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Influence of the Hostile Neck on Restenosis after Carotid Stenting

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Abstract

INTRODUCTION—Carotid artery stenting (CAS) for carotid stenosis is favored over carotid endarterectomy (CEA) in patients with a hostile neck from prior CEA or cervical irradiation (XRT). However, the restenosis rate after CAS in patients with hostile necks is variable in the literature. The objective of this study was to quantify differences in the ISR/occlusion and re-intervention rates after CAS in patients with and without a hostile neck. Here we hypothesize that patients with hostile necks have an increased ISR, and that this increase may add morbidity to these patients.

MATERIALS AND METHODS—All patients undergoing CAS from 2007 to 2013 for carotid artery stenosis with follow-up imaging at our institution were queried from our carotid database (N=236). Patients with hostile necks, including both CAS after prior CEA (N=65) and prior XRT (N=37), were compared to patients who underwent CAS for other reasons including both anatomical (N=46) and medical comorbidities (N=88). The primary end points were in-stent restenosis (ISR), repeat intervention, and stent occlusion. Secondary endpoints of the study were stroke/MI/death at 30 days, perioperative CVA, TIA, MI, groin access complications, hyperperfusion syndrome, and periprocedural hypotension or bradycardia.

RESULTS—Despite the hostile neck cohort being younger and having lower incidence of COPD, CAD, and renal insufficiency, they had a greater incidence of ISR (11% versus 4%; $P=.03$) and required more re-interventions (8% vs. 2%; $P=.04$). Stent occlusion and peri-procedural morbidity/mortality were not different between groups.

CONCLUSIONS—Patients with hostile necks have increased risk of restenosis and need for re-interventions after CAS compared to patients without a hostile neck. However they do not appear to have higher rates of stent occlusion or per-procedural events.

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Introduction

Stroke is a major cause of morbidity and mortality for patients with vascular disease, and the fourth leading cause of death in the United States. Carotid endarterectomy (CEA) is the gold standard therapeutic intervention for patients with symptomatic carotid stenosis of 50% or greater^{1,2}. Recently large trials have established carotid artery stenting (CAS) to be an alternative therapeutic option for treating carotid artery stenosis which may be less taxing on the heart than CEA under general anesthesia^{3–7}.

CAS is a particularly attractive option in patients with prior cervical irradiation (XRT) or a history of ipsilateral carotid endarterectomy because of the technical challenges of open surgery in these patients with “hostile necks.” Here patients with “hostile necks” undergoing CEA, have higher rates of cranial nerve palsy and longer operative times^{8,9}.

The literature to date has not clearly defined the risk of in stent restenosis (ISR) in patients undergoing CAS for patients with 1) prior neck irradiation or 2) restenosis after prior CEA (“hostile necks”) compared to patients who undergo CAS for other reasons. Overall ISR ranges from 3–17% in the literature^{10,11}.

The objective of this study was to quantify differences in the ISR/occlusion and re-intervention rates after CAS in patients with and without a hostile neck. Here we hypothesize that patients with hostile necks have an increased ISR, and that this increase may add morbidity to these patients.

Materials and Methods

Medical records of consecutive patients undergoing CAS from a single institution’s experience were collected in an IRB-approved database and analyzed for this study. Patient demographics, imaging, indications for treatment, and perioperative and postoperative outcomes were queried and compared between patients undergoing CAS with and without a hostile neck, defined here as prior neck irradiation or CAS after post-CEA restenosis. (Fig 1)

Both symptomatic and asymptomatic patients with atherosclerotic occlusive disease were included in the analysis. We excluded from the analysis, patients undergoing CAS for aneurysmal disease, rupture, dissection, and pseudoaneurysms and patients who did not have follow-up imaging at our institution.

Carotid duplex ultrasound (CDUS), magnetic resonance arteriography, digital subtraction arteriography (DSA), or computed tomography arteriogram imaging was used to evaluate patients for ISR postoperatively. All patients who followed up at our institution had CDUS at one month, six-months, and one year post-procedure. In the absence of changes in symptomatology or velocity, patients underwent annual duplex ultrasound surveillance thereafter. The last imaging study in the patient’s record or the last study prior to re-intervention was analyzed for ISR. ISR was defined as >70% cross sectional stenosis by arteriography or having peak systolic velocity (PSV) >230cm/s and end diastolic velocity (EDV) >100cm/s by CDUS. Primary end points of this study were ISR, repeat interventions, and stent occlusion. Secondary endpoints were death within 30 days, TIA/CVA within 30

days, hyperperfusion syndrome, or groin complications. All patients undergoing repeat intervention first had selective carotid angiography to confirm the ISR. Repeat intervention was performed for asymptomatic patients with confirmed ISR >80% or for symptomatic patients with ISR >50%. This criteria was used for both hostile neck and the non-hostile neck group. Once confirmed, patients underwent either conventional balloon angioplasty or repeat CAS. All reinterventions utilized embolic protection devices.

Chi-square and Fischer's exact test were used for statistical analysis of categorical variable. Students t-test was used for continuous variable analysis. P-values of <0.05 were used to define statistical significance.

