Efficacy and safety of stereotactic radiosurgery for glomus jugulare tumors

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Object. Since the mid-1990s the use of radiosurgery for glomus jugulare tumors has grown in popularity. Despite its increased use, follow-up periods for radiosurgery are short and the numbers of patients reported are small. To add to the available information, the authors report their experience with the application of linear accelerator (LINAC) or CyberKnife modalities in 13 patients with 16 tumors.

Methods. All patients were treated with frame-based LINAC or CyberKnife radiosurgery, with doses ranging from 1400 to 2700 cGy. Patients were retrospectively assessed for posttreatment side effects, which included hearing loss, tongue weakness, and vocal hoarseness. The patients’ most recent magnetic resonance (MR) images were also assessed for changes in tumor size.

The median follow-up duration was 41 months and the mean follow-up period was 60 months. All tumors remained stable or decreased in size on follow-up MR images. All patients had stable neurological symptoms, and one experienced transient ipsilateral tongue weakness and hearing loss, both of which subsequently resolved. One patient experienced transient ipsilateral vocal cord paresis; however, this individual had received previous external-beam radiation therapy.

Conclusions. The authors’ findings continue to support radiosurgery as an effective and safe method of treatment for glomus jugulare tumors that results in low rates of morbidity.

KEY WORDS • glomus jugulare tumor • radiosurgery • linear accelerator • CyberKnife
CLINICAL MATERIAL AND METHODS

Before we began the study, the Stanford Internal Review Board committee first approved the proposed patient treatment and follow-up protocol. A retrospective analysis of the Stanford University Hospital radiosurgery database was then conducted to identify patients with glomus jugulare tumors who were treated with LINAC or CyberKnife modalities between 1991 and 2004 (Fig. 1). Patient records were examined for the following data: age, sex, laterality of tumor, dose, number of isocenters, pre- and post-treatment symptoms, largest dimension of tumor on MR images before and after therapy, and duration of follow-up review in which neuroimages and clinical symptoms were assessed (Table 1). Clinical symptoms were also documented by telephone interviews, and the patients’ MR images were obtained to confirm the findings.

Patient Population

Patients ranged in age from 21 to 80 years, with a mean age of 52 years. Of the 13 patients included in the study (five men and eight women) there were 16 tumors; two patients had multiple lesions. Four patients had previously undergone open surgeries for their tumors; two of them underwent multiple resections. Nine of the 13 patients were treated exclusively with radiosurgery. Tumor sizes ranged from 1.2 to 6.2 cm at the largest measurable diameter, with a mean size of 3 cm. Of the five patients who presented with recurring tumors (all previously resected, with histological features consistent with glomus tumors), the lesion extended up to the cavernous sinus in one, whereas the remainder had local recurrences. Presenting symptoms involved the ninth (five patients), 10th (four patients), 11th (four patients), and 12th (two patients) cranial nerves.

Five tumors were treated using a frame-based LINAC system, and the remaining 11 were treated with the CyberKnife. Prescribed doses to the periphery of the tumor (typically to the 80% isodose line) ranged from 1400 to 2700 cGy. Patients who underwent LINAC radiosurgery were treated with one to three isocenters and those treated with the CyberKnife received nonisocentric-based treatments.
Follow-up durations ranged from 4 to 139 months with neuroimages (mean 44 months, median 27 months) and 4 to 172 months with clinical follow-up visits (mean 60 months, median 41 months).

**RESULTS**

After treatment, two patients experienced transient worsening of preoperative cranial nerve deficits: the first noted transient ipsilateral tongue atrophy and hearing loss that both began 2 months posttreatment and resolved over the following 2 months, and the second reported worsened vocal hoarseness (confirmed with laryngoscopy) that began 1 month posttreatment and resolved over 8 months. The remaining patients experienced no side effects.

All 16 tumors were stable at the time of follow-up review of MR images, which ranged from 4 to 139 months (all images were obtained with 5-mm slices and a zero skip gap). Two patients who were treated with stereotactic radiosurgery alone experienced a tumor regression. The patient in Case 8 had a tumor whose largest diameter on neuroimaging studies was 3.8 cm before treatment, and at 15 months after treatment the lesion had decreased to a maximal diameter of 3.4 cm. The patient in Case 15 had a tumor whose largest diameter on neuroimaging studies was 6.2 cm before treatment, and at 8 months after treatment the lesion had decreased to a maximal diameter of 5 cm.

