Radiation arteritis: A contraindication to carotid stenting?

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Background: **Carotid artery stenting (CAS) for high-risk anatomic lesions is accepted practice. Neck irradiation and radiotherapy-induced arteritis are common indications. The clinical outcomes of CAS for radiation arteritis have been poorly defined.**

Methods: **A prospective database of patients undergoing CAS at a tertiary referral academic medical center was maintained from 1999 to 2006. Patients undergoing primary carotid artery stenting for significant atherosclerotic (ASOD) and radiotherapy (XRT)-induced occlusive disease were analyzed. Life-table analyses were performed to assess time-dependent outcomes. Cox proportional hazard analysis or Fisher's exact test was performed to identify factors associated with outcomes. Data are presented as the mean ± SEM unless otherwise indicated.**

Results: **During the study period, 150 patients underwent primary CAS, 75% with embolic protection. Fifty-eight percent were symptomatic. One hundred twenty-seven (85%) were treated for ASOD, and 23 (15%) had XRT. The 30-day all-cause mortality rate was 1% for ASOD and 0% for XRT (P = NS); overall survival at 3 years was equivalent. There was no significant difference in major adverse event rates as defined by the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial between the groups. The 3-year neurologic event-free rate was 85% for ASOD and 87% for XRT (P = NS). Late asymptomatic occlusions were seen only in XRT patients. The 3-year freedom from restenosis rate was significantly worse for the XRT group, at 20%, vs 74% for the ASOD group ($P < .05$). Likewise, the 3-year patency rate was also worse for the XRT group, at 91%, vs 100% for ASOD by Kaplan-Meier analysis ($P < .05$). No factor was predictive of occlusion or stenosis by Cox proportional hazards analysis.**

Conclusion: **CAS for radiation arteritis has poor long-term anatomic outcome and can present with late asymptomatic occlusions. These findings suggest that these patients require closer postoperative surveillance and raise the question of whether CAS is appropriate for carotid occlusive lesions caused by radiation arteritis. (J Vasc Surg 2007;45:110-7.)**

Extracranial carotid stenosis as a result of accelerated atherosclerosis is a recognized complication of external beam radiation in patients with head and neck malignancy.[1-5] Cervical irradiation is a known risk factor for accelerating carotid stenosis progression.[6,7] Carmody et al[5] demonstrated a 22% prevalence of >70% carotid stenosis in patients with previous neck radiotherapy compared with 4% in controls. Eighty percent of patients with significant stenosis in the irradiated group were symptomatic.[5]

Carotid endarterectomy (CEA) in these patients is hindered by previous surgical reconstructions and radiation-induced fibrosis that obliterates the endarterectomy plane and, as a result, is often associated with interposition graft placement. Carotid surgery in these patients is not associated with a greater risk of stroke; however, a higher incidence of arterial damage, cranial nerve palsy, prosthetic infection, anastomotic breakdown, restenosis, and an increased rate of wound complications have been reported.[8] These patients are thus at a higher risk than nonirradiated patents, and as a result, neck irradiation and radiation arteritis are common high-risk indications for carotid artery stenting (CAS).

The clinical outcomes of CAS for radiation arteritis are not well defined and we sought retrospectively to define our outcomes for primary CAS in radiation arteritis within our vascular service line.

METHODS

Study setting. This study was performed at the University of Rochester Medical Center, an academic medical center in a metropolitan area of 300,000 population and a surrounding rural county of about 1 million in western New York State. The center is a tertiary referral center with a dedicated vascular service line.

Experimental design. A prospective database of patients undergoing endovascular treatment for carotid artery occlusive disease between 1999 and 2006 was maintained. Patients undergoing primary CAS for significant atherosclerotic (ASOD) and radiotherapy-induced (XRT) occlusive disease were analyzed. Vessels treated for intimal hyperplasia or trauma were excluded. Data utilization fell under the category of secondary use of pre-existing data.

Procedures. Procedures were performed with local Institutional Review Board approval or as part of an approved multicenter clinical trial, or both, and followed Centers for Medicare and Medicaid Services regulations. For each patient, demographics, symptoms, existing co-

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morbid conditions, and risk factors for atherosclerosis were identified. Periprocedural data were obtained from the record. Follow-up was by clinical assessment and carotid duplex ultrasound scans performed at 1, 6, and 12 months after the intervention and every 6 months thereafter. Patients underwent carotid stenting where carotid stenosis ≥80% was detected on duplex imaging and was confirmed on computed tomography (CTA) or magnetic resonance angiography (MRA).

