AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
2015, Vol. 153(2) 225–230

DOI: 10.1177/0194599815586719
http://otojournal.org
SAGE

Carotid Artery Sacrifice and Reconstruction in the Setting of Advanced Head and Neck Cancer

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No sponsorships or competing interests have been disclosed for this article.

Abstract

Objective. To determine oncological and neuromorbidity outcomes in patients with advanced head and neck cancer (stage IVB) requiring sacrifice and reconstruction of the carotid artery.

Study Design. Case series with chart review.

Setting. Tertiary care referral center.

Subjects and Methods. Overall, 51 patients underwent carotid artery sacrifice during surgical treatment of the neck, in both the primary and salvage setting. All patients underwent autogenous in-line carotid artery bypass grafting with either saphenous vein or the deep femoral vein in conjunction with vascular surgery. In all, the study included 39 males and 12 female subjects, with age ranging from 39 to 82 (mean, 62.7).

Results. Two patients (3.9%) had a cerebral vascular accident in the immediate postoperative period. The remaining 49 patients (96%) had no neurologic sequela. Serial ultrasonic evaluation revealed 4 patients with intra-luminal thrombus within the site of reconstruction. Perioperative mortality occurred in a single patient. Disease-related mortality occurred in 9.8% (5) of patients, with an overall 2-year survival of 82%.

Conclusions. We presently report the largest series of surgical treatment for advanced head and neck cancer with carotid artery involvement. We document an overall 2-year survival of 82% in the setting of low perioperative neuromorbidity and mortality rates. We therefore consider carotid artery sacrifice and autogenous vein graft reconstruction in the absence of distant metastatic disease as a viable treatment option for what was once thought to be a palliative procedure.

Keywords

carotid artery sacrifice, radical neck dissection, head and neck cancer, squamous cell carcinoma, unresectable disease

Received November 17, 2014; revised March 18, 2015; accepted April 23, 2015.

Introduction

Staple to the management of head and neck cancer is the ability to obtain clear resection margins in an attempt to control loco-regional disease. The management of advanced head and neck squamous cell carcinoma with carotid artery involvement, however, presents a challenge to many head and neck surgeons. Several management options are available, underpinned only by the potential for severe neurologic complications. Nonsurgical treatment options include radiation therapy in combination with chemotherapy, interstitial radiation brachytherapy, or a combination of these modalities. Surgical options include carotid artery stripping, resection of the carotid artery with reconstruction, or resection of the carotid artery without reconstruction.[1-6]

In consideration of surgical options, stripping of the arterial wall was advocated by authors who identified clean planes of resection.[1,7-9] However, later histopathologic studies of carotid artery specimens demonstrated microscopic invasion of the arterial wall in more than 40% of specimens.[3,4,10-14] The presence of such microscopic disease may lead to increased rates of recurrence and inferior oncologic outcomes.[4,14-17] Furthermore, stripping or shaving of the carotid arterial wall may weaken the artery, predisposing to rupture, particularly in the setting of radiation or in the presence of salivary fistula or infection.[1,3] The use of autogenous venous grafting in the reconstruction of the carotid artery was first described by Conley[1] in 1953 utilizing the superficial femoral vein and the great saphenous vein. More recent publications indicate improved morbidity and mortality rates with autogenous venous and arterial grafting.[3,4,10,13,14]

Consensus regarding the management of carotid artery involvement and reconstructive methods remains elusive.

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Studies evaluating long-term postoperative outcomes following carotid artery sacrifice are limited in size and follow-up data. We currently present the largest study series evaluating the en bloc removal of the carotid artery with autogenic venous graft reconstruction. We evaluated overall graft success rate, neurologic outcomes, as well as oncological outcomes following the procedure.

Materials and Methods

Following John Peter Smith Hospital Institutional Review Board approval, a single surgeon retrospective case series with chart review was performed from 1997 to 2014. In total, 2040 neck dissections were performed during this time period. The subset of patients undergoing en bloc tumor resection with carotid artery sacrifice were further reviewed. Study design included only patients with either primary or recurrent head and neck squamous cell carcinoma, with extensive neck disease without evidence of distant metastatic disease during presurgical evaluation. All patients who underwent sacrifice of the common carotid or internal carotid artery were identified. The anticipation for carotid artery sacrifice was based on preoperative imaging (computed tomography [CT] or magnetic resonance imaging [MRI]) or in the presence of clinically suspicious involvement (Horner's Syndrome, fixation). Furthermore, it is our institutional practice to always anticipate and plan for the need for carotid artery sacrifice in all cases of advanced head and neck disease in the presence of significant neck metastases. Vascular surgery is routinely consulted and involved in the care of these patients.

