Cerebral revascularization and carotid artery resection at the skull base for treatment of advanced head and neck malignancies

Clinical article

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Object. Resection of cancer and the involved artery in the neck has been applied with some success, but the indications for such an aggressive approach at the skull base are less well defined. The authors therefore evaluated the outcomes of advanced skull base malignancies in patients who were treated with bypass and resection of the internal carotid artery (ICA).

Methods. The authors retrospectively reviewed the charts of all patients with advanced head and neck cancers who underwent ICA sacrifice with revascularization in which an extracranial-intracranial bypass was used between 1995 and 2010 at the Barrow Neurological Institute.

Results. Eighteen patients (11 male and 7 female patients; mean age 46 years, range 7–69 years) were identified. There were 4 sarcomas and 14 carcinomas that involved the ICA at the skull base. All patients underwent ICA sacrifice with revascularization. One patient died of a stroke after revascularization. A second patient died of the effects of a fistula between the oral and cranial cavities (surgery-related mortality rate 11.1%). Eight months after the operation, 1 patient developed occlusion of the bypass and died. Complications associated with the bypass surgery included 1 case of subdural hematoma (SDH) with blindness, 1 case of status epilepticus, and 1 case of asymptomatic bypass occlusion (bypass-related morbidity rate 16.7%). Complications associated with tumor resection included 3 cases of CSF leakage requiring repair and shunting, 1 case of hydrocephalus requiring shunting, 1 case of SDH, and 1 case of contralateral ICA injury requiring a bypass (tumor resection morbidity rate 33.3%). In 1 patient treated with adjuvant therapy before surgery, the authors identified only a radiation effect and no tumor on resection. In a second patient the bypass was occluded, and her tumor was not resected. The other 16 patients underwent gross-total resection of their tumor. Excluding the surgery-related deaths, the mean and median lengths of survival in this series were 13.2 and 8.3 months, respectively (range 1.5–48 months). Including the surgery-related deaths, the mean and median lengths of survival were 11.8 and 8 months, respectively (range 17 days–48 months). At last follow-up all patients had died of cancer or cancer-related causes.

Conclusions. Despite maximal surgical intervention, including ICA sacrifice at the skull base with revascularization, patient survival was dismal, and the complication rate was significant. The authors no longer advocate such an aggressive approach in this patient population. On rare occasions, however, such an approach may be considered for low-grade malignancies.

Key Words • skull base • malignant tumor • carotid artery sacrifice • extracranial-intracranial bypass • carcinoma • sarcoma • oncology

Abbreviations used in this paper: CA = carotid artery; ICA = internal CA; MCA = middle cerebral artery; RAG = radial artery graft; SCC = squamous cell carcinoma; SDH = subdural hematoma; STA = superficial temporal artery; SVG = saphenous vein graft.

HEAD and neck cancers involving the CA at the skull base usually have a poor prognosis because they are frequently diagnosed at advanced stages, and their recurrence rate is high even after surgery or chemoradiotherapy.2,8 The optimal management for advanced head and neck cancers remains resection to microscop-ically negative (“clean”) margins, coupled with adjuvant therapy. Tumors are considered operable if negative margins can be obtained safely. These tumors may arise from the bony skull base itself or from the intracranial compartment and may secondarily involve the skull base. However, they typically arise from soft tissues, respiratory or digestive tracts, and

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
Growing tumors may involve the CA at the neck or the skull base, thereby increasing the challenge of treatment. The decision to intervene in cases of CA involvement depends on tumor type, tumor location, and systemic disease status. Treatment options for advanced head and neck cancers involving the CA include hospice care, nonsurgical adjuvant therapy, CA peeling, and CA resection with or without revascularization.

The risks of stroke and death involved with sacrificing the CA are significant. To decrease the overall morbidity and mortality rates associated with CA sacrifice, revascularization may be performed. Related complications, such as bypass rupture and occlusion, and the inability of existing tests to predict cerebral vascular reserve, pose further challenges to this strategy.

