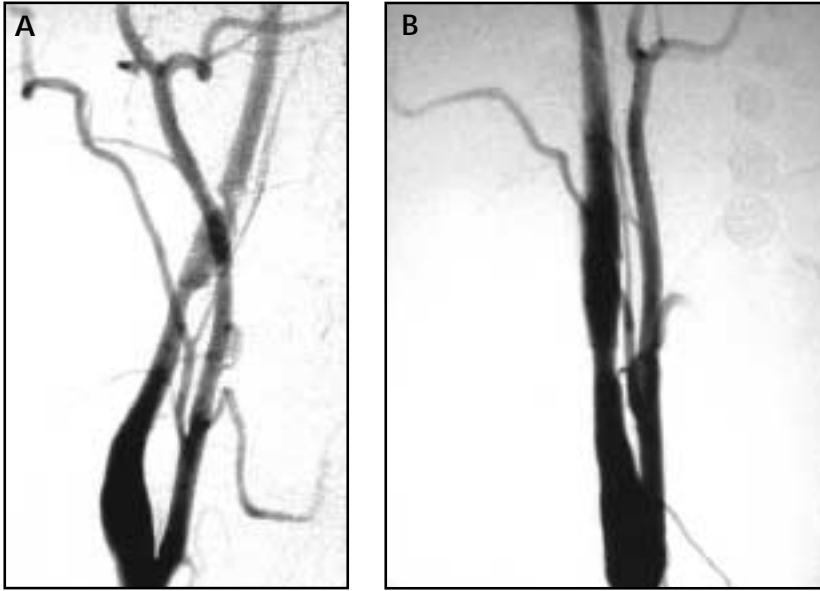
ing. A total of 5210 procedures were performed at 36 medical centers. These medical centers reported a technical success rate of 98.4%. The combined periprocedural stroke and death rate was reported to be 5.1%. The quality of data collection at each of these institutions is difficult to ascertain. Also, this type of survey information is subject to the bias of those reporting the information. This bias will almost certainly lead to an underreporting of complications. Therefore, this type of survey data cannot be viewed as a substitute for rigorous clinical trials.

What is really important is how carotid angioplasty and stenting compare with surgery and with the natural history of symptomatic and asymptomatic carotid stenosis. This can be best determined by simply measuring and comparing the proportions of patients who reach specific clinical end points (especially stroke and death). The data from the published case series of carotid angioplasty and stenting is generally presented in a favorable light because only a small

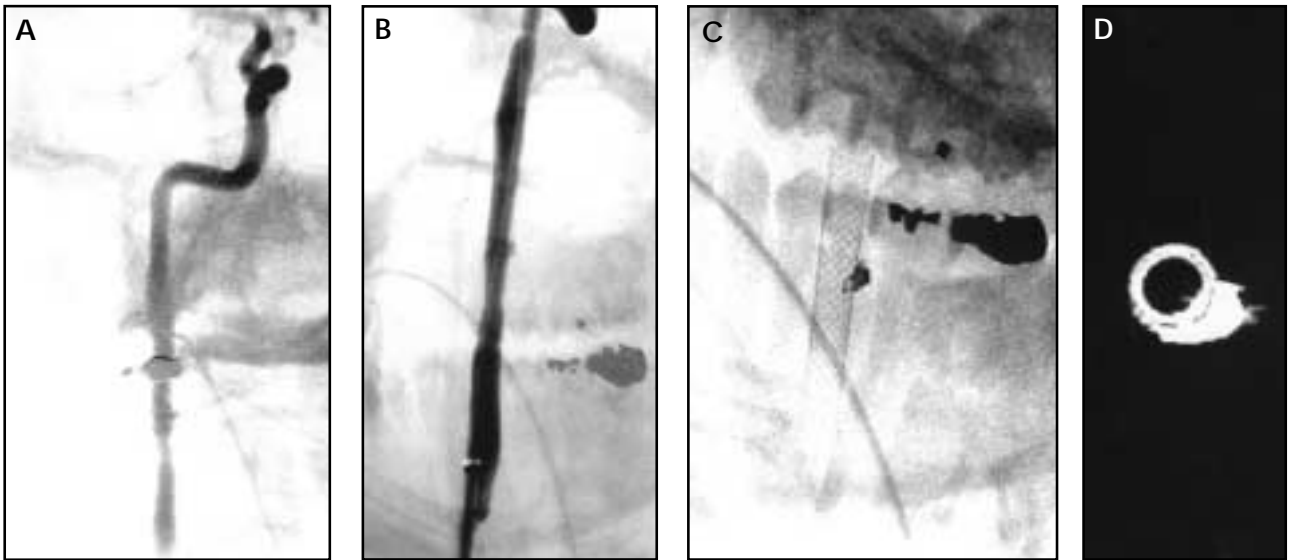
fraction of the patients treated have a complicating neurological event. This data appears less favorable, however, when one considers that 88% of symptomatic patients and at least 95% of asymptomatic patients would not have a stroke during the first year of medical therapy (i.e., if they had not undergone surgery or carotid angioplasty and stenting).<sup>12</sup>