A preoperative carotid duplex was obtained prior to surgical resection. In addition, vein mapping of the deep and superficial veins of the lower extremities was done with ultrasonography if the deep femoral vein was to be utilized. Absence of distant metastatic disease was verified on whole body positron emission tomography (PET)-CT evaluations or in conjunction with CT neck and chest along with normal liver function tests. Preoperative CT angiography or balloon occlusion testing is not done due to rates of false negatives and potential for serious sequelae.[4,14,16] Furthermore, balloon occlusion studies do not alter intraoperative management. For example, in the event that patients demonstrate adequate collateral perfusion, carotid artery reconstruction would still be performed due to the possibility of a false negative study.

All patients were reconstructed with autogenous venous grafts following carotid artery sacrifice. The decision for en bloc resection of the carotid artery was performed intraoperatively, in the presence of gross carotid wall involvement, with an inability to achieve free dissection in a subadventitial plane. Patients undergoing the procedure from 1997 to 2007 were reconstructed with a saphenous vein graft. From 2007 onward, reconstruction was performed utilizing the superficial femoral vein. If sternocleidomastoid muscle resection was performed in conjunction with arterial sacrifice, in-line carotid bypass grafts were subsequently covered with regional flaps (ie, trapezius or pectoralis major). During carotid artery clamping, all patients received systemic anticoagulation with weight-based heparin, at a dose of 100 units per kilogram, beginning 5 minutes prior to arterial clamping. A carotid arterial shunt was also used during the creation of the bypass to maintain cerebral perfusion. Protamine reversal was given after the bypass was completed. Intraoperative Doppler assessment was used on the bypass to assess patency after the reconstruction was completed. Postoperatively, patients were placed on perioperative antibiotics and subcutaneous heparin for deep venous thrombosis (DVT) prophylaxis.

Basic demographic information was collected, including age and gender. Oncologic parameters including treatment history, head and neck subsite, nodal stage, disease stage, and human papillomavirus (HPV) status were determined. Long-term oncologic follow-up data were also analyzed, including survival and disease outcomes. Operative resection and reconstruction details, including type of flap coverage (if any) was also considered. All potential perioperative neuromorbidity and mortality outcomes were further assessed. Ultrasonic evaluation of the reconstructed in-line bypass was performed 1 to 2 months postoperatively and every 6 months thereafter for 1 year to assess for patency.

Results

In total, 51 patients with primary or recurrent head and neck squamous cell carcinoma had undergone carotid artery sacrifice and reconstruction with autogenous vein grafting. The study included 39 male and 12 female subjects, with ages ranging from 39 to 82 (mean, 62.7). Primary surgery was performed in 41 patients (**Table 1**). All 41 patients received subsequent external beam radiation treatment of at least 60 Gy. Further chemotherapy was given as adjuvant therapy to only 30 patients (11 patients received erbitux, and 19 received cisplatin/5FU). The remaining patients did not receive chemotherapy due to coexistent medical comorbidities as well as patient preferences. Salvage surgery was performed in the remaining 10 patients. Of these, 7 patients had only received single modality definitive radiation therapy. The remaining patients had previously received chemoradiation, 2 of which received cisplatinum/5FU, while the other patient received erbitux.

Of the 51 patients, 12 patients had carotid artery resection in conjunction with resection of primary site lesions. The remaining 39 patients underwent isolated carotid artery resections without surgical resection of the primary site. The common carotid artery was sacrificed in 42 patients and included only the internal carotid artery in the remaining 9 patients. The external carotid artery was resected in 47 patients due to locally advanced disease. In total, 38 patients underwent carotid artery reconstruction with a saphenous vein graft, and 13 patients underwent reconstruction with the deep femoral vein (**Table 2**). In all, 42 patients underwent regional flap coverage, either with a trapezius muscle flap (28) or pectoralis major muscle flap (14).

In total, of the 51 patients undergoing reconstruction, 3.9% of patients (2) had a cerebral vascular accident (CVA) in the immediate postoperative period. One patient

Table 1. Demographic Information of the 51 Patients Undergoing Carotid Artery Sacrifice and Reconstruction.