Patients were given clopidogrel (75 mg) and aspirin (81 mg) beginning 3 days before the intervention. Patients were asked not to take their β-blocker medications the day of the procedure, and we did not begin giving prophylactic β-blockers before the procedure. Patients with a baseline heart rate of 60 beats/min were given prophylactic atropine. Patients who demonstrated a bradycardia on angioplasty before stenting were prophylactically treated. Routine preprocedural and postprocedural neurology consultations were not requested unless the patient was symptomatic.

After the stenting procedure, clopidogrel was continued for 1 month, and aspirin was continued for life. All patients undergoing carotid stenting received an intravenous heparin bolus (100 U/kg) to achieve systemic anticoagulation during the carotid intervention.

All carotid stenting procedures were performed in fixed-imaging procedure rooms under conscious sedation. The technique of stenting with an embolic protection device has been described previously.[9] A self-expanding monorail carotid stent was deployed across the internal carotid stenosis and consisted of Wallstent (Boston Scientific, Natick, Mass) Precise (Cordis, Miami Lakes, Fla), or Acculink (Guidant, Santa Clara, Calif) stents. Balloon angioplasty after stenting was performed with an angioplasty balloon (diameter, 5 or 6 mm), depending on the appearance of the completion angiogram.

Patients were routinely kept in the hospital overnight and discharged home the next day. Follow-up visits with carotid duplex ultrasound scans were performed as previously indicated. Patients who required interventions for clinically significant restenosis after CAS were evaluated with duplex ultrasound scans at 3-month intervals. We did not perform immediate duplex scanning in the perioperative period. All duplex ultrasound scans were performed at approved vascular laboratories accredited by the Intersociety Commission on Accreditation of Vascular Laboratories using the University of Washington criteria.

Restenosis was defined as the development of >50% stenosis. Clinically significant stenosis was defined as luminal reduction of 80% or higher. The presence of a high-grade stenosis was verified by biplanar carotid angiography. Patients that were defined as restenosed by University of Washington criteria were subsequently re-evaluated using modified criteria for in-stent restenosis by Stanziale et al,[10] peak systolic velocity ≥225 cm/s and internal carotid artery (ICA)/common carotid artery (CCA) ≥2.5 for ≥50% stenosis.

Carotid angioplasty and possible stenting were subsequently performed by following the standard protocol upon confirmation of the restenotic lesions. Patients with >50% stenosis and no symptoms were monitored. Patients with >80% stenosis or >50% stenosis with symptoms were offered angiography. Our policy is to watch restenosis <80% that is asymptomatic. Reintervention was offered to patients with >80% stenosis.

Definitions. The XRT patients were defined as having irradiation directed at head and neck cancers and XRT had been received for 17 laryngeal cancers, 4 lymphomas, 1 oral cancer, and 1 parotid cancer. Coronary artery disease was defined as a history of angina pectoris, myocardial infarction, congestive heart disease, or prior coronary artery revascularizations. Cerebrovascular disease included a history of stroke, transient ischemic attack (TIA), or carotid artery revascularization. Hypertension was defined as a systolic blood pressure >150 mm Hg or diastolic blood pressure >90 mm Hg on three occasions during a 6-month period. Hyperlipidemia was defined as fasting cholesterol >200 mg/dL, a low-density lipoprotein cholesterol of >130 mg/dL or triglycerides >200 mg/dL, or active therapy for hyperlipidemia. Diabetes was defined as a fasting plasma glucose >110 mg/dL, an HbA_{1c} >7%, or active therapy for diabetes. Metabolic syndrome was defined as previously described,[11] with the exception of abdominal circumference, which is not routinely recorded. We substituted a body mass index score ≥27.0 as a positive score instead of an abdominal circumference >102 cm for men or >88 cm for women.

A death ≤30 days of the procedure was considered procedure-related. A major complication was defined as any event, regardless of how minimal, not routinely observed after endoluminal therapy that required treatment with a therapeutic intervention or rehospitalization ≤30 days of the procedure. The major adverse event rate was defined using Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) criteria.[12] Unlike SAPPHIRE, patients did not have a troponin series performed or formal neurologic consultations.

Primary patency was defined as a patent carotid segment without recurrent stenosis or the need for further intervention. Assisted primary patency was defined as a patent carotid segment, which underwent further intervention within the inflow, treated vessel segment or outflow of the treated vessel segment to improve patency. Secondary patency was defined as an occluded carotid vessel or a carotid with hemodynamic failure resulting in a surgical bypass. Loss of patency was defined according to accepted Society of Vascular Surgery (SVS) reporting standards.