### Patient selection

Most patients treated with carotid angioplasty and stenting have symptomatic atherosclerotic carotid stenosis (figure 1). For asymptomatic patients, the complication rate for the procedure must be below 3% and the patient must have a survival expectancy of at least 5 years to realize any benefit from correction of their carotid stenosis by surgery.<sup>4</sup> Patients thought to be too ill for carotid endarterectomy<sup>13</sup> may be poor candidates, since this patient population may not survive long enough to accrue any benefit from the procedure. However, patients who are poor candidates for surgery because of previ-



**FIGURE 2.** (A) Symptomatic traumatic dissection causing stenosis. (B) Successful stenting with Smart Stent (Cordis Endovascular, Miami Lakes, FL).



**FIGURE 3.** (A) Traumatic pseudoaneurysm caused by a gunshot wound. (B) A Wallstent (Boston Scientific Corp., Natick, MA) was placed across the pseudoaneurysm. (C) Guglielmi detachable coils (Target Therapeutics, Inc., Fremont, CA) were placed into the pseudoaneurysm. (D) Three-dimensional rotational angiography demonstrates coils outside of stent.

ous neck surgery or previous radiation therapy to the neck are potential candidates for carotid angioplasty and stenting.<sup>14</sup> Contralateral carotid occlusion has been proposed as an indication for angioplasty and stenting.<sup>15</sup> Dissection, with or without pseudoaneurysm, may also occasionally be treated effectively with angioplasty and stenting (figures 2 and 3).<sup>16</sup>

### Technical aspects

Carotid angioplasty and stenting is generally performed from a transfemoral approach. The vessel is selectively catheterized with a diagnostic catheter, and a diagnostic angiogram is performed. Patients are generally anticoagulated with 5000 to 10000 units of heparin to achieve an activated clotting time >300 seconds.

They should also be treated with an antiplatelet agent, such as clopidogrel, during and after the procedure.

No angioplasty balloon or stent has been approved for use in the carotid artery by the U.S. Food and Drug Administration (FDA). Stents that have been used in the carotid have included Palmaz (Cordis Endovascular, Miami Lakes, FL), Strecker, Wall-

stents (Boston Scientific Corp., Natick, MA), and Smart Stents (Cordis Endovascular).<sup>5,17</sup> Most of these stents require a 7F lumen for their introduction, but some Wallstents can now be introduced through a 6F lumen. Lower profile delivery systems are under development.

Self-expanding stents are now used primarily because they are not permanently deformed when exposed to compressive forces. Palmaz stents and other balloon-expandable stents are also sometimes useful because they can be more precisely positioned than Wallstents. They have increased "hoop strength" relative to self-expanding stents, but once they are deformed, they remain deformed.<sup>8,17</sup> They should be used only if they will not be exposed to crushing forces, such as when they are positioned high in the carotid artery behind the mandible.

