Endovascular management of carotid artery disease after radiation therapy and radical neck dissection

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Object. More patients with head and neck cancers who undergo radical neck dissection and adjuvant radiation are experiencing prolonged survival times. Because of their improved survival, patients are living long enough to suffer the delayed effects of radiation therapy. Radiation-induced carotid artery (CA) stenosis in patients with or without radical neck dissection often requires extensive exposure and vessel reconstruction. The aim of this study was to evaluate the efficacy of endovascular treatment as an alternative therapy for radiation-induced CA stenosis.

Methods. Coinciding with the improved longevity of these patients, CA angioplasty and stent placement has become a definitive treatment strategy for this particularly challenging group of individuals. Long lesions are easily addressed with multiple telescoped stents. The tendency toward early restenosis can now be addressed with cutting balloon angioplasty. A review of the authors’ institutional database yielded five patients (four men and one woman) with a history of radiation treatment ipsilateral to their CA stenosis. Three of five patients were symptomatic, and the interval between radiation therapy and endovascular treatment ranged from 1 to 47 years (mean 16.6 years). Four of the five patients were treated using distal embolic protection devices, and all patients underwent balloon dilation after stent placement.

Conclusions. As advancements are made in the technology and techniques for CA angioplasty and stent placement, the safety and durability of treatments in patients with radiation-induced atherosclerotic disease will improve.

KEY WORDS • radiation therapy • radical neck dissection • carotid artery angioplasty • carotid stent placement • cutting balloon

OVERVIEW

There are three categories of radiation-induced arterial disease, as follows: 1) vessel rupture; 2) early vessel occlusion; and 3) delayed atherosclerosis superimposed on a proliferative response to radiation. The prevalence of critical CA stenosis in patients who have received radiation therapy for head and neck cancer has been reported to be as high as 22%. As survival times for patients with head and neck malignancies improve, the number of individuals requiring CA intervention is likely to increase. Carotid endarterectomy in an irradiated field is complicated because the normal anatomical planes are obliterated, the atherosclerotic plaques are extensive, and the normal cleavage points between the plaque and intima do not exist (histologically, the plaque is a heavily thickened intima). Radical neck dissection adds another level of complexity to the surgical approach because of the destruction of normal tissue planes and potentially poor wound healing. Additionally, restenosis occurs more frequently after endarterectomy in patients with radiation-induced atherosclerotic disease.

Carotid artery disease that occurs as a result of radiation therapy or radical neck dissection is considered a clear indication for endovascular therapy. The endovascular approach entirely avoids the complicated tissue dissection and healing problems likely to be found in a previously irradiated field. Long lesions can be addressed with multiple telescoped stents. Restenosis can be tackled with repeated angioplasty with or without stent placement or with cutting balloon angioplasty. In this manuscript we review our experience with CA angioplasty with or without stent placement in patients who have undergone radical neck dissection and are suffering from radiation-induced CA stenosis.

CLINICAL MATERIAL AND METHODS

Patient Population

We reviewed our institutional database, which contains more than 5000 records of endovascular procedures performed between 1998 and 2004, to identify patients with a history of radiation treatment ipsilateral to their CA stenosis. Institutional Review Board approval was obtained for this study. Five patients were identified who met the review criteria. The medical charts of these patients were...
inspected, and relevant clinical data were entered onto a computer spreadsheet. The patients’ angiograms were reviewed for this publication.

The ages of the five patients who met the criteria for this study ranged from 68 to 83 years (mean 73.2 years); four were men. Patient demographic data, clinical characteristics, and technical and angiographic results are presented in Table 1. Three of the five were symptomatic, and the interval between radiation therapy and endovascular treatment ranged from 1 to 47 years (mean 16.6 years). Only one patient had undergone radiation therapy without a radical neck dissection. Four of the five patients were treated using distal embolic protection devices, including EPI FilterWires (Boston Scientific, Natick, MA) in three and a GuardWire (PercuSurge Medtronic, Inc., Santa Rosa, CA) in the other. All patients underwent balloon dilation after stent placement.