Patient Characteristic	Total (n)
Gender	
Male	39
Female	12
Previous therapy	
None	41
Adjuvant therapy	
Radiation	11
Chemoradiation	30
Radiation	7
Chemoradiation	2
Primary site	
Oral cavity	9
Oropharynx	18
Hypopharynx	6
Larynx	12
Cervical esophagus	2
Maxilla	1
Unknown	3
Clinical staging	
IVB	51
Nodal staging	
N3	51
Human papillomavirus status	
Positive	10
Negative	41

Table 2. Resection and Reconstruction Details during Arterial Carotid Artery Sacrifice.

Operative Detail	Total (n)
Procedure	
Isolated resection	39
With primary site resection	12
Arterial sacrifice	
Isolated ICA	9
CCA	42
Arterial reconstruction	
Saphenous vein	38
Deep femoral vein	13
Regional flap	
Pectoralis major	14
Trapezius/sternomastoid	28

Abbreviations: CCA, common carotid artery; ICA, internal carotid artery.

developed residual upper extremity weakness, while the second patient had profound hemiplegia. The remaining 49 patients (96%) had no neurologic sequela. Serial ultrasonic evaluation at 2 months postoperatively showed 4 thrombosed bypass grafts. Of these 4, one patient was reconstructed with the superficial femoral vein, while the remaining 3 patients had undergone saphenous vein grafts. Both CVA events were in the saphenous vein bypass group. Patient complications included 4 postoperative wound infections (7.8%) managed conservatively with antibiotics. Two of the 4 postoperative infections were in patients with thrombosed bypass grafts, but neither had any resultant complications. Furthermore, there were no reported incidences of salivary fistulas or carotid artery blowouts.

Patients were followed for a mean of 49 months (range, 1-108 months). The minimum follow-up for patients who did not die of unrelated causes was 2 years. In all, 5 patients died of disease related to their cancer. Two of the disease-related mortalities were in the primary surgery group, with the remaining 3 in the salvage surgical group. One patient developed recurrence within the neck and died of disease at 8.5 months following the surgery. The remaining 4 patients developed disseminated metastatic disease in the absence of local or regional neck recurrence and died at an average of 9.2 months following surgery (range, 5-13 months). Overall, 2-year disease-free survival was 82% within our patient series. One patient had died as a direct consequence of a CVA. Four other patients died of unrelated causes, including motor vehicle accident, unrelated myocardial infarction, and aspiration pneumonia. The aspiration pneumonia occurred more than 6 months postoperatively and was unrelated to neurologic sequelae related to carotid artery sacrifice.

Discussion

Advanced head and neck squamous cell carcinoma with involvement of the carotid artery are staged as IVB tumors. Traditionally, IVB tumors are considered surgically unresectable and subsequently have poor long-term survival. Typical management of IVB disease with carotid artery involvement involves chemoradiation therapy with surgery reserved for the salvage setting. However, some studies suggest that chemoradiation may result in an incomplete response in patients with advanced neck disease, with subsequent residual subclinical nodal disease.[18] Furthermore, large retrospective reviews have documented that the vast majority of metastatic disease occurs in the setting of locoregional recurrence, indicating the potential role for aggressive treatment of local and regional disease.[4,19]

Management of carotid artery involvement ranges from nonsurgical methods through the use of aggressive multimodality therapies with radiation and chemotherapy to the surgical extirpation of tumor. However, invariably long-term survival is directly linked to the ability to resect all tumor, achieving negative resection margins.[4,11] Surgical intervention ranges from directly peeling or shaving tumor from the arterial wall to en bloc carotid resection with or without reconstruction.[9,13-15,20,21] Potential for neurologic sequelae following carotid resection has led to the development of various reconstructive and bypass techniques to

Table 3. Comparing Survival Rates of Patient Cohorts to the Proportion of Patients Who Had Received Previous Treatment in the Form of Radiation or Chemoradiation.[a]

Study	Sample Size (n)	Previous Treatment (%)	1-Year Survival (%)	2-Year Survival (%)
Sessa et al[3]	30	67	60	31
Freeman et al[26]	47	93	40	<30
Biller et al[27]	23	100	25	10
McCready et al[25]	16	63	44	—
Okamoto et al[28]	6	100	44	—

[a]Only squamous cell carcinoma was included in the analysis.

attempt to ameliorate subsequent neuromorbidities and mortalities.