When putting the guiding catheter into the common carotid artery, it is usually preferable to place the tip of the exchange wire in the external carotid artery with a diagnostic catheter, and then exchange it for the guiding catheter. Before stent placement, it is usually necessary to predilate the stenosis with a 3.5- to 4.0-mm diameter balloon. The shortest appropriate balloon is used to optimize inflate/deflate characteristics and to minimize trauma to the artery adjacent to the stenosis. The stent is deployed following predilatation. Residual stenosis is dilated with another angioplasty balloon as appropriate.

## Complications

Prevention of stroke is the primary goal of carotid angioplasty and stenting. Stroke is also the most worrisome complication of the procedure. Carotid angioplasty and stenting theoretically cannot be performed with less risk than cerebral angiography. The risk of stroke from cerebral angiography in the ACAS trial was 1.5%.<sup>4</sup> The risk of permanent stroke from cerebral

angiography in patients with a transient ischemic attack or stroke as an indication for angiography in 3 prospective studies (1148 patients) was 0.7%.<sup>18</sup> Therefore, it is doubtful that the risk of stroke during carotid angioplasty and stenting could ever be less than approximately 1%, perhaps even with distal protection devices.

The risk of stroke complicating carotid angioplasty and stenting may be reduced by capturing and removing emboli during the procedure, which has become known as distal protection. Theron<sup>5</sup> was the first to promote use of a distal protection device to reduce the risk of thromboembolic complications during carotid angioplasty and stenting. Ohki et al<sup>19</sup> performed angioplasty and stenting on carotid endarterectomy explants and found that the procedure generally produced numerous small plaque emboli. This *ex vivo* experiment has generated much interest in the issue of distal protection, and a number of devices are now under development.<sup>20,21</sup> It has not yet been proven that any of these devices will reduce neurological complications of carotid angioplasty and stenting. At the present time, these devices are experimental and are not used by most operators. Abciximab may be a means of reducing thromboembolic complications of carotid angioplasty and stenting, and, as in coronary angioplasty and stenting, other such pharmacological adjuncts are likely to be useful.

Carotid stenting is sometimes complicated by bradycardia and hypotension during or after the procedure.<sup>10,13,22-24</sup> Bradycardia and hypotension result from stimulation of the carotid baroreceptor by the expanding balloon or stent. Hypotension (systolic pressure <90 mm Hg) has been reported to occur in 17% to 22% of cases.<sup>10,22-24</sup> Vasopressors were required to treat hypotension in 8% to 16% of cases in some series.<sup>10,22-24</sup> Postprocedural hypotension has been reported to last as long as 4 days.<sup>10</sup>

Postprocedural hypotension seems to occur more commonly with balloon expandable-stents (26%) than with self-expanding stents (9%).<sup>10</sup> Postprocedural hypotension seems to occur less frequently in patients with previous ipsilateral carotid endarterectomy,<sup>10</sup> which may be due to surgical disruption of the carotid baroreceptor system. Because of the potential for hemodynamic instability, all patients undergoing carotid angioplasty and stenting should be well hydrated.

Mendelsohn et al<sup>24</sup> reported new onset bradycardia in 6 of 19 procedures (32%). In 5 of these 6 patients, the nadir heart rate occurred within 4 minutes of balloon dilatation or stent delivery. One patient required temporary pacing for 21 hours beyond the conclusion of the procedure. Bradycardia has been reported to occur in 28% of cases by Qureshi et al,<sup>22</sup> with 1 of 14 patients with bradycardia requiring transvenous pacing. Yadav et al<sup>17</sup> reported bradycardia persisting for a few minutes after balloon inflation in 71% of 107 patients. Some interventionalists have recommend routine prophylaxis with atropine.<sup>5,10,24</sup> At some institutions, a temporary pacemaker is inserted routinely.<sup>10,24</sup> Others have advocated obtaining femoral venous access in all patients and making sure that a transvenous pacemaker is available immediately.<sup>17</sup>

The rather large femoral sheath required for angioplasty and stent placement can result in significant complications, such as fatal retroperitoneal hemorrhage, which accounted for the single death in the series reported by Yadav et al.<sup>17</sup> Smaller stent delivery systems are under development, which should result in fewer arterial access site complications. Closure devices may reduce serious access site complications, but such a reduction remains to be proven.<sup>25</sup> These devices also might add significant financial cost to the procedure.

