Impact of Surgical Resection on Survival in Patients With Advanced Head and Neck Cancer Involving the Carotid Artery

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IMPORTANCE The present study addresses the survival benefit of aggressive surgical treatment of head and neck cancer involving the carotid artery.

OBJECTIVE To assess survival outcomes in patients treated for advanced squamous cell carcinoma involving the carotid artery using different treatment strategies.

DESIGN, SETTING, AND PARTICIPANTS Retrospective study at a tertiary care center of 44 consecutive patients with squamous cell carcinoma involving the carotid artery from 2005 to 2012 with a median follow-up of 12 months. The radiologist was blinded to the outcome of surgical procedures.

INTERVENTIONS Surgery with or without radiotherapy, and definitive chemoradiation.

MAIN OUTCOMES AND MEASURES Overall survival and rates of locoregional and distant failures. The hypothesis was formulated before data collection.

RESULTS Of 44 patients, 35 (80%) were treated with curative intent with surgery with or without adjuvant therapy (n = 27 [61%]) or definitive chemoradiation therapy (n = 8 [18%]), while 9 patients (21%) were treated in a palliative fashion. Patients treated with curative intent had improved overall survival (median survival, 13.5 months) compared with the palliative group (median survival, 3.6 months) (P = .001). Of patients treated with curative intent, those with previously untreated disease (n = 14 [40%]) had an improved outcome relative to patients with recurrent or persistent disease (n = 21 [60%]), with median survival of 38.7 and 9.6 months, respectively (P = .008). Patients were treated with curative intent using 3 different treatment strategies (ie, carotid artery resection with or without reanastamosis) (n = 6 [17%]), curative peeling with or without adjuvant therapy (n = 21 [60%]), and definitive chemoradiation therapy (n = 8 [23%]). Survival outcome was not significantly different between subgroups treated with curative intention (P = .47). When reviewed by a head and neck radiologist in a blinded fashion (n = 30), preintervention imaging had a positive predictive value of 72.7% for resectability of cancer involving the carotid artery. In cases with almost circumferential involvement (>270°) and narrowing of the carotid artery, the disease was unresectable (n = 3).

CONCLUSIONS AND RELEVANCE Advanced head and neck cancer involving the carotid artery can be treated with curative intent with favorable results in most patients. If disease burden merits, an aggressive approach involving resection with or without reanastamosis of the carotid artery can be used without significant added morbidity.
Involvement of the carotid artery is a potential result of advanced squamous cell carcinoma of the head and neck, with an incidence of 5.5% of all patients treated with radical neck dissections in 1 series. It is associated with poor patient survival, with overall survival rates ranging from 22% to 35% at 1 to 2 years. Optimal treatment of these patients is unclear, as the survival benefit of aggressive surgical treatment has not been clearly established. Aggressive treatment of disease involving the carotid artery leads to better locoregional control of the disease.

Patients with squamous cell carcinoma involving the carotid artery represent a heterogeneous group. Carotid artery involvement occurs proportionally more often in patients treated for recurrent or persistent disease; however, a minority will present with this finding at the initial evaluation for previously untreated disease. Treatment strategies likewise vary, with options including surgery, chemoradiation, and palliation. While a surgical peel may suffice for some, those with circumferential involvement or frank invasion of the carotid artery may require resection of the carotid artery with or without reconstruction. Advances in vascular surgery, such as interposition bypass grafts, have decreased the neurologic morbidity associated with aggressive surgical intervention, but there is limited evidence describing survival or quality-of-life benefits to justify this aggressive approach.

In patients with clinical suspicion of carotid artery involvement with head and neck cancer, preintervention imaging is crucial to delineate the extent and resectability of disease. Preoperative magnetic resonance imaging (MRI) has been noted to be beneficial in predicting unresectable involvement of the carotid artery in cases with near-circumferential involvement. While computed tomography (CT) is a common imaging tool, its utility at predicting carotid artery invasion has been questioned because of poor sensitivity for carotid artery involvement.

In the present study, we examined survival outcomes in patients treated with various strategies for recurrent and previously untreated squamous cell carcinoma involving the carotid artery. We also investigated the predictive value of preoperative imaging, primarily CT, at successfully identifying cases in which direct invasion of the carotid artery would preclude removal of disease without removing the involved artery (unresectability).