Results

466 CAS procedures were performed between February 2007 and July 2013. 67 of the 230 patients without follow-up in our system had hostile necks. 236 of these patients had follow-up imaging in our institution and were included in the analysis. 90% of the hostile neck patients and 96% of the non-hostile neck patients had duplex ultrasound as the follow up imaging modality ($P=0.55$). Of the procedures with follow up imaging available 201 (85%) were performed by vascular surgeons and the other 35 CAS were performed by interventional cardiologists or interventional radiologists.

There were significant differences between the patients undergoing CAS with a hostile neck compared to the non-hostile neck patients. The hostile neck patients were younger ($p=0.002$) and there was a trend for them having a longer mean follow-up (12.7 months vs. 9.3 months; $P=.07$). Since medical indications for CAS were commonly encountered, the increased prevalence of medical comorbidities in the non-hostile neck patients compared to hostile neck patients was not surprising. (Table I) 42% of both the hostile and non-hostile neck groups were symptomatic at time of presentation. Preoperative medications and all other recorded demographics were similar between the two cohorts.

The rate of ISR was significantly increased in patients with hostile necks compared to those without ($N=12$ vs. 5 respectively, $P=0.02$). They were also more likely to undergo repeat interventions ($N=8$ vs. 3 respectively, $P=0.04$). (Table II) High-grade carotid stenoses ranging from 76–90% was confirmed on DSA at the time of re-intervention. For patients with repeat CAS, there was no difference in symptomatic versus asymptomatic presentation or degree of stenosis at the time of initial CAS between the two groups ($P>.05$). Furthermore, there was no difference in symptomatic versus asymptomatic presentation at the time of reintervention ($N=3$ vs. 1 respectively). (Table III)

In the hostile neck cohort three patients with ISR (25%) presented with symptoms at the time of reintervention and one of the patients in the non-hostile group (20%) presented with symptoms (NS). Best medical management was similar between the two groups who had ISR or repeat interventions ($P=1$ and 0.5 respectively). Of the three patients who were symptomatic at the time of re-intervention, only one was not on a statin. This was intentional due to prior adverse reaction to statins. The one patient who presented in the non-hostile neck group with symptoms was also compliant with best medical management. (Table II)

There were no significant differences in perioperative death, MI, CVA rates, hyperperfusion syndrome, bradycardia/hypotension or groin complication between the two groups. (Table IV)

Discussion

This is the largest series in the literature to date evaluating the ISR and reintervention rate of CAS in patients with a history of XRT or CAS after CEA restenosis. Here we demonstrate an increased ISR (11%) and reintervention (8%) rate in the hostile neck population compared to that of patients undergoing CAS for other reasons. However, this increase did not lead to increased rates of stent occlusion or perioperative morbidity.

Others have attributed risk of ISR to the hostile neck^{10–13}, but to our knowledge this is the first report demonstrating an increased rate of ISR and re-intervention in patients with a hostile neck compared to patients without hostile necks. Cam et al. recently published a case series of CAS procedures in irradiated necks and had results similar to our study with ISR rate of 10.8% with a 47 month mean follow-up¹⁴. However Cam et al. did not analyze patients without cervical irradiation and therefore lacked comparative data. Fokkema et al. performed a systematic literature search and evaluated patients with irradiated necks and compared patients undergoing CAS to those undergoing CEA. In this study the ISR rates in the CAS group varied from 12–43% and were significantly worse than restenosis after CEA. This study did not examine non-hostile necks undergoing CAS and therefore conclusions regarding ISR and repeat intervention could not be drawn from this data. However, and similar to our study, this search found that most patients with ISR presented without symptoms¹⁵. This study has a number of limitations that should be considered when interpreting the results. There were a significant number of patients undergoing CAS who did not have follow-up imaging in our institution. While we are a referral center for patients requiring CAS, the incorporation of outside imaging into our data set would be very helpful in increasing the confidence of these results. However, our institutional review board approval only covers data acquired at our own institution, and the results of outside imaging were not collected from the various referral centers for this study. Additionally, while there was a trend toward decreased duration of follow-up in the non-hostile neck cohort, this did not reach statistical significance and represented an absolute difference of only 3 months. Thus this trend is unlikely to have a significant impact on our results. Further our database includes data entered retrospectively over a number of years and by a variety of practitioners. Here the real-world nature of patient selection and clinicians may actually increase the usefulness of this report to clinicians. Finally while there are no standard and universally accepted duplex velocity criteria for stented carotid arteries and the literature on duplex US of the stented carotid varies, there is literature supporting the need for establishing and validating velocity criteria in each individual vascular lab¹⁶. Lal et al compared DUS to CTA and Carotid angiograms after carotid stenting and found PSV>220cm/s and ICA/CCA ratio >2.7 correlated with a >50% ISR¹⁷. Zhou et al also examined this topic by comparing DUS velocities to carotid angiograms and found an EDV >90cm/s had a 89% sensitivity, 100% specificity, 100% positive predictive value and 67% Negative predictive value for a >70% ISR¹⁸. Because most ISR estimates in this study were made by duplex, without formal validation, overestimation of ISR is a possibility. However most

patients identified by duplex criteria with ISR underwent carotid angiography at the time of repeat intervention. Here there were no patients identified without high grade restenosis (>75%). This data has been used to validate our vascular laboratory's criteria and gives us confidence that the ISR rates identified in this study are real. Despite these limitations, our study is still the largest series to date and because we are the referral center for these patients, improved adherence to imaging protocols within our institution or improved collaboration with our referring physicians may only increase the statistical confidence of the results.