Statistical analysis. All statistical analyses were performed on an intention-to-treat basis. Measured values are reported as percentages or means ± 1 SD. Survival, patency, and neurologic-free and major adverse event rates were calculated using Kaplan-Meier analysis and are reported using current SVS criteria. Standard errors are reported in Kaplan-Meier analyses. The log-rank test was used to determine differences between life tables. Multivar-

Table I. Patient characteristics*

	ASOD n = 127(%)	*XRT n = 23(%)*
Age years (mean ± SD)	71 ± 11	71 ± 8
> 80 years	28 (22)	4 (17)
Sex (male)	76 (60)	14 (61)
Symptoms		
Asymptomatic	55 (43)	12 (52)
Stroke	26 (20)	3 (13)
Transient ischemic attack	29 (23)	5 (22)
Amaurosis fugax	10 (8)	3 (13)
Vertebrobasilar stroke	17 (9)	1 (4)
Contralateral Lesion		
>50% Stenosis	49 (39)	11 (48)
>80% Stenosis	20 (16)	6 (26)

ASOD, patients with atherosclerotic occlusive disease; *XRT,* patients with radiotherapy-induced arteritis.
**P* = NS for all data.

Table II. Patient Comorbidities*

	ASOD n = 127(%)	*XRT n = 23(%)*
Coronary artery disease		
Congestive heart failure	38 (30)	8 (35)
Myocardial infarction	60 (47)	9 (39)
Atrial fibrillation	13 (10)	1 (4)
COPD	25 (20)	3 (13)
Hypertension	119 (94)	22 (96)
Diabetes mellitus		
Insulin dependent	7 (6)	0 (0)
Noninsulin dependent	42 (33)	4 (17)
Hyperlipidemia	107 (84)	18 (78)
Metabolic syndrome	58 (46)	9 (39)
Renal insufficiency		
Creatinine >1.5 mg/dL	35 (28)	3 (13)
Hemodialysis dependent	2 (2)	0 (0)
Hypothyroid*	22 (17)	15 (65)
Nicotine abuse		
Current	25 (20)	1 (4)
Former	84 (66)	18 (78)
No history	18 (14)	4 (17)
Body mass index (kg/m^2)		
≥ 27.0	72 (57)	8 (35)
≥ 30.0	42 (33)	5 (22)

ASOD, patients with atherosclerotic occlusive disease; *XRT,* patients with radiotherapy-induced arteritis; *COPD,* chronic obstructive pulmonary disease.
**P* = NS except for hypothyroid (*P* < .05).

Table III. Procedure

	ASOD n = 127(%)	*XRT n = 23(%)*	P
Lesion location			
Common carotid only	14 (11)	6 (26)	NS
Internal and common carotids	4 (3)	6 (26)	<.05
Internal carotid only	105 (83)	10 (44)	<.05
Technical failure	4 (3)	1 (4)	NS
Embolic protection device			
Successful deployment	101 (93)	11 (92)	NS
Unsuccessful deployment	8 (7)	1 (8)	NS

ASOD, patients with atherosclerotic occlusive disease; *XRT,* patients with radiotherapy-induced arteritis.

iate stepwise regression analysis was used to determine the influence of preprocedural and periprocedural factors on outcomes.

The significance level $P \leq .10$ was used to include or eliminate a covariate from the model. Covariates were considered to be significantly associated with the outcome if they were included in the final model and their significance level was $P \leq .05$. Interactions between statistically significant covariates were checked. Logistic regression models were used for outcomes that were measured shortly after the procedure (complications, short term clinical benefits). The dependence of each covariate on the outcome was first checked separately using the χ^2 test. Covariates with the significance level of $P \leq .10$ were included in the multivariate stepwise analysis.

RESULTS

Patient population. During the study period, 150 patients (60% men) underwent primary CAS, 75% with embolic protection; 58% of these patients were symptomatic. The most common presenting symptom was TIA (36%), followed by cerebrovascular accident (31%), vertebrobasilar stroke (19%), and amaurosis fugax (14%). No statistical differences were present between groups for symptoms (Table I). A total of 127 (85%) were treated for ASOD, and 23 (15%) had XRT. The mean age was 71 ± 0.03 years (range, 46 to 95 years) for ASOD patients and 71 ± 0.12 years (range: 56 to 85 years) for XRT patients (*P* = NS). Among the comorbidities between the two groups, only hypothyroidism was found to be significantly different (Table II).

