From the Society for Clinical Vascular Surgery

Carotid artery stenting may be performed safely in patients with radiation therapy-associated carotid stenosis without increased restenosis or target lesion revascularization

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Objective: **Neck radiation therapy (XRT) can induce carotid artery stenosis and may increase the technical difficulty of endarterectomy. It is considered a relative indication for carotid angioplasty and carotid artery stenting (CAS). This study sought to evaluate differences in CAS embolic potential and restenosis performed on XRT and non-XRT patients.**
Methods: **At three institutions, 366 CAS procedures were performed on 321 patients (XRT, n = 43; non-XRT, n = 323). Mean follow-up was 410 days (median, 282 days; range, 7-1920 days). Patients were observed with duplex ultrasound to assess for restenosis. Additional end points included target lesion revascularization (TLR), myocardial and cerebrovascular events, and perioperative complications. Captured particulate from embolic protection filters was analyzed with photomicroscopy and image analysis software for 27 XRT and 214 non-XRT filters.**
Results: **XRT patients were more likely to be male and had lower rates of hypertension, coronary artery disease, and diabetes mellitus, although the mean age at procedure did not differ. There was no increase in severe internal carotid tortuosity among XRT patients (XRT: 50% vs non-XRT: 34.7%; $P = .06$). Indication for CAS did not differ between the two groups, including the number of CAS procedures performed for symptomatic carotid stenosis (XRT: 39.7% vs non-XRT: 39.0%; P = NS). Perioperative outcomes, including the composite 30-day stroke, myocardial infarction, and mortality, were not significantly different (XRT: 2.6% vs non-XRT: 3.9%; P = NS.) There were no significant differences in restenosis rate at the 50% (XRT: 9.4% vs non-XRT: 8.6%; P = NS) or 70% (XRT: 3.5% vs non-XRT: 8.6%; P = NS) threshold. Filter particle analysis revealed that filters from XRT patients had more numerous large particles per filter (1.4 vs 0.7; $P < .05$) and larger mean particle size (464.1 μm vs 320.0 μm; $P < .05$). TLR did not differ significantly between the groups.**
Conclusions: **In contrast to earlier studies, this analysis reveals that there are significant differences in XRT and non-XRT patients undergoing CAS in terms of medical comorbidities and embolic material captured in embolic protection filters. The decreased incidence of atherosclerotic risk factors was observed in XRT patients probably because XRT was the primary factor responsible for carotid stenosis. Despite increased embolic particle size, CAS can be performed safely with no increased morbidity, TLR, or restenosis in XRT patients. (J Vasc Surg 2015;62:624-30.)**

Carotid artery stenosis is a major cause of embolic stroke. Carotid endarterectomy (CEA) has a proven role in reducing the risk of stroke in patients with symptomatic carotid stenosis and in asymptomatic patients with critical stenotic lesions. Carotid artery stenting (CAS) with embolic protection has also been shown to be safe and effective in treating carotid stenosis.[1-3] However, recent comparative randomized prospective trials have established CEA as first-line therapy for patients who require carotid intervention because of the lower risk of periprocedural stroke.[4] There are still data to support the selective use of CAS in those patients who are at higher risk of complication from CEA. One such cohort includes patients with "hostile necks" who have undergone previous neck radiation therapy (XRT) for malignant disease with or without previous neck dissection. These patients are at higher risk for cranial nerve injuries, wound complications, and increased use of interposition grafting during open carotid surgery.[5,6] Given the acceptable safety profile of CAS with embolic protection, many practitioners employed CAS as an alternative to CEA in these patients who otherwise would pose an elevated operative risk.

Neck XRT used in the treatment of malignant disease can lead to radiation arteritis, which can progress into significant stenotic and occlusive lesions in affected vessels.

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The pathophysiologic mechanisms underlying radiation arteritis are not fully understood. The process appears to be primarily inflammatory in nature, and although it shares similarities to atherosclerosis, the plaque characteristics and natural history of these lesions may be distinct. There have been reports that stenotic lesions in radiation arteritis may be more concentric than atherosclerotic plaques, and the vessels may develop more severe tortuosity.[7] It is unknown if these differences in pathophysiology result in different outcomes after carotid stenting.