Conclusions

Patient's with hostile necks undergoing CAS are at an increased risk of restenosis and re-interventions. However this subgroup of patients does not have increased perioperative morbidity or mortality compared to those undergoing CAS for other indications. CAS in the hostile neck population would likely still benefit over CEA due to the decreased risk of cranial nerve injury and complexity of repair. However, the durability of CAS in patients with hostile necks may be decreased compared to patients without hostile necks. The role of medical therapy alone in this population is not known, but may be reasonable in asymptomatic patients with hostile necks.

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Fig. 1.

Table I

Patient Demographics at time of primary CAS

Variable	CEA/XRT	No history of CEA/XRT	P Value
<i>Demographics</i>			
Patients (No.)	102	134	
Age (mean, range)	66 (47–88)	70 (45–88)	0.0016
Gender (M; mean)	72 (70)	83 (62)	0.17
Follow up (mean Mo., std dev)	12.7 (16.5)	9.3 (11.6)	0.07
Symptomatic (N, %)	42 (42)	56 (42)	1
<i>Comorbidities (N, %)</i>			
Smoking	37 (45)	40 (43)	0.88
Diabetes	29 (29)	54 (42)	0.05
HTN	84 (82)	121 (92)	0.04
HLD	69 (69)	93 (72)	0.78
CKD	4 (4)	19 (15)	0.01
COPD	10 (10)	28 (23)	0.01
CAD	28 (27)	77 (57)	<0.001
CHF	6 (6)	17 (14)	0.08
<i>Post-operative Treatment (N, %)</i>			
ASA	78 (78)	111 (86)	0.12
Plavix	98 (98)	128 (98)	1
Statin	60 (65)	81 (69)	0.66
Coumadin	4 (4)	9 (7)	0.4

Table II

Primary Endpoints

End Point	Hostile Neck		No Hostile Neck		P Value
	<i>XRT</i> (N=37)	<i>CEA</i> (N=65)	<i>Unfavorable Anatomy</i> (N=46)	<i>Medical Comorbidities</i> (N=88)	
Repeat Intervention					
(N,%)	3 (8)	5 (8)	1 (2)	2 (1)	0.04
Average Restenosis					0.58
(N)	83(3)	79(5)	76(1)	90(2)	
Symptomatic (%)	0(0)	3(60)	0(0)	1(50)	1
Dual Antiplatelet (At time of Reintervention)					
And Statin	3(100)	3(60)	1(100)	2(100)	0.5
In-stent Restenosis (PSV>230 EDV>100)					
(N,%)	3 (8)	9 (14)	1 (2)	4 (5)	0.02
Dual Antiplatelet (At time of ISR)					
And Statin	3(100)	7 (78)	1 (100)	3 (75)	1
Stent Occlusion					
(N,%)	1 (3)	1 (2)	0 (0)	1 (1)	0.4

Table III**Preoperative Demographics by Group**

End Point	Hostile Neck		No Hostile Neck		P Value
	XRT (N=37)	CEA (N=65)	Unfavorable Anatomy (N=46)	Medical Comorbidities (N=88)	
Symptomatic					
N (%)	17(46)	27(41)	16(35)	40(45)	0.89
Imaging Modality					
N (%)					
CDUS	33(89)	58(89)	32(96)	84(95)	0.55
CTA	3(8)	5(8)	0(0)	3(3)	0.06
MRA	0(0)	1(2)	1(2)	1(1)	1
Arteriogram	1(3)	1(2)	1(2)	0(0)	0.58

Table IV

Secondary Endpoints

End Point	Hostile Neck		No Hostile Neck		P Value
	XRT (N=37)	CEA (N=65)	Unfavorable Anatomy (N=46)	Medical Comorbidities (N=88)	
N (%)					
Stroke/MI/Death (30 days)	0 (0)	2 (2)	0 (0)	4 (3)	0.7
Death (30 Days)	0 (0)	1 (1)	0 (0)	0 (0)	0.43
CVA (30 Days)	0 (0)	1 (1)	0 (0)	4 (5)	0.28
TIA (30 Days)	0 (0)	0 (0)	2 (2)	0 (0)	0.32
MI (30 Days)	0 (0)	0 (0)	0 (0)	0 (0)	1
Access Issues	0 (0)	0 (0)	0 (0)	3 (2)	0.18
Cerebral Hyperperfusion	2 (2)	1 (1)	0 (0)	0 (0)	0.08
Bradycardia Hypotension	3 (3)	1 (1)	1 (1)	7 (5)	0.34