The mean length of follow-up was 14.4 months. Preoperative evaluations consisted of ultrasound imaging only (45%); ultrasound imaging with MRA (20%), CTA (12%), or angiography (4%); ultrasound imaging, MRA, and CTA (2%); MRA and angiography (4%); MRA alone (3%), and angiography alone (6%).

Preoperative hemodynamics evaluated the degree of vessel stenosis as occluded (0%), 80% to 99% stenosis (84%), 70% to 79% stenosis (14%), and 50% to 69% stenosis (2%). Sixty patients (40%) presented with contralateral disease >50%, and 26 (17%) presented with contralateral disease >80% (no difference between groups). No patients presented with vessel occlusion. There was a positive correlation between preoperative ultrasound imaging and intraoperative angiography.

Procedures. Procedural details are shown in Table III. The 30-day all-cause mortality rate was 1% for ASOD and 0% for XRT (*P* = NS), and overall survival at 3 years was equivalent. There was no significant difference in major adverse event rates, as defined by the SAPPHIRE trial, or local complications between the two groups.

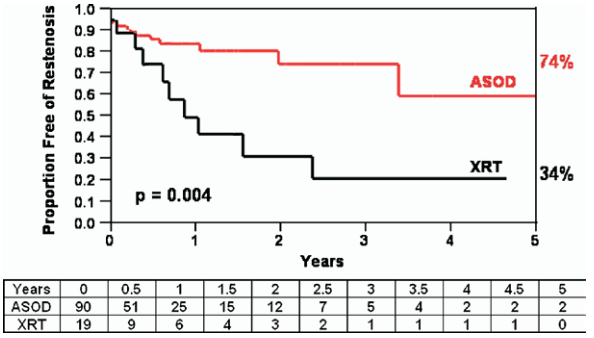
Table IV describes the frequency of systemic, regional, and local complications encountered perioperatively.

Table IV. Complications*

	ASOD n = 127(%)	*XRT n = 23(%)*
Systemic		
Cardiac (MI)	2 (2)	0 (0)
Pulmonary	3 (2)	0 (0)
Renal	2 (2)	0 (0)
Regional		
Stroke	7 (6)	1 (4)
TIA	7 (6)	0 (0)
Bradycardia	18 (14)	2 (9)
Hypotension	14 (11)	0 (0)
Vasospasm	12 (9)	2 (9)
Local		
Dissection	2 (2)	0 (0)
Occlusion	0 (0)	0 (0)
Hematoma	7 (6)	1 (4)
Groin AV fistula	0 (0)	0 (0)
Groin hemorrhage	1 (1)	0 (0)
Groin pseudoaneurysm	2 (2)	0 (0)

ASOD, patients with atherosclerotic occlusive disease; *XRT,* patients with radiotherapy-induced arteritis; *MI,* myocardial infarction; *TIA,* transient ischemic attack; *AV,* arteriovenous fistula
*P = NS.

Briefly, the most common complications were bradycardia (13%), hypotension (9%), vasospasm (9%), hematoma (5%), stroke (5%), and TIA (4%). Four procedures (3%) for ASOD and one procedure (4%) for XRT resulted in technical failure (P = NS). Disease was more extensive in the XRT group: 3% of ASOD stenoses and 26% of XRT stenoses involved the ICA and CCA ($P < .05$). Successful deployment of embolic protection devices was achieved in 93% and 92% of attempts for ASOD and XRT, respectively (P = NS). There was no difference in residual stenosis of <30% between the two groups, 97% of ASOD and 96% of XRT, as determined by the completion angiogram.



Years	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
ASOD	90	51	25	15	12	7	5	4	2	2	2
XRT	19	9	6	4	3	2	1	1	1	1	0

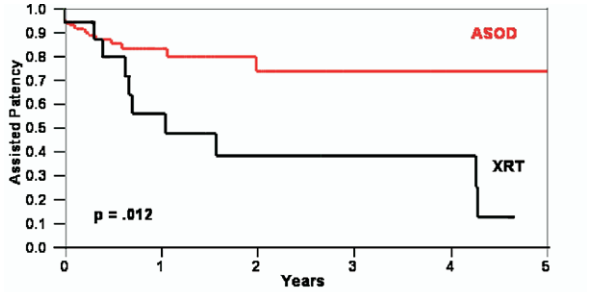
Fig 1. Freedom from restenosis. Sixteen (13%) patients with atherosclerotic occlusive disease *(ASOD)* and 10 patients (43%) with radiotherapy-induced *(XRT)* arteritis restenosed ($P < .05$). The 3-year rates for freedom from restenosis were 74% for ASOD and 20% for XRT. Error bars are omitted for clarity. The number of procedures at risk at each time interval is shown below the figure. The standard error did not exceed 10% at all time intervals that were analyzed.