**Protocol for CA Angioplasty With or Without Stent Insertion**

The following is a summary of the treatment protocol for patients who undergo CA angioplasty with or without stent placement at our institution. Patients receive aspirin (325 mg/day) for 3 to 4 days before the procedure, along with a loading dose of clopidogrel (300 mg). Carotid artery stenosis is measured on pretreatment angiography studies according to criteria applied in the North American Symptomatic Carotid Endarterectomy Trial. The procedure is performed after administration of local anesthesia and intravenous sedative hypnotic agents. Heparin is given intravenously before the lesion is crossed with any device, with the goal being to maintain an ACT of greater than 250 seconds during the procedure. Predilation of the stenotic lesion is accomplished with an angioplasty balloon that is undersized compared with the diameter of the distal ICA. Atropine is given before predilation angioplasty if the patient’s heart rate is less than 70 beats per minute and the lesion is near the carotid bulb, or when dilation leads to a drop in heart rate to less than 60 beats per minute that does not recover within a few seconds. If a stent is used, it is deposited before angioplasty is performed. For cases in which distal embolic protection is used, the protective device is deposited distal to the stenotic lesion in a straight segment of the ICA before crossing the lesion with the predilation balloon. The patient is observed overnight in the intensive care unit and is discharged the next day after CA Doppler ultrasonography studies have been obtained. After the procedure a 4-week course of clopidogrel (75 mg/day) is prescribed, along with aspirin (325 mg/day) for life.

**RESULTS**

There were no immediate complications in any patient. None suffered significant bradycardia or hypotension during balloon inflation or stent insertion. One patient was lost to follow up. In the four patients in whom follow-up information was available (range 1–24 months), the National Institutes of Health Stroke Scale score was 0. The in-stent PSVs ranged from 78 to 157 cm/second. In accordance with our standard protocol, follow-up Doppler ultrasonography studies are obtained in each patient at 3, 6, and 12 months, and then yearly thereafter. A follow-up angiogram is performed if the PSV on the Doppler ultrasonography study is greater than 300 cm/second.

**ILLUSTRATIVE CASES**

**Case 1**

This 66-year-old man presented with asymptomatic 80 to 90% left-sided CA stenosis documented by CA Doppler ultrasonography imaging and magnetic resonance angiography. One year earlier, the patient had undergone a radical neck dissection for squamous cell carcinoma of the tongue, and had required adjuvant treatment with radiation and chemotherapy. Diagnostic angiography studies revealed a 75% stenosis according to North American Symptomatic Carotid Endarterectomy Trial criteria. After a discussion of treatment risks, benefits, and alternatives, the patient chose to proceed with CA angioplasty with stent placement. He underwent an uncomplicated procedure in which an EPI FilterWire and the Endotex stent system (Boston Scientific, Natick, MA) were used.

On routine follow-up evaluation performed 2 years later, the patient’s Doppler ultrasonography PSVs were 363/160 cm/second. Diagnostic angiography revealed greater than 80% in-stent stenosis (Fig. 1 left). Heparin was given to achieve an ACT greater than 250 seconds. Using a Sim-2 catheter (Cook, Inc., Bloomington, IN) to gain access to the CCA, a stiff exchange wire was placed in the left external CA and exchanged for a No. 6 French Cook shuttle (Cook, Inc.) that was placed into the CCA. The lesion was crossed with an EPI FilterWire. A 3.5 × 15-mm cutting balloon was deployed with no complication. Immediately following balloon angioplasty, the PSV fell to 155 cm/second, with no in-stent stenosis (Fig. 1 right). The patient tolerated the procedure with no complications and has remained asymptomatic on follow-up evaluation 1 year later.

**TABLE 1**

Demographic and other data in five patients undergoing endovascular therapy for radiation-induced CA disease*

<table>
<thead>
<tr>
<th>Age (yrs), Sex</th>
<th>yrs. Btw DEP &amp; FU</th>
<th>DEP Device</th>
<th>FU (mos)</th>
<th>PSV (cm/sec)</th>
<th>NIHSS Score on FU</th>
<th>Stenosis (%) Pretreatment &amp; Posttreatment</th>
<th>Location of Stenotic Lesion</th>
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<td>70, F no 18 yes 5 157 0 70 &lt;10</td>
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* DEP = distal embolic protection; ET = endovascular therapy; FU = follow up; NA = not available; NIHSS = National Institutes of Health Stroke Scale; RT = radiation therapy; sx = symptoms.
balloon was advanced over the FilterWire into the most stenotic portion of the ICA/CCA. The balloon was inflated to 10 atm and left in place for 4 minutes. Angiographic studies obtained after balloon deflation demonstrated only 10 to 20% residual stenosis (Fig. 1 right). The EPI filter was recaptured, the Cook shuttle was exchanged for a stiff wire, and the femoral access site was closed with a No. 8 French AngioSeal device (St. Jude Medical, St. Paul, MN). The patient remained asymptomatic at the 1-year follow-up evaluation, with a Doppler in-stent PSV of 122/41 cm/second.