When cancers involve the CA in the neck, carotid sacrifice improves the 2-year survival rate but is associated with a significant risk of neurological deficits, stroke, and delayed ischemic complications. The perioperative mortality rate ranges from 0% to 45%, and the rate of de novo aneurysm formation ranges from 1% to 10%. Involvement of the ICA at the skull base (cavernous sinus, petrous, or infratemporal segments) has been considered a contraindication for resection. However, some surgeons have argued that there may still be a role for such an approach. To evaluate this possibility we analyzed our approach, which consisted of bypass and resection for treatment of CA involvement with tumors at the skull base.

Methods

We retrospectively reviewed the charts of all patients with recurrent or progressive advanced head and neck cancers involving the ICA at the skull base who underwent ICA sacrifice with revascularization in which an extracranial-intracranial bypass was used between 1995 and 2010 at the Barrow Neurological Institute. Follow-up was based on telephone calls to patients, families, and primary care physicians, as well as on our office records. Patient hospital and office records were evaluated retrospectively.

Altogether, 18 patients (11 male and 7 female patients; mean age 46 years, range 7–69 years [Table 1]) with recurrent or progressive malignancies involving the ICA at the level of infratemporal fossa, petrous bone, or cavernous sinus were treated. Nine of these patients have been reported in other studies from our group. However, only 5 of these 9 patients were analyzed for survival outcomes; the other 4 were described as a part of a technical report.

The MRI studies showed that the infratemporal ICA was involved by tumor in 9 patients, the petrous ICA in 3 patients, and the cavernous ICA in 6 patients. All patients underwent preoperative angiography, but their cerebrovascular reserve was not evaluated because vascular reconstruction was planned in all cases. All patients underwent an extracranial-intracranial bypass, which included a direct ipsilateral bypass with a SVG in 7 cases, a RAG in 1 case, a so-called bonnet bypass (STA to contralateral MCA) with a SVG in 3 patients, and a bonnet bypass with a RAG in 7 cases (Figs. 2 and 3). Revascularization was performed after mild hypothermia was established and barbiturate protection was provided. Electroencephalographic monitoring was conducted intraoperatively. The tumor was resected in a second-stage procedure. Postoperatively, all patients were maintained on aspirin (325 mg) for life.

Results

Table 2 summarizes the outcomes of the patients. Immediately after surgery (within the first 24 hours) the bypass was functional and patent in all 18 patients (immediate patency rate 100%), but 1 bypass failed (overall patency rate 94.4%) in the postoperative period. Three complications (16.7%) were associated with the bypass surgery: 1 SDH associated with blindness (Case 1), 1 stroke (Case 12), and 1 asymptomatic bypass occlusion (Case 18). The patient with the stroke (Case 12) died within the postoperative period. At surgery another patient (Case 15) was found to have radiation effect instead of tumor; consequently, this patient unnecessarily underwent ICA sacrifice and bypass.

The tumors were resected in the remaining 16 patients (88.9%). Six complications (33.3%) were associated with the resection of tumors: 3 cases of CSF leakage (16.7%—Cases 2, 11, and 14); 1 case each of hydrocephalus (Case 8) and iatrogenic vascular injury to the contralateral ICA (Case 17); and the patient who was found to have radiation effect at surgery (Case 15) suffered an SDH related to anticoagulation therapy and had status epilepticus.

Two patients died (surgery-related mortality rate 11.1%). Besides the patient who had a stroke from occlusion of the bypass, a second patient (Case 6) died of infection and pneumocephalus related to a fistula between his oral and cranial cavities. Histological evaluation of the ICA for tumor invasion was available in 7 cases. In a single case, histological examination of the specimen confirmed invasion of the ICA wall by tumor (Fig. 4). Histologically, except in the case of treatment effect, all resected specimens were confirmed to be malignancies.