Outcomes. During follow-up, the rate of restenosis was 13% for ASOD and 43% for XRT ($P < .05$), with an average time to restenosis of 1.0 ± 0.01 years and 0.8 ± 0.04 years, respectively (P = NS) (Table V). Freedom from restenosis was significantly worse for the XRT group, with rates of 55%, 39%, and 32% at 1, 2, and 3 years, respectively, vs 89%, 82%, and 72% for the ASOD group ($P < .05$) (Fig 1). For the patients who restenosed, five of the 16 ASOD and four of the 10 XRT patients had a prior postoperative duplex ultrasound examination that showed freedom from restenosis (Fig 2). Vessel occlusion only occurred in the XRT group (8.6% vs 0% for ASOD patients; $P < .05$) (Fig 3). The two vessel occlusions in the XRT group occurred at 0.8 and 1.9 years; one was symptomatic, with episodes of visual field loss, and the other was asymptomatic (Table V).

Table V. Clinical outcomes

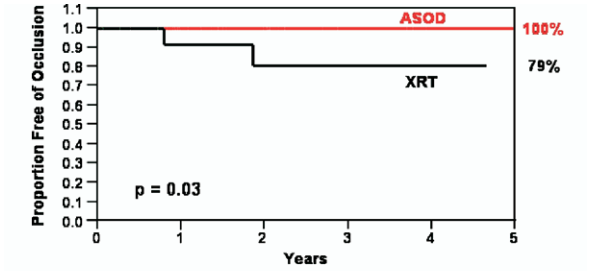
	ASOD n = 127(%)	*XRT n = 23(%)*	*P*
Technical failure	4 (3)	1 (4)	NS
Restenosis of all patients	16 (13)	10 (43)	<.05
Years to restenosis, mean ± SD	1.0 ± 1.81	0.83 ± 0.67	
Restenosis of patients*	12 (9)	9 (39)	<.05
Years to restenosis, mean ± SD	1.33 ± 1.96	0.92 ± 0.66	
Vessel occlusion	0 (0)	2 (8.6)	<.05
Years to occlusion, mean ± SD	0	1.34 ± 0.77	
Reintervention(s)	1 (1)	3 (13)	<.05
Recurrent symptoms	19 (15)	4 (17)	NS
Cerebrovascular accident			
≤30 days	9 (7)	2 (9)	NS
During entire length of follow-up	13 (10)	2 (9)	NS
Myocardial infarction			
≤30 days	0 (0)	0 (0)	NS
During entire length of follow-up	4 (3)	1 (4)	NS
Mortality			
≤30 days, all causes	1 (1)	0 (0)	NS
During entire length of follow-up	1 (1)	2 (9)	NS

ASOD, patients with atherosclerotic occlusive disease; *XRT,* patients with radiotherapy-induced arteritis.
*Excluding technical failures.



Years	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
ASOD	90	51	25	15	12	7	5	5	3	3	3
XRT	19	10	7	5	4	4	3	3	3	1	0

Fig 2. Freedom from restenosis, assisted. One patient with atherosclerotic occlusive disease *(ASOD)* and three patients with radiotherapy-induced *(XRT)* arteritis underwent reintervention. Restenosis rates remained significantly different between the two groups. Error bars are omitted for clarity. The number of procedures at risk at each time interval is shown below the figure. Standard error did not exceed 10% at all time intervals that were analyzed.

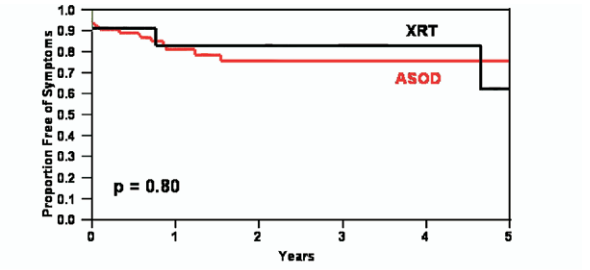


Years	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
ASOD	90	55	25	16	13	8	6	6	3	3	3
XRT	19	13	10	8	6	5	4	3	3	2	0

Fig 3. Vessel patency. No patient (0%) with atherosclerotic occlusive disease *(ASOD)* and two patients (8.6%) with radiotherapy-induced *(XRT) arteritis* occluded postoperatively ($P < .05$). The 3-year rates for freedom from occlusion were 100% for ASOD and 79% for XRT. Error bars are omitted for clarity. The number of procedures at risk at each time interval is shown below the figure. Standard error did not exceed 10% at all time intervals that were analyzed.