We hypothesized that we would be able to identify significant epidemiologic differences in patients undergoing CAS for atherosclerotic de novo lesions and those patients previously exposed to XRT, with XRT patients having less burden of atherosclerotic comorbidities. We also hypothesized that we would be able to detect anatomic differences in XRT vs non-XRT lesions, with more tortuosity in the postradiation carotids, but that given the low rates of major adverse outcomes and restenosis, we would not see any differences in the two groups. Finally, it was hypothesized that there would be measurable differences in the embolic material generated by post-XRT plaques vs non-XRT plaques.

METHODS

This study consisted of a retrospective review of a multi-institutional database as well as examination of embolic protection filters. The database began in August 2003 and included data up to September 2013. The database included patients from three institutions, and the patients were entered in a single database, on an unselected consecutive basis. The database and waiver of informed consent for retrospective research were approved by Institutional Review Boards at each institution. Patients were stratified according to whether they had a history of previous neck XRT.

Patient characteristics. Patient demographics were obtained by searching the medical record for comorbidities and patient characteristics. Patients with a life expectancy >1 year were considered for carotid intervention if they were found on imaging to have a stenosis >70% or a symptomatic lesion >50%. Patients were offered carotid stenting on the basis of factors that made them higher risk for CEA; this included high cardiac or pulmonary risk, previous neck irradiation, and previous neck dissection or CEA. CAS was not offered to XRT patients undergoing treatment for active malignant disease. Many of the patients included were enrolled in clinical trials at the time of the intervention.

Lesion characteristics. Anatomic characteristics of lesions based on intraoperative angiograms were analyzed individually. Angiograms were assessed for lesion percentage stenosis, lesion length, and presence of contralateral disease. Stent type and measurements were recorded as well.

Tortuosity scoring was also performed for all available angiograms. Tortuosity scores were based on a 3-point system, which consisted of a measurement of the degree of deviation of the internal carotid from the axis between the common carotid and the distal internal carotid. Axis deviation <45% was classified mild; axis deviation between 45% and 90% was classified moderate; and axis deviation >90% was considered severe tortuosity.

Procedures. All procedures were performed by vascular surgeons or interventional cardiologists, with the participation of vascular surgeons. Formal neurologic assessment was performed before the CAS procedure by a trained research associate. In the absence of suspected clinical neurologic events, postoperative assessments were performed by vascular surgeons; however, in the event of a suspected neurologic event, urgent consultation with an independent neurologist was obtained. Procedures were performed under local anesthesia through femoral access. During the procedure, neurologic assessment was performed; preprocedure and postprocedure cerebral angiograms were obtained. After placement of introducer sheaths, patients were heparinized and monitored with activated clotting levels with a goal between 250 and 300 seconds. Patients were started or continued on 81 mg of aspirin daily, and clopidogrel-naive patients were begun on 75 mg of clopidogrel 5 days preoperatively and continued it for 4 weeks in the absence of other indications.

Embolic protection filters were used in all patients. The filters analyzed included Accunet (Abbott Laboratories, Chicago, Ill), Angioguard (Cordis Corporation, Miami Lakes, Fla), Emboshield (Abbott Laboratories), EPI FilterWire (Boston Scientific Corp, Natick, Mass), and SpiderFX (ev3 Inc, Plymouth, Minn).

End points. Patients were observed with clinical examination and duplex ultrasound at 1, 3, 6, 9, and 12 months and then annually. Duplex ultrasound examinations were performed by high-volume vascular laboratories certified by the Intersocietal Commission for the Accreditation of Vascular Laboratories. Restenosis was determined by the presence of a hemodynamically significant lesion on B-mode ultrasound in addition to velocity criteria. Two cutoff points were used for this study, 50% and 70% restenosis; 50% restenotic lesions required a peak systolic velocity of 125 cm/s or an end-diastolic velocity of 40 to 99 cm/s; 70% lesions required a peak systolic velocity >230 cm/s, end-diastolic velocity >100 cm/s, or internal carotid artery/common carotid artery ratio >4.0. Target lesion revascularization (TLR) was determined by identifying patients in whom there was more than one ipsilateral intervention; for those patients, operative reports and angiograms were individually reviewed to determine whether the intervention constituted TLR of a restenotic lesion or if the interventions were occurring at a de novo lesion. For the purposes of the review, reinterventions were considered to be TLR if the treatment area fell within a previously placed carotid stent or immediately proximal or distal, contiguous with a previously placed stent.

Perioperative complications including myocardial infarction, stroke, and mortality were quantified. Myocardial infarction was defined by positive electrocardiographic