**DISCUSSION**

Glomus jugulare tumors are indolent, well-vascularized lesions that cause symptoms primarily through mass effect on neighboring structures such as cranial nerves and vasculature.14 Historically, surgical treatment for glomus jugulare tumors was thought to result in a high rate of morbidity because of the cranial nerve and vascular structures with which these lesions are intimately associated. In addition, the overall mortality rate was between 5 and 13%.15 With the advent of improved microsurgical techniques and the use of combined approaches, the mortality rate has lowered substantially; however, cranial nerve injury continues to be a problem.18–21 In a retrospective series of 176 patients treated between 1972 and 1998 and reported by Jackson, et al.,12 in 85% complete surgical control was described. The remaining 15% of their patients had a subtotal resection or recurrence. Complications included 4.5% of patients with cerebrospinal fluid leaks; deficits of the ninth (39%), 10th (25%), 11th (26%), and 12th cranial nerves (21%); and a mortality rate of 2.7%. Although the mortality rates have improved significantly, a relatively high rate of cranial nerve dysfunction remains. The higher rate of morbidity, however, may be attributed to the fact that patients treated in 1972 were included in the analysis; the authors indicated that more complications occurred before 1987.

In reporting on a series of 43 patients in 2002 (of whom 28 were surgically treated by the authors), Al-Mefty and Teixeira1 claimed that a gross-total resection was achieved in 24 (86%) of 28 patients, with tumor recurrence in only two (7%) of 28. In addition, their patients’ mortality rate was 0%. Complications reported in their study included one patient with a hemiplegia from a carotid artery thrombosis that was reversed with urokinase treatment, four patients with cerebrospinal fluid leaks, and five with infection. Nevertheless, new cranial nerve deficits developed in 11 patients (39%), with five requiring a tracheostomy and four requiring a gastrostomy at a mean follow-up duration of 38 months. Many of the patients in this series presented with symptomatic, large, complex tumors, and lower rates of cranial nerve deficits may be seen in smaller lesions.
Green, et al., however, reported better results for cranial nerve function. In their series of 52 tumors, in which 43 patients were treated surgically via the infratemporal fossa approach, 95% of their patients had at least a Grade I or II on the House scale with respect to facial nerve function at a mean follow-up time of 4.2 years (note that 88% of patients presented with a normal [House Grade I] function). As for the other cranial nerves, 23% of patients presented with a ninth nerve deficit; however, 49% of their patients had a ninth cranial nerve deficit postoperatively. Although 34% presented with a 10th cranial nerve deficit, 46% had a postoperative deficit in the same nerve. Whereas 18% presented with an 11th cranial nerve deficit, 43% had a postoperative deficit in this nerve. Lastly, 20% presented with a 12th cranial nerve deficit and 27% had a postoperative deficit in this nerve. These authors also reported that 85% of their patients were able to resume all preoperative activities. Nevertheless, 15% of their patients had been unable to perform activities of daily living preoperatively.

Patel, et al., published their results in a series of 12 patients; they achieved complete resection in 10 of them by using combined approaches. These authors again demonstrated no surgically related deaths or episodes of stroke; however, three patients (33%) required facial nerve resection during the procedure, followed by nerve grafting. Another patient experienced a postoperative hemiparesis from hydrocephalus and brainstem distortion that resolved in the course of 2 years. Only one patient also experienced mild persistent swallowing difficulty. These improvements in surgical techniques indicate that resection is a viable and safe option for many patients and may be the best choice for large tumors with mass effect.

External-beam radiation therapy, which was initially introduced as an adjuvant treatment for subtotal resections, was later used as primary therapy in patients who were not surgical candidates. Investigators in centers in which external-beam radiation therapy was used have reported tumor control (defined as stable or decreased tumor size) in as many as 61% of their cases, with 71% of patients reporting improvement of their clinical symptoms.

The drawbacks associated with external-beam radiation therapy are the large field sizes, which include the upper neck and skull base. Reported complications include radionecrosis of bone, possible induction of secondary malignancies, and xerostomia. The introduction of intensity-modulated radiation therapy has reduced the amount of normal tissue exposed to radiation, to avoid the side effects. Despite these drawbacks, the introduction of radiosurgery has offered a new technique to deliver radiation precisely.

Glomus jugulare tumors are ideally suited for radiosurgery; they are well-defined, noninfiltrating lesions, and they usually present with a reasonably small size. Unlike conventional radiation therapy, the steep dose gradient achievable with radiosurgery minimizes irradiation of neighboring normal tissue and allows delivery of a larger dose of radiation to this slowly proliferating tumor without exceeding the radiation tolerance of normal tissues.