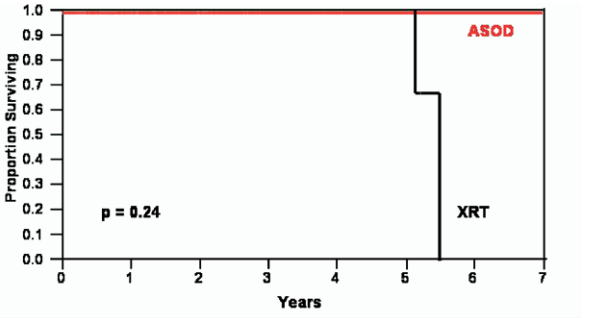
By Cox proportional hazard analysis, only prior head and neck irradiation (relative risk, 3.0) hypothyroidism (relative risk, 2.3), and insulin-dependent diabetes mellitus (relative risk, 2×10^{-6}) altered the rate of restenosis among patients; all other patient characteristics, comorbidities, and presenting symptoms were insignificant risk factors for increasing the likelihood of restenosis.

The respective symptom-free rate at 1, 2, and 3 years was 87%, 85%, 85% for ASOD, respectively, and 87%, 87%, 87% for XRT (Fig 4). During the entire length of follow-up, the rate of recurrent symptoms was 16% for ASOD and 17% for XRT (P = NS). Cerebrovascular accident ≤30 days of procedure did not differ between ASOD (9, 7%), and XRT (2, 9%; P = NS). Only one death, which was in the ASOD group, occurred ≤30 days of the procedure (P = NS) (Fig 5). Only one ASOD patient (1%) required reintervention, whereas three XRT patients (13%) underwent reintervention ($P < .05$). The three XRT patients were stented again, and the one ASOD patient underwent a common carotid cut-down and cryoplasty. Two of the reinterventions were for in-stent restenosis, and the third was for 99% stenosis proximal to the stent. The three patients that required reintervention all had excellent anatomic outcomes on final postoperative imaging during the original procedure. All three patients were asymptomatic before reintervention. Assisted patency rates remained significantly different between the two groups (Figs 2 and 3).



Years	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
ASOD	127	72	35	25	17	11	7	6	3	2	2
XRT	23	13	10	10	10	8	8	4	4	4	2

Fig 4. Freedom from recurrent symptoms. Twenty patients (16%) with atherosclerotic occlusive disease *(ASOD)* four patients (17%) with radiotherapy-induced *(XRT)* arteritis experienced recurrent symptoms postoperatively (P = NS). Error bars are omitted for clarity. The number of procedures at risk at each time interval is shown below the figure. Standard error did not exceed 10% at all time intervals that were analyzed.



Years	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
ASOD	127	75	40	30	21	12	8	7	4	3	3
XRT	23	15	12	11	10	8	8	4	4	3	3

Fig 5. Patient survival. One patient (1%) with atherosclerotic occlusive disease *(ASOD)* and two (9%) with radiotherapy-induced *(XRT)* arteritis died during follow-up (P = NS). Error bars are omitted for clarity. The number of procedures at risk at each time interval is shown below the figure. Standard error did not exceed 10% at all time intervals that were analyzed.

DISCUSSION

General. Patients with a past history of head and neck irradiation are thought to be poor candidates for CEA owing to the loss of fascial planes from radiation-induced

Table VI. Carotid artery stenting for radiation-induced stenosis—literature review

	Houdart et al[18]	*Ting et al*[20]	*Harrod-Kim et al*[21]	*Al-Mubarak et al*[19]
Patients (N)	7	16	16	14
EPD	2/7	*	0/16	*
Peri-op mortality	0/7	0/16	1/16	0/14
Peri-op morbidity	1/7	4/16	2/16	1/14
Stroke rate	0/7	1/16	1/16	1/14
Freedom from recurrence	100%	100%	82.4%	79%
Patency	100%	100%	88%	100%
Reintervention(s)	0	1	3	0
Follow-up (months)	Mean: 8	Median: 30	Mean: 28	6

EPD, embolic protection device

Table VII. Carotid endarterectomy for radiotherapy-induced stenosis—literature Review

