Comparison of Radiosurgery and Surgery for the Treatment of Glomus Jugulare Tumors

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Running head: Comparison of Treatments for Glomus Jugulare

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Abstract

Objective. The optimal management of glomus jugulare tumors remains controversial. Available treatments were once associated with poor outcomes and significant complication rates. Advances in skull base surgery and the delivery of radiation therapy by stereotactic radiosurgery have improved the results from these treatment options. We summarize and compare the contemporary outcomes and complications for these therapies.

Methods. We reviewed papers regarding treatment of glomus jugulare tumors with radiosurgery or surgery published from 1994 to 2004. Eight radiosurgery (142 patients) and 7 surgical (374 patients) studies were evaluated on neurological outcome, change of tumor size (radiosurgery)/percent of total resections (surgery), recurrences, tumor control, need for further treatment, and complications.

Results. The mean age at treatment for surgical and radiosurgical patients was 47.3 and 56.7 years, respectively. Mean follow-up was 49.2 and 39.4 months, respectively. The surgical control rate was 92.1%, with 88.2% of tumors totally resected on the first surgery. CSF leak occurred in 8.3% of surgeries and recurrences in 3.1%; mortality was 1.3%. Among radiosurgical patients, tumors diminished in 36.5%, 61.3% had no change in tumor size, and subjective or objective improvements occurred in 39.0%. Despite residual tumor in 100% of radiosurgical cases, recurrences occurred in only 2.1%, morbidity was 8.5%, and there was 0% mortality.

Conclusions. Mortality and recurrences after these treatments are infrequent, and therefore, both treatments are safe and efficacious. Although surgery is associated with higher morbidity, it immediately and totally eliminates the tumor. The radiosurgery
results are very promising, although the incidence of late recurrence (10-20 years) is unknown.
Introduction

Glomus jugulare tumors are rare, with an estimated incidence of one per 1.3 million population.\textsuperscript{33} Glomus jugulare tumors are typically radiosensitive, highly vascularized lesions arising from the chief cells of the paraganglia in the adventitia of the dome of the jugular bulb. Although only 1-5\% are malignant with metastatic spread,\textsuperscript{3-5,32} the more common benign tumors are commonly locally aggressive with compression and infiltration of adjacent bone, cranial nerves, or blood vessels,\textsuperscript{10} despite an estimated growth rate of only 0.8 mm per year.\textsuperscript{6,25}

Early attempts at surgically treating these benign, slow-growing lesions were associated with poor local tumor control, high rates of recurrences, and significant morbidity and mortality.\textsuperscript{24} In 1968, Rosenwasser\textsuperscript{24} noted a recurrence rate of 80\% and mortality of 50\% after surgery for paragangliomas involving the skull base. Reports in 1973\textsuperscript{41} and 1982\textsuperscript{40} noted that the standard treatment for glomus jugulare tumors was a radical mastoidectomy, that complete surgical excision was seldom possible, and that radiotherapy was commonly used for residual or unresectable disease. Since that time, advances in imaging, in the understanding of the surgical anatomy related to glomus jugulare tumors, in microsurgical techniques, and in the delivery of radiation have improved treatment efficacy and safety. Today, the treatment options for patients with glomus jugulare tumors include microsurgical resection, radiosurgery, vascular embolization, conventional fractionated external beam radiotherapy, or a combination of these modalities. The goal of any treatment is to control tumor growth and prevent further neurological compromise, and it is important select the intervention with the greatest chance of tumor control with the lowest risk of complications.
For many patients, the primary treatment modality is surgery, and it is the only treatment option that can offer immediate and complete tumor elimination. Although the goal of surgery is a total resection, because of the vascularity and involvement of critical vascular and neural anatomy in glomus jugulare tumors, the total removal of these lesions, historically, has been accompanied by significant morbidity, including new cranial nerve deficits and occasional mortality. However, the ability to combine various skull base approaches, and advances in microneurosurgical techniques, anesthesia, post-operative care, nerve grafting, embolization, cranial nerve intra-operative monitoring, and pre-operative evaluation with cerebral blood flow studies have increased the possibility of obtaining a total resection with fewer complications. With current techniques, large lesions, lesions involving cranial nerves, or complex glomus jugulare tumors that were deemed inoperable in the past and were treated with radiotherapy as a primary modality are being safely and totally resected.

Conventional radiotherapy with fractionated external beam radiation has been used as a primary, combined, or salvage treatment in patients who could not undergo surgery because of advanced age or other comorbidities, more aggressive or larger or unresectable tumors, or residual disease. Its use, however, is associated with frequent recurrences at lower radiation doses and significant radiation-induced complications with higher doses. These complications include radiation-induced otitis, mastoiditis, altered taste, alopecia, mucositis, and dermatitis, which all may occur acutely. Other complications that have been reported to occur in a delayed manner have included facial nerve palsy, hearing loss, temporal bone necrosis, brain necrosis, secondary malignancy including osteosarcoma, late metastasis to bone and
lungs 17 years after irradiation, cerebrospinal fluid leak from radiation-induced dural and
temporal bone necrosis, and pituitary-hypothalamic insufficiency.\textsuperscript{10,14,16,34,38,42,44,49} It is
important to note that the goal of radiotherapy is disease control or growth inhibition
rather than tumor elimination,\textsuperscript{43} as higher doses of radiation are associated with increased
complications to the temporal bone and brain stem.\textsuperscript{9} Radiation therapy is noted to
eliminate the entire tumor in only 30\% of cases.\textsuperscript{47} Interestingly, the mechanism of growth
inhibition of glomus jugulare tumors by radiotherapy is not entirely understood. It is
thought to work by