Despite the aforementioned benefits of using radiosurgery to treat glomus jugulare tumors, there are issues of precise target delineation. Given the complexity of the neck anatomy, both the LINAC and CyberKnife modalities have small treatment delivery errors (< 2 mm) that translate into potential underdosing of a tumor edge or inclusion of neighboring cranial nerves. Modern neuroimaging cannot reliably separate tumor from adjacent cranial nerves when targeting for radiosurgery treatment, whereas such concerns are less important with external-beam radiation therapy. In addition, although radiosurgery minimizes the dose of radiation that normal neighboring tissue receives, there remains the risk that normal tissue will be exposed to radiation. Permanent cranial nerve deficits are rare, but they are still possible side effects of stereotactic radiosurgery.

In 1995, the first published series on the use of GKS for glomus tumors was reported. Since then, several additional studies have been reported in the literature. Using GKS, Foote and colleagues treated nine patients with glomus tumors. In all nine, no tumor growth was seen after treatment and no long-term complications were reported. Jordan, et al., reported on eight patients treated with GKS, noting no tumor progression and no delayed cranial neuropathies. Both groups of investigators remarked on the minimal number of side effects. Liscak, et al., however, reported a complication from their study of 14 patients treated with radiosurgery. Although this study also showed 100% control in tumor progression, with all patients reporting at least some clinical improvement, three patients experienced worsening hearing. One must also note that not all groups achieved 100% control of tumor growth. Recently, Eustacchio, et al., reported their experience in 19 patients treated using GKS. They reported a 94.7% tumor control rate, with no complications. In addition, Feigenberg, et al., only reported tumor control in three of five patients in whom LINAC therapy was administered.

The longest follow-up duration was reported by Bari, et al. They treated eight patients with glomus jugulare tumors by using GKS. Their follow-up duration was between 52 and 97 months. In their group, all patients were clinically stable and five of the eight had a decrease in the size of the lesion. They cautioned, however, that a 10-year follow-up period would be more conclusive.

As for the LINAC experience, Feigenberg, et al., reported on a series of five patients with glomus tumors who were treated with LINAC radiosurgery. Their median follow-up duration was 27 months. Their results were not as encouraging; two of the five tumors had grown at 6 and 40 months after radiosurgery. Nevertheless, their patient numbers were small. In a more recent series by M. Lim, et al., the authors reported their experience with LINAC therapy in 12 patients with glomus jugulare tumors. In their study the median dose was 15 Gy and the median follow-up period was 4 years. All patients attained a stable or decreased tumor size with stable or improved clinical symptoms. What was interesting was that at Feigenberg and colleagues’ institution a higher median dose of 25 Gy was used, but their tumor control was inferior, even with a shorter follow-up duration. In our earlier experience with the LINAC and CyberKnife modalities, we reported our results in 10 tumors treated with a dose be-
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tween 16 and 25 Gy. Our median follow-up duration was 21.5 months, and we achieved 100% control of tumor growth and stable clinical symptoms.\(^\text{15}\)

As for complications, because of the proximity of glomus jugulare tumors to the lower cranial nerves, we must first consider the susceptibility of these nerves to injury with either surgery or radiosurgery.\(^\text{4}\) An encouraging finding in our study, which has been confirmed in other reports, is the radiation resistance of the cranial nerves. In our series there were two patients with transient cranial nerve deficits that resolved completely. The rate of cranial nerve injury in the majority of the aforementioned studies was also very low.\(^\text{9,14,17}\)

As encouraging as these results are, we must still be cautious about the initial studies. As Bari, et al.,\(^\text{2}\) have previously emphasized, the indolent growth rate of the glomus jugulare tumor still requires a 10-year follow-up period to determine the treatment’s true efficacy. In our three patients who have completed more than 10 years of follow up, they continue to report stable clinical symptoms with no side effects. We are optimistic that outcomes in the more recently treated patients will continue to be good.

**CONCLUSIONS**

Our study is the largest single-center series in which a LINAC-based treatment has been used. We report a 100% control rate of tumors, with stable clinical symptoms. Our results continue to demonstrate that tumor control, preservation of cranial nerves, and minimal side effects are maintained within a larger cohort. Stereotactic radiosurgery remains a safe and efficacious form of treatment for glomus jugulare tumors, and is associated with minimal morbidity.

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**Disclosure**

Dr. Adler is the Chief Medical Officer of and a shareholder in Accuray, Inc., which manufactures the CyberKnife.

**References**


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