	Kashyap et al[14]	*Leseche et al*[15]	*Friedell et al*[13]	*Rockman et al*[16]
Patients (N)	24	27	10	10
Peri-op mortality	0/24	1/27	0/10	0/10
Peri-op morbidity	10/24	3/27	0/10	2/10
Stroke rate	0/24	0/27	0/10	1/10
Freedom from recurrence	21/24	24/27	9/10	10/10
Reintervention(s)	1	2	0	0
Patency rate	96%	100%	90%	100%
Follow-up	1-156 months	Mean: 40 months	Mean: 37 months	1-5 year

fibrosis. Multiple studies have found an increased prevalence of carotid artery stenosis among patients who previously underwent head and neck radiotherapy.[1-5] The proportion of patients who were previously irradiated and later developed significant carotid stenosis ranged from 18% through 7.5 years of follow-up as reported by Brown et al,[1] to 40% through 10 years of follow-up as reported by Steele et al.[4]

The literature is conflicting on whether endovascular stenting or endarterectomy/bypass is most effective (Tables VI and VII). Some reports indicate CEA for previously irradiated patients is acceptable and results in the same outcomes as for nonirradiated patients.[13-16] Friedell et al[13] reviewed their experience in treating 13 previously irradiated patients with CEA for carotid artery stenosis. There were no perioperative deaths, cranial nerve injuries, or cerebral infarctions, and after an average follow-up of 37 months, all remained living and asymptomatic, with one vessel occlusion. Kashyap et al[14] treated 24 previously irradiated patients. They also found no perioperative deaths or cerebral infarctions, and over the course of follow-up, no CVAs, one occlusion, two restenoses, and one reintervention occurred.

In the largest study, by Lesèche et al,[15] 27 previously irradiated patients were followed-up and one perioperative death owing to hemorrhage and one TIA occurred. All patients remained asymptomatic throughout follow-up, and the risk of recurrent stenosis at 18 months was 16.6%, with two vessels requiring reintervention.[15] Rockman et al treated nine previously irradiated patients with the following outcomes: no perioperative mortality, one perioperative stroke, one procedural complication (a carotid artery pseudoaneurysm), and no signs of recurrent stenosis during follow-up.[16] A recent Cochrane Systematic Review concluded no significant difference between major risk of treatment for CAS and CEA.[17]

Meanwhile, other authors suggest carotid stenting is safe and comparable to surgical intervention for radiotherapy-induced stenoses. Both Houdart et al,[18] who monitored seven XRT patients for a mean of 8 months, and Al-Mubarak et al,[19] who monitored 14 XRT patients for 6 months, found 100% of the patients free of restenosis and no reinterventions performed during the course of follow-up. Ting et al[20] and Harrod-Kim et al[21] both monitored 16 XRT patients for 30 and 28 months, respectively, and found the freedom from recurrence was 82.4% and 79%, respectively. Our findings differ greatly. With a mean follow-up of 14.4 months, 57% of our XRT patients were free from restenosis.

We sought to find a reason why our restenosis rates differed from these authors. There was no difference in defining restenosis as >50%. The difference between our findings and those of Houdart et al[18] and Al-Mubarak et al[19] could result from the differences in length of follow-up. Houdart et al lost 36% of their patients to follow-up, whereas our rate, at 17%, was less than half. Their patients may not have been given enough time to restenose; however, Ting[20] and Harrod-Kim[21] both monitored their patients for twice the duration and found freedom of recurrence rates for their XRT patients to be comparable with our ASOD patients.

We differed with Ting et al[20] in our inclusion of technical failures as immediate restenosis. By excluding technical failures, our restenosis rate drops to 39%, and Ting et al, when including technical failures, increases to 22%. Harrod-Kim et al[21] calculated their freedom from restenosis based on the number of occlusions out of total vessels stented. If a patient had the CCA and ICA stented, then we would view this intervention as having the potential for one future restenosis, rather than two vessels with the potential to restenosis. The interventions for our 23 XRT patients were 10 ICA only, six CCA only, and six CCA and ICA. Thus, 28 vessels were stented, and our restenosis rate would become 36% when including technical failures, and 32% when not including technical failures. Our reported 43% restenosis rate for XRT patients does drop when we apply the same approach as the mentioned authors, but a significant difference still exists between our ASOD and XRT patients regardless of the approach taken. This difference between ASOD and XRT patients was not examined by the previous four studies. Although our XRT restenosis rates are higher than the 0% to 21% reported elsewhere, these studies do not provide a baseline restenosis rate for their ASOD patients.