Tumor stripping provides a potential method for surgical removal of tumor while maintaining intact circulation to the central nervous system.[3,8-10,22] However, histopathologic analysis of carotid artery specimens following tumor stripping technique revealed microscopic disease within the arterial wall of the carotid artery.[10,12] This likely lends to the low survival outcomes associated with such surgical management. In 1977, Kennedy et al[15] reported a recurrence rate of 50% following surgical shaving.[10] This has led authors to attempt to predict the level of extraluminal tumor invasion based on the degree of encasement on CT scan for better preoperative evaluation and planning.[23,24] Yoo et al[23] found less than 1.8 mm depth of invasion in patients with less than 180° of carotid encasement, with a statistically higher overall survival.

However, such surgical manipulation of the carotid artery may weaken the adventitial lining, predisposing to postoperative complications, particular in the setting of post-radiation effects. Radiation-induced changes may result in arteritis, luminal obstruction, arterial aneurysm, and further wall weakening that may cause dreaded complications such as a carotid artery blowout.[2,5,6] Furthermore, such weakening to the arterial wall in close proximity to the aerodigestive tract may lead to increased rates of complications in the setting of wound breakdown, infection, and fistula.[4] Such suboptimal oncologic outcomes of tumor stripping in the setting of an increased risk for postoperative complications has led to the development of various techniques involving carotid artery sacrifice and reconstruction.

Oncological outcomes following carotid resection of stage IVB disease has been a question of debate. Management of advanced carotid disease may range and varies by institution. In a cohort analysis by Roh et al,[7] patients with carotid involvement were treated either palliatively, definitively with chemoradiation, or with carotid resection and reconstruction. No patients within the former 2 groups survived beyond 15 months, with patients in the sacrifice group demonstrating a 2-year survival of 24.5%. Other authors have reported a 2-year disease-free survival of up to 40%.[3,11] Meta-analysis performed by Snyderman and Damico[4] demonstrated a 2-year disease-free survival of 22%. They further determined that 77% of patients were free of metastatic disease.

Within our series, 5 patients died of disease related to their cancer. One patient developed regional recurrence in the neck and died of disease at 8.5 months following surgery. Four patients developed distant metastatic disease and died at an average of 9.2 months following surgery (range, 5-13 months). Overall, 2-year survival was higher within our series than most cases reported in the literature, calculated to be 82%.

The significantly higher survival rates within our study may be attributed to aggressive early surgical management of the advanced neck, as is common practice within our institution. Stage IVB disease is traditionally treated with chemoradiation, with surgery reserved in the salvage setting. However, despite clinical response to primary chemoradiation therapy, subclinical disease oftentimes may persist. Sabatini and Ducic[18] demonstrated active nodal disease in planned neck dissection specimens following chemoradiation even when patients were thought to have responded clinically. Furthermore, surgery in the salvage setting is more challenging due to radiation effects obscuring clean subadventitial dissection of the carotid artery, potentially compromising oncological outcomes. Therefore, rather than reserve aggressive surgery and potential carotid sacrifice in the setting of salvage therapy after failed chemoradiation, we propose performing aggressive initial surgical tumor extirpation followed by adjuvant therapy. Within our study, 41 (80%) of patients received aggressive neck dissections prior to any subsequent intervention. Of those 41, 2-year survival was calculated to be 88% (37/41).

The majority of patient case series reporting on carotid artery sacrifice involve cohorts with a significant proportion of patients having received prior radiation or chemoradiation (**Table 3**). These previously treated patient groups may be undertreated, consequently leading to suboptimal salvage surgery. In a study of 16 patients undergoing carotid sacrifice by McCready et al,[25] 1-year survival was determined to be 44%. However, in the subgroup of 6 treatment-naïve patients who underwent subsequent resection and adjuvant therapy, the disease-free 1-year survival was determined to be 67%.[25]

The potential morbidity and mortality resulting from carotid sacrifice have led some authors to attempt reconstruction following resection. In 1953, Conley[1] was the first to describe carotid artery reconstruction utilizing autogenous grafting material. In 1956, he described the technique in a