Case 2
This 76-year-old man presented with a transient episode of numbness and weakness in his right arm. In 1957, the patient had undergone radical neck dissection and radiation therapy for neck cancer. At the time of his evaluation at our institution, Doppler ultrasonography and magnetic resonance angiography indicated a 70% stenosis of the left ICA. Cerebral angiography revealed a long segment of stenosis in the left CCA that extended into the ICA (Fig. 2 left). Maximal stenosis was present in the midportion of the CCA. The therapeutic risks, benefits, and alternatives were discussed with the patient, and he chose to proceed with an endovascular approach.

After achieving an ACT of greater than 250 seconds, the left ICA was engaged with a glide wire. A Vitek catheter (Cook, Inc.) and a No. 6 French Select shuttle (Cook, Inc.) were placed with minimal purchase in the proximal CCA. The lesion was crossed with an EPI FilterWire, and the maximal point of stenosis was predilated with a 3.5 × 30–mm angioplasty balloon. An 8 × 36–mm Wallstent (Boston Scientific) was placed from the ICA to the maximal stenotic lesion in the CCA; a second Wallstent was then deposited from the middle of the first stent to the proximal portion of the diseased vessel. Good restoration of flow was demonstrated on angiographic follow-up studies (Fig. 2 right). The filter and sheath were removed. The femoral access site was successfully closed with a No. 8 French AngioSeal device. The patient was dismissed home the next day; he was neurologically intact with in-stent PSVs of less than 100 cm/second.

**DISCUSSION**

Five-year survivors of head and neck cancer who have received radiation therapy may have at least twice the incidence of symptomatic cerebrovascular disease compared with age-matched patients who do not undergo neck irradiation, and in nearly 20% CA disease develops. Three (60%) of our five patients presented with symptomatic disease; each had survived at least 10 years after undergoing cervical irradiation. Treatment of this group of patients often requires complex arterial reconstruction because of the extensive amounts of plaque and the difficulty involved in dissecting the plaque from the normal vessel wall. Although carotid endarterectomy and CA reconstructive surgery can be performed safely by experienced practitioners, the frequency of arterial and cranial nerve injuries is higher, and poor wound healing is a potentially disastrous consequence.

During the last 10 years, CA angioplasty with or without stent placement has emerged as an excellent treatment alternative for this group of patients. Dissection through a previously irradiated surgical field is avoided, and long-segment stenosis is easily handled with multiple stents. Restenosis reportedly occurs at a rate of 4.8 to 17.6% more than 1 year after CA stent placement for radiation-induced disease. Nevertheless, cutting balloon angioplasty, as illustrated in the patient in Case 2, has emerged as an excellent treatment strategy for in-stent stenosis. Repeated performance of standard balloon angioplasty with or without secondary stent placement remains another viable alternative.
Since 1980, interventional cardiologists have used cutting balloons for the treatment of in-stent stenosis.\textsuperscript{10} This device is a noncompliant balloon with three or four ath-erotomes (which are 0.005-in thick microsurgical blades) that are mounted longitudinally on the balloon’s outer sur-face (Fig. 3). With the device’s expansion, the blades (which were previously shielded by the balloon) score the plaque or neointimal hyperplasia, cracking it evenly. The-oretically, cutting balloon angioplasty leads to the ac-complishment of revascularization with lower pressure, greater precision, and less vessel injury than conventional repeated angioplasty. Although clinical experience is lim-ited to small series, cutting balloon angioplasty for early in-stent CA restenosis (the source of which is believed to be neointimal hyperplasia) appears to be the treatment of choice.\textsuperscript{2,14,15}

The only stroke in their series occurred before the routine use of distal embolic protection devices. The use of these devices has led to a significant decrease in thromboem-bolic complications.\textsuperscript{2,14,15} With the further development of CA angioplasty and new stent devices and delivery tech-niques, the management of CA stenosis in patients with this particularly difficult-to-treat condition will become both safer and more durable.

**Fig. 3.** Graphic rendering of the cutting balloon (Boston Scientific Interventional Technologies) (left) and photograph of the ath-erotome (right). Depictions of the cutting balloon are reproduced with permission from the manufacturer of the device. Printed with permission from Bendok BR, Roubin GS, Katzen BT, et al: Cutting balloon to treat carotid in-stent stenosis: technical note. \textit{J Invasive Cardiol} \textbf{15}:227–232, 2003.

### References


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### Disclosure

Dr. Hopkins is a consultant for and receives research support from Boston Scientific, Cordis Corporation, Guidant, Medtronic, and Micrus. He has a financial interest in Boston Scientific, Medtronic, and Micrus.

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