Methods

Patient Selection

Patients were identified by retrospectively screening electronic medical records using a combination of current procedural terminology (CPT) and International Classification of Diseases, Ninth Revision (ICD-9), codes pertinent to advanced regional metastatic head and neck cancer. We screened patients using CPT codes for different types of neck dissection and used preintervention imaging and operative reports to identify patients with involvement of the carotid artery. We also screened databases of vascular surgery as well as radiation oncology to identify patients. From August 2005 to December 2012, 44 patients were identified as having regional metastatic disease that involved the carotid artery and were treated at the Head and Neck Institute of the Cleveland Clinic Foundation, Cleveland, Ohio. Only patients with squamous cell carcinoma were included, with other cases, including those with thyroid carcinoma, specifically excluded. These remaining patients had overt or suspected carotid artery involvement based on clinical examination and subsequent imaging studies. In this study, the gold standard for assessing carotid artery involvement was intraoperative findings, except in those patients in whom nonsurgical treatment was used. In those cases, imaging criteria cited in the literature and the opinion of a head and neck radiologist were sought to ascertain if the carotid artery was involved. In patients treated with surgical therapy, intraoperative assessment of disease in the pericarotid area was used to determine resectability. In cases in which carotid artery involvement was either near the skull base or bilateral, the disease was considered to be unresectable.

Outcomes Examined

There were 2 main objectives of this study. The primary aim was to study the impact of different treatment strategies on overall survival within this patient population. Patients were divided in 2 main groups based on whether the treatment was with curative intent or palliation. The main outcome measure was overall survival, which was defined as the time from initiation of treatment for carotid artery involvement until death. Secondary outcomes were rates of locoregional and distant metastasis in different treatment groups. The secondary aim was to assess whether preintervention imaging with contrast-enhanced CT scan or MRI predicts successful resection of tumor involving the carotid artery, and to study particular radiological signs that may predict unresectability of disease involving the carotid artery. Institutional review board approval was given, and the requirement for informed consent was waived.

Imaging

Preintervention imaging (positron emission tomography/CT with contrast-enhanced diagnostic CT of the neck, soft-tissue protocol MRI neck without and with contrast) was assessed by a single board-certified neuroradiologist (A.B.) who was blinded to the outcome of surgical intervention. Imaging was assessed for degree of encasement of vascular structures wherein the tumor was deemed unresectable in cases of vascular encasement by 270° or more and in cases in which there was both vascular encasement as well as narrowing of the vessel. Cases were also deemed unresectable in the presence of additional imaging findings of a stage T4b unresectable tumor, such as prevertebral space invasion and/or invasion of mediastinal structures. An overall opinion on whether the disease involving the carotid artery was invading in a manner that would preclude resection of disease without surgical removal (with or without reconstruction) of the involved artery (unresectable disease) was also provided by the neuroradiologist.
For patients who underwent carotid artery resection and reanastomosis or ligation (n = 6), a preoperative balloon occlusion test was part of the workup to ensure vascular sufficiency. Vascular surgery was involved in these procedures pertaining to resection and reanastomosis using interposition venous grafts as appropriate.

**Statistical Analysis**
Patient survival was documented until a terminal event or last follow-up. A terminal event was verified from a national Social Security Death Index. Survival analysis was conducted using the Kaplan-Meier probability method using GraphPad Prism software (version 5.0), and the log-rank test was used to ascertain significance between survival curves for different groups, and P < .05 was considered significant.

**Results**
Clinical characteristics of patients are detailed in Table 1. The median age (range) was 65 (31-84) years, and 34 (77%) were male. Most patients (29 [66%]) presented with recurrent or persistent disease at the time carotid artery involvement was suspected. At initial presentation, 36 (82%) had stage IV disease. The most common primary sites were the larynx (in 13 [30%]) and oropharynx (in 13 [30%]).

**Carotid Artery Disease and Details of Treatment**
Based on patient-specific factors and treatment history, disease involving the carotid artery was treated with either curative or palliative intent. Different treatment groups and proportions of previously untreated vs recurrent disease are detailed in Table 2. The curative strategy in recurrent or persistent disease involved salvage surgery aimed at complete extirpation of disease (including curative peeling from carotid adventitia where indicated or carotid artery resection with or without reconstruction) with or without subsequent adjuvant therapy. In previously untreated cases or in select recurrent or persistent cases, definitive chemoradiation therapy was also used with a curative intent. In cases with unresectable disease and exhaustion of other treatment modalities, palliative debulking of regional metastatic disease and/or palliative chemotherapy was used with end-of-life care.

As shown in Table 2, most patients treated with surgical or palliative intervention had recurrent or persistent disease (67%-89%). This is in contrast to the definitive chemoradiation group, which was primarily treatment naïve (75%). In the carotid artery resection or ligation group (n = 6), 4 patients were treated with interposition grafting of greater saphenous vein, 1 with grafting of femoral-popliteal vein, and 1 with carotid artery ligation. In the group in which curative peeling of tumor was used (n = 21), 9 patients received postoperative adjuvant therapy, of whom 4 underwent reirradiation because they had high-risk disease. In the carotid artery resection group, 3 patients underwent pectoralis major myocutaneous flaps, 2 underwent anterolateral thigh flaps, and 1 patient underwent a rectus abdominis flap reconstruction.