series of 17 patients, with a subsequent operative mortality of 41%.[1] It was not until 1981 that Lore and Boulos[10] described the enhanced survival outcomes associated with carotid artery reconstruction in 10 patients utilizing both saphenous vein grafts and Teflon grafts. No operative mortality occurred, with 2 patients (20%) having postoperative CVA. In a meta-analysis by Snyderman and Damico[4] in 1992, 22 case series were reviewed with carotid artery resection, of which 65% of patients had some form of reconstruction performed, either with autogenous graft material (82%) or alloplastic materials (7%). The remaining 11% underwent bypass anastamoses from the external carotid to the internal carotid system.[4] Of the 158 patients reviewed, major cerebral vascular accidents occurred in 17%, resulting in permanent morbidity. Transient neurological deficits were further observed in another with 10% of patients. To the surprise of the authors, no difference in neurologic outcomes was observed between ligation groups and reconstructed group. They, however, called for better risk stratification of patients based on collateral blood flow.[4] In Katsuno et al's[11] analysis of 11 series, including 148 patients, overall mortality was found to be 6.8%, and neurologic complications occurred in 4.7% of patients undergoing carotid sacrifice with reconstruction.

Within our series, all reconstructions were performed with venous autogenous grafts, either the greater saphenous vein, or the superficial femoral vein. Postoperative ultrasound revealed 4 thrombosed bypass grafts, 3 of which were from the saphenous vein group. Our series neuromorbidity and mortality outcomes are in line with that found within the literature, with a CVA rate of 3.9% (2 patients) and overall perioperative mortality rate of 1.9% (1 patient). All CVA events occurred in the saphenous vein group. It was also determined that all neuromorbidities and the single mortality occurred in our salvage surgery patients and not in the primary surgical group.

Due to unfavorable radiated soft tissue and potential for wound infection, some authors have attempted extracranial bypass techniques to the distal internal carotid artery system, circumnavigating the radiated field.[20,21] Other authors attempted to elucidate the ideal conduit to use in the reconstruction of the carotid artery.[3,10,22] Lore and Boulos[10] documented an increased rate of infection and fistulization putting the vessel graft at risk for exposure and subsequent anastamotic breakdown or occlusion.[2,4-6] In their study, there was a higher rate of autogenous graft occlusion compared to the alloplastic graft group. Lore and Boulos[10] recommended the use of alloplastic conduits.[7-9] Other authors have postulated that the use of arterial graft conduits may be more resistant to the inflammatory changes that induces intimal hyperplasia and fibrosis that may lead to venous graft thrombosis, particularly in the setting of wound infection and salivary fistula.[3,11,12,22] Sessa et al[3] documented a series of 30 patients with autogenous arterial graft, of which no suture line breakdown occurred, even in the setting of active wound infection and fistula, with only 1 documented case of late onset thrombosis.[4,15,17]

Within our study, we document a graft patency of 92% (47 patients) through the sole use of autogenous vein grafts. We had no subsequent persistent fistulas develop or any carotid blowouts. However, in 8% (4 patients) of the patients, wound infections developed that responded to conservative management with antibiotics. In 2 of these patients, the autogenous grafts thrombosed, but there were no neurologic sequelae. Utilization of a deep vein bypass in the latter part of this study allowed for a conduit that was both large caliber (better size match with the carotid artery) and durable (resistant to infection). The low rate of fistulization is likely due to the routine use of regional muscle flaps in the reconstructions.

Conclusions

Surgical management of advanced head and neck cancer with carotid artery involvement presents a surgical dilemma for the head and neck surgeon. Recent advances in carotid artery sacrifice and in-line reconstructive techniques by various methods have documented increased rates of survival and palliation in an otherwise virulent disease entity. Based on our study, we have demonstrated an overall 2-year disease-free survival of 82%, with an acceptable complication rate following carotid resection. Furthermore, due to the potential for incomplete response to conservative management with chemoradiation and its impact on surgical extirpation, we recommend initial surgical management of all advanced neck disease, followed by adjuvant medical therapy. We therefore consider carotid artery sacrifice and autogenous vein graft reconstruction, in the absence of distant metastatic disease, as a viable treatment option for what was once thought to be a palliative procedure.

Author Contributions

Moustafa Mourad, primary author, acquisition of data, drafting, final approval, accountability of all work; **Masoud Saman**, acquisition of data, drafting, final approval, accountability of all work; **David Stroman**, vascular surgeon, acquisition of data, drafting, final approval, accountability of all work; **Thomas Lee**, acquisition of data, drafting, final approval, accountability of all work; **Yadranko Ducic**, senior author, primary surgeon, acquisition of data, analysis of data, revision of draft, verifying intellectual and clinical concepts, final approval of manuscript, and accountability of all work.

Disclosures

Competing interests: None.

Sponsorships: None.

Funding source: None.

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