The interval between revascularization and tumor resection ranged from 1 to 37 days (mean 9.1 days, median 7 days). The length of hospitalization ranged from 13 to 43 days (mean 22, median 20 days). Eight patients (44.4%) were discharged to home, 2 (11.1%) to rehabilitation, and 3 (16.7%) to a skilled nursing facility. Data were unavailable for 3 patients (16.7%).

All patients died of progression of their disease, but no information was available on local versus distant recurrence of disease in most cases. The overall mean and median follow-up (excluding the surgery-related deaths) was 13.2 and 8.3 months, respectively (range 1.5–48 months). Including the surgery-related deaths, the mean and median follow-up of patients was 11.8 and 8 months, respectively (range 17 days–48 months).

Five patients survived longer than 12 months (overall 1-year survival rate 27.8%). Of these patients, 1 had a palatal SCC, 1 had a rhabdomyosarcoma (in which the final pathological finding was consistent with treatment effect),
and 3 had an adenocystic carcinoma. Only 2 patients survived longer than 24 months (overall 2-year survival rate 11.1%). One of them had a palatal SCC, and the second had an adenocystic carcinoma. Based on subgroup analysis, patients with adenocystic cancers survived an average of 28.7 months (range 18–48, median 20 months), whereas those with nonadenocystic cancers (excluding the patient with the treatment effect and no viable cancer) survived an average of 7.4 months (range 17 days–23 months, median 5.5 months).

Discussion

Three collaborative international studies have established the morbidity, mortality, and median survival rates for patients with skull base malignancies following craniofacial resections.\textsuperscript{13–15} Surgical complications were noted in one-quarter to one-third of patients with skull base malignancies (range 25%–36.3%), and their rate of postoperative mortality ranged from 1.4% to 4.8%. These studies reported 5-year overall and recurrence-free survival rates of 61%–62% and of 55%–57%, respectively.\textsuperscript{13–15} In separate studies of patients undergoing infratemporal resections of skull base malignancies, complications occurred an average of 7.4 months (range 17 days–23 months, median 5.5 months).

Our morbidity and mortality rates were 33.3% and 11.1%, respectively. The median survival rate in our series was 8 months. Although our morbidity rate is within the published range, our mortality and survival rates are worse than those reported by others.\textsuperscript{13–15}

Sacrifice of the CA in the neck has been associated with better results than sacrifice of that vessel in the skull base.\textsuperscript{3,5,21,28} Malignancies that extensively involve the skull base or that extend into the cavernous sinus, pituitary gland, or orbit are usually contraindications for surgical intervention.\textsuperscript{36} Several studies have challenged this view and suggested that there may be an indication to pursue aggressive tumor resection and CA sacrifice with concomitant revascularization.\textsuperscript{6,16,28} Gormley et al.\textsuperscript{16} focused on adenocystic carcinomas with an intracranial extension. Of 16 such patients who underwent bypass and carotid resection at the skull base, 8 died (mean follow-up 137 months, range 33–216 months) and 6 were alive without evidence of local disease (mean follow-up 72 months, range 25–204 months). One patient had evidence of local disease but was still alive 56 months after surgery, and 1 died of complications associated with the procedure at 63 months. Brisman et al.\textsuperscript{6} evaluated 7 patients who underwent revascularization and aggressive resection of tumors and CA at the skull base. Four patients were alive.
in good condition, 1 died 2.5 years after surgery without evidence of local recurrence, and 2 experienced vascular occlusion of their bypass with 1 major stroke. Nayak et al.\textsuperscript{28} described 6 patients who underwent revascularization and carotid sacrifice at the skull base. None of these patients survived beyond 2 years, but 2 survived 9 and 12 months after surgery, respectively, and a third survived 14 months before dying.