With the idea of whether a true group of high-risk patients exists, for whom CEA may not be ideal for and thus should be managed endovascularly, we found it pertinent to determine our effectiveness in endovascularly treating a subset of the high-risk group, irradiated patients.[22]

Procedural events. Four of the five technical failures were the result of vessel tortuosity, and the fifth procedure was terminated owing to the fear of disrupting the extensive plaque formation and the patient exhibiting severe nausea and retching. No difference existed in the success rate of embolic protection device deployment between the two groups. However, XRT patients were significantly more likely to not have deployment of an embolic protection device attempted, 48% (XRT) vs 14% (ASOD). Some of this reflects that fact that these patients were treated before the clinical release of embolic protection devices.

Others have found XRT patients to exhibit a higher prevalence of bilateral disease and a higher rate of CCA lesions.[3] We did not find a significant difference between the two groups with respect to CCA lesions; however, we did find the XRT patients to have more extensive disease within the carotid artery (ie, involving both the ICA and CCA). The only significant factor for predicting postoperative stroke was if an attempt to deploy the embolic protection device was unsuccessful. A successful deployment of an embolic protection device was not seen as protective, and not attempting placement of an embolic protection device was not seen as a risk factor for postoperative stroke. No differences existed between the two groups with regards to systemic complications, regional complications at the carotid artery and brain, or local complications at the access site.

Although not significantly different from the ASOD group, none of the XRT patients became hypotensive during the procedure. Perhaps this was due to the lack of lesions at the carotid bulb in the XRT group, or that the previous cervical irradiation damaged the glossopharyngeal and resulted in a loss of the baroreceptor reflex. Our two most common perioperative complications, bradycardia (13%) and hypotension (9%), were roughly half the rate in previous reports.[23,24] Among the patient comorbidities screened, only hypothyroidism differed significantly between the two groups. A greater proportion of hypothyroid patients (65%) were in the XRT group vs the ASOD group (17%), which was expected owing to the XRT patients' previous history of neck irradiation.

Cumulative patency. No significant difference was found in the proportion of technical failures between the two groups; however, even if the technical failures are excluded from analysis, the freedom from restenosis still differs significantly between ASOD and XRT patients. One ASOD patient (1%) required reintervention at 3.4 years after operation, and the vessel remained patent at the last follow-up. Meanwhile, three XRT (13%) patients required reintervention at 0.08, 0.89, and 4.26 years after operation. All three patients restenosed again for a second time, and one required reintervention for a second time. It is of interest that despite a roughly threefold greater rate in vessel restenosis and a significant difference in reintervention rates, no difference existed in rate of recurrent symptoms between groups.

The rates for freedom from recurrent symptoms at 1, 2, and 3 years were, respectively, 87%, 85%, 85% for ASOD, and 87%, 87%, 87% for XRT (P = NS). Of the patients experiencing recurrent symptoms, CVAs occurred in 13, TIAs in 4, both upper extremity paresthesia and episodes of aphasia in 2, and 1 patient each had perioperative CVA and later a left homonymous hemianopsia, loss of auditory function, upper extremity paresthesia, and an episode of aphasia.

There have been discussions that the current guidelines for evaluating in-stent restenosis are insufficient and overestimate restenosis.[10,25] Because all of our patients were stented, both groups should be equal in the proportion of overestimates. We chose to follow recommendations from Stanziale et al[10] and used $\geq$225 cm/s and an ICA/CCA $\geq$2.5 as the cutoffs for $\geq$50% stenosis.[10] Using the new criteria, five ASOD and one XRT patient were excluded from the restenosis population, resulting in 9% of ASOD and 39% of XRT patients restenosing ($P < .05$).

CONCLUSION

Technical failure and 30-day event rates are similar among ASOD and XRT patients. CAS is equally as effective in preventing recurrent symptoms in XRT patients as in ASOD patients. However, XRT patients show increased rates of restenosis, reintervention, and occlusion. CAS for radiation arteritis has poor long-term anatomic outcome and can present with late occlusions. These findings suggest that these patients require closer postoperative surveillance and raise the question of whether CAS is appropriate for carotid occlusive lesions caused by radiation arteritis.

AUTHOR CONTRIBUTIONS

Conception and design: CDP, AMB, MGD
Analysis and interpretation: CDP, AMB, MGD
Data collection: CDP, AMB, MGD
Writing the article: CDP, AMB, MGD
Critical revision of the article: CDP, AMB, MGD, WAS, KAI, DLW
Final approval of the article: CDP, AMB, MGD, WAS, KAI, DLW
Statistical analysis: CDP, AMB, MGD
Overall responsibility: CDP, AMB, MGD

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