## Clinical trials

The primary issues that determine if carotid angioplasty and stenting should be widely applied are safety, efficacy, and durability. Angioplasty and stenting are getting safer with time, but carotid endarterectomy also seems to be safer than it was during NASCET for many surgeons. Therefore, it is important to directly compare state-of-the-art carotid endarterectomy with state-of-the-art carotid angioplasty and stenting in order to assess the relative merits of each procedure realistically and relevantly. This type of comparison can be made only with a prospective, randomized, controlled trial.

Some trials have suggested that carotid angioplasty and stenting are not yet as safe as carotid endarterectomy. The Schneider Wallstent trial of carotid angioplasty and stenting was stopped prematurely because of safety considerations regarding the angioplasty and stenting procedure.<sup>26</sup> Naylor et al<sup>27</sup> reported the results of a single-center trial in England in which 5 of 7 patients treated with angioplasty and stenting suffered a stroke. We are left to wonder whether these trials were not successful because of problems specific to the devices tested, because of problems with carotid artery angioplasty and stenting in general, or because of relative operator inexperience.

A multicenter, prospective, randomized, controlled trial comparing carotid endarterectomy with carotid artery stenting (Carotid Revascularization Endarterectomy and Stent Trial [CREST]) has been funded by the National Institute for Neurological Disease and Stroke and is scheduled to begin enrollment soon. This trial will allow a much more objective comparison of surgery and stenting than has been previously possible. A limited number of experienced operators will participate in the trial. The CREST trial will utilize the Acculink stent (Guidant Corporation, Indianapolis, IN).

At least two industry-sponsored trials are planned for the near future. The ARCHeR (Acculink for Revascularization of Carotids in High-Risk Patients) trial has been designed and funded by Guidant Corporation to evaluate the Acculink stent in symptomatic and asymptomatic patients who are at high risk for carotid endarterectomy. The SAPPHERE (Stenting and Angioplasty with Protection in Patients at High-Risk for Endarterectomy) trial has been designed and funded by Cordis Endovascular. In this trial, symptomatic and asymptomatic patients will be randomized for treatment with either carotid angioplasty and stenting performed with a distal protection device or carotid endarterectomy.

## Conclusion

The most compelling argument to perform carotid angioplasty and stenting would be that it is safer than carotid endarterectomy. No reliable data to support this argument exists. It is hoped that trials will provide some reliable data to address this question. Currently, carotid angioplasty and stenting is useful in patients who are poor candidates for carotid endarterectomy because of anatomically inaccessible lesions, restenosis following previous endarterectomy, radiation-induced stenosis, and other high-risk conditions.

Another argument made to support the use of carotid angioplasty and stenting is that it seems less invasive than surgery. While one could intelligently argue that endarterectomy performed under local anesthesia is not really any more invasive, such an argument may be irrelevant because many patients will probably perceive endarterectomy to be more invasive and choose to have angioplasty and stenting. An increasing number of patients will know carotid angioplasty and stenting exists as an option because it is being publicized on the

Internet and in other media. Since patients are taking an more active role in medical decision making, the perception of carotid angioplasty and stenting as less invasive by patients could be very important.

There are also cultural forces that are influencing the medical decision-making process. There is a widespread sense that "everyone else is doing it," and physicians do not want to miss the development of new technology for fear of being left behind. Doctors and patients like new devices, so there is a tendency to embrace treatments that involve new technology. As this new technology develops, there may be devices to sell, so the medical device industry is highly motivated to develop the technology and encourage its use. The stent industry, which has been highly successful in selling coronary stents, has become quite competitive and is looking for new markets. In 1996, 130,000 carotid endarterectomies were performed in the United States,<sup>2</sup> and it is possible that a similar number of carotid angioplasty and stent procedures might be performed in the near future. *AR*

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