The argument that CA sacrifice and bypass may improve survival for patients with malignancies at the skull base may be specific to the histological type of the cancer. In our series the 1- and 2-year survival rates were 27.8% and 11.1%, respectively. Of the 5 patients who survived beyond 1 year, 3 had adenocystic carcinomas, 1 had a rhabdomyosarcoma (which intraoperatively was noted to be scar tissue and not tumor), and 1 had an SCC. A prior study had highlighted the improved outcome of patients with adenocystic cancers after carotid resection and revascularization.\textsuperscript{16} We also noted that patients with this type of tumor survived longer after aggressive resection and bypass compared with patients with nonadenocystic tumors.

The actual ability of tumor to invade the CA has been
TABLE 2: Summary of characteristics and outcomes in patients with advanced head and neck cancers that involved the CA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>18</td>
</tr>
<tr>
<td>pathological findings</td>
<td></td>
</tr>
<tr>
<td>sarcoma</td>
<td>4</td>
</tr>
<tr>
<td>carcinoma</td>
<td>14</td>
</tr>
<tr>
<td>types of bypass</td>
<td></td>
</tr>
<tr>
<td>regular w/ RAG</td>
<td>1 (5)</td>
</tr>
<tr>
<td>regular w/ SVG</td>
<td>7 (39)</td>
</tr>
<tr>
<td>bonnet w/ RAG</td>
<td>7 (39)</td>
</tr>
<tr>
<td>bonnet w/ SVG</td>
<td>3 (17)</td>
</tr>
<tr>
<td>patent bypass</td>
<td>17 of 18 (94.4)</td>
</tr>
<tr>
<td>morbidity from bypass</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>morbidity from tumor resection</td>
<td>6 (33.3)</td>
</tr>
<tr>
<td>surgery-related mortality</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>1-yr survival rate</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>2-yr survival rate</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>mean survival</td>
<td>11.8 mos</td>
</tr>
<tr>
<td>median survival</td>
<td>8 mos</td>
</tr>
<tr>
<td>range survival</td>
<td>17 days–48 mos</td>
</tr>
</tbody>
</table>

debated. In some case reports of microscopically evaluated cancer-invaded cavernous sinus, no invasion of the ICA by the tumor was found—only encasement of the artery. One of our patients had pathologically proven invasion of the vessel by tumor. Although physical vascular invasion may be rare, extensive encasement without malignant invasion of the vessel wall would still require sacrifice of the ICA to attempt to achieve microscopically negative margins. Due to the paucity of data, we could not demonstrate that resection of the ICA at the skull base for malignancies allowed us to achieve a microscopically negative margin.

With high rates of morbidity and mortality, poor postresection survival rates, and improved survival with chemoradiotherapy, the role of aggressive resection has been questioned. In some series of skull base tumors treated with adjuvant therapies, overall survival rates at 2 and 3 years have been reported at 80% and 36%, respectively. Our data indicate that despite resection, the presence of ICA involvement in advanced head and neck cancers portends a worse prognosis, with higher morbidity and mortality rates, compared with patients without ICA involvement. Given this trend toward poor outcomes, the futility of this procedure outweighs its benefits in most cases. It should be used with caution and only after careful patient selection.

Conclusions

The ideal treatment regimen for malignant tumors involving the CA at the skull base remains nonsurgical. On certain occasions, carotid sacrifice and bypass may have a role in the treatment of tumors with less aggressive biological behaviors, such as adenocystic carcinomas. Given the high rates of surgery-related mortality and poor survival despite aggressive measures, we interpret our results and those of other authors as indicating that in cases of aggressive malignancies, CA involvement at the skull base is a relative contraindication to revascularization and aggressive resection.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Acquisition of data: Kalani, Kalb, Martirosyan. Analysis and interpretation of data: Feiz-Erfan, Kalani. Drafting the article: Kalani. Critically revising the article: Feiz-Erfan, Kalani. Reviewed submitted version of manuscript: all authors. Statistical analysis: Kalb. Administrative/technical/material support: Kalb, Martirosyan. Study supervision: Feiz-Erfan, Spetzler, Porter.

References