**Survival Outcomes in Different Groups**
Patients treated with a curative intent had a statistically better overall survival compared with the palliative group (Figure 1A) (P = .001). The palliative group had a median overall survival of 3.6 months, whereas patients treated with curative intent had a median overall survival of 13.5 months. Within the group treated with curative intent, patients with previously untreated disease had a favorable prognosis compared with patients with recurrent or persistent disease (P = .008). Previously untreated patients had a median overall survival of 38.7 months compared with a median overall survival of 9.6 months in patients with recurrent or persistent disease (Figure 1B). Patients treated with a curative intent but with different treatment strategies did not show any significant difference in overall survival (Figure 2A). The median overall survival in the carotid artery resection/ligation group was 10.3 months, which was not significantly different from the group in which curative peeling of the tumor was used as the treatment strategy (median overall survival, 13.5 months). Further analysis of the subgroup treated with curative peeling showed no significant overall survival difference between patients who received postoperative adjuvant therapy and those who did not (Figure 2B).

**Regional and Distant Failures**
During the course of follow-up, 50% to 60% patients developed locoregional recurrences. One-third of the patient population had some form of lymph node involvement, and 30% of patients developed distant metastatic disease.
Complications

There were no perioperative neurological complications in all 6 patients who underwent either carotid artery resection and reanastamosis or ligation. One patient experienced an intraoperative anastamosis breakdown, which was repaired. One patient experienced a carotid artery blowout 6 weeks after resection and reanastamosis necessitating ligation of the common carotid artery. This patient experienced a stroke as a consequence. There were no other complications noted among this group.

Role of Imaging

Preintervention imaging was reviewed in 30 patients (26 diagnostic contrast-enhanced CT scans and 4 contrast-enhanced MRI examinations of the neck) who subsequently underwent a surgical intervention. Preintervention imaging was also reviewed in 7 patients treated with definitive chemoradiation. The radiologist’s opinion had a sensitivity of 84.2% and a positive predictive value of 72.7%. However, it was not very specific (45.5%) and had a marginal negative predictive value of 62.5%. Of note, the degree of carotid artery encasement was not a determinant of unresectable disease (Figure 3). However, in cases in which the radiologist’s opinion was based on circumferential involvement and narrowing of the carotid artery (Figure 3) (3 cases treated subsequently with surgery), the prediction of unresectable carotid artery involvement was 100%. In the definitive chemoradiation group, imaging was assessed in 7 patients, and all had near-total circumferential involvement of the carotid artery (Figure 3).

Discussion

In the present study, we examined preoperative imaging as well as survival outcomes in a heterogeneous cohort of patients with advanced head and neck cancer involving the carotid artery. As demonstrated in Figure 1A, patients who were candidates for curative therapy did demonstrate a survival advantage compared with the palliative group (P = .001). Figure 1B, Patients with recurrent or persistent disease had a worse survival rate than previously untreated patients with advanced regional metastatic disease involving the carotid artery (P = .008).

Table 2. Characteristic of Disease Involving the Carotid Artery and Its Outcome With Different Strategies

<table>
<thead>
<tr>
<th>Characteristic (No. of Patients)</th>
<th>Recurrent or Persistent Disease</th>
<th>Previously Untreated Disease</th>
<th>Median Survival, mo</th>
<th>Locoregional Failure</th>
<th>Distant Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid artery resection or ligation (6)</td>
<td>5 (83)</td>
<td>1 (17)</td>
<td>10.3</td>
<td>3 (50)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Curative peel, with or without adjuvant treatment (21)</td>
<td>14 (67)</td>
<td>7 (33)</td>
<td>13.5</td>
<td>12 (57)</td>
<td>7 (33)</td>
</tr>
<tr>
<td>Definitive chemoradiation (8)</td>
<td>2 (25)</td>
<td>6 (75)</td>
<td>38.7</td>
<td>5 (63)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Palliative debulking (9)</td>
<td>8 (89)</td>
<td>1 (11)</td>
<td>3.6</td>
<td>NA</td>
<td>1 (11)</td>
</tr>
</tbody>
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Abbreviation: NA, not applicable.
strated overall survival (median survival, 10.3 months), comparable with some of the larger series in the literature. Furthermore, it compares favorably with the median survival of those patients who were not treated in a curative fashion (median survival, 3.6 months). Other than a single instance of carotid artery rupture with a subsequent stroke, there were no instances of perioperative complications in this group. This would suggest that careful selection of patients for carotid artery resection with preoperative planning as part of a curative oncologic procedure can be accomplished without significantly increasing morbidity.

Treatment of cancer contiguous to the carotid artery becomes a challenge in recurrent or persistent disease secondary to fibrosis adjacent to carotid adventitia owing to previous radiation or surgical procedures. Similarly, previously untreated disease can present with various degrees of carotid artery encasement. In many of these cases, intraoperative assessment of the carotid adventitia can guide a surgeon to attempt a resection in a subadventitial plane (“curative peel”). In our study, 21 patients were treated with a curative peel after intraoperative assessment, and subsequent dissection resulted in complete extirpation of cancer. In 9 of these cases, postoperative adjuvant treatment was used as well, including 4 cases of reirradiation. Overall survival was comparable with survival in the group treated with carotid artery resection (median survival, 13.5 months and 10.3 months, respectively). Although some authors have suggested violation of oncologic principles with such an approach, rates of locoregional failure were comparable between this subgroup and the one treated with carotid artery resection. It has also been suggested that such an approach may increase the risk of carotid artery rupture, especially in irradiated patients. In our study,
there was no such complication. This could be due to meticulous coverage of the ipsilateral vascular structures with tissue or other methods.

The third treatment strategy used with curative intent was definitive chemoradiation therapy, which was largely used in previously untreated patients (6 of 8). Although there was no gold standard (intraoperative method) to assess carotid artery invasion in this subgroup, preoperative imaging assessment by a radiologist predicted unrespectability based on almost complete encasement in 5 out of 6 previously untreated cases. The median overall survival was highest in this subgroup (median survival, 38.7 months), yet it was not statistically significant from other subgroups in which surgical therapy was used. This trend toward benefit could be explained by factors such as the treatment-naïve nature of these patients. In addition, human papillomavirus (HPV) status was not included as a part of this study. Even advanced-stage HPV-positive squamous cell carcinoma of the head and neck has been noted to respond favorably to treatment, which could have provided a potential bias. Although our data show no significant difference in survival among the 3 treatment groups treated with curative intent, this conclusion should be interpreted cautiously because of unadjusted survival analysis as well as the low power of current study.

The rates of locoregional and distant failures after completion of treatment were comparable in all 3 subgroups treated with curative intent and are similar to findings reported in larger series of carotid artery resection. This largely reflects the inherent dismal prognosis with advanced extranodal metastatic disease in these unfortunate patients. Historically, the major goal of aggressive procedures in such patients includes alleviation of symptoms such as pain and frank invasion of skin or vascular structures with potential catastrophic results. In this series, however, we were able to demonstrate a survival benefit when patients were treated with a curative intent.

Use of preoperative imaging to gauge extent of disease and predict successful extirpation of cancer involving the carotid artery has been studied previously. A CT scan-based prediction was also found to lack sensitivity based on the criteria of 180° encasement. However, a study using MRI found 270° or more circumferential involvement to be an accurate predictor of carotid artery invasion in 29 patients with squamous cell carcinoma of the head and neck. In our study, predominantly contrast-enhanced CT scan imaging was used to assess the extent of neck disease. Although the degree of encasement was not a determinant of resection, circumferential (>270°) involvement with associated narrowing of carotid artery was an accurate predictor of unresectable disease.

There are limitations to this study. First, the retrospective nature is an obvious potential source of bias, which we have attempted to control. In addition, the heterogeneous patient population makes results more difficult to generalize. Variations, such as HPV status, treatment history, and myriad patient factors, add levels of complexity to any retrospective study. Finally, while the number of patients treated compares favorably with those in other studies on this topic, the limited number of patients in each treatment arm allows significant bias by patients who would otherwise be recognized as outliers.

In conclusion, treatment of carotid artery involvement with squamous cell carcinoma is a therapeutic challenge with poor overall survival. Despite this, there does seem to be a survival advantage to pursuing curative treatment. Primary radiation therapy with concurrent chemoradiation therapy may be an acceptable alternative in some patients with previously untreated disease. Preoperative imaging can be useful in predicting the resectability of a tumor, especially when there is circumferential encasement and narrowing of the carotid artery, but it does not replace direct intraoperative examination. Decisions regarding unresectable disease can only be made intraoperatively by direct assessment of the arterial anatomy. In most cases, carotid artery dissection and preservation can be accomplished without altering complication and failure rates. In cases in which there is high index of suspicion of unresectable disease invading the carotid adventitia, carotid artery resection should be used along with careful preoperative assessment and imaging to maximize outcome.

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Analysis and interpretation of data: Manzoor, Russell, Burkey, Khan.
Drafting of the manuscript: Manzoor, Russell, Burkey, Khan.
Critical revision of the manuscript for important intellectual content: Russell, Bricker, Koyfman, Scharpf, Burkey, Khan.
Statistical analysis: Manzoor, Russell, Bricker, Khan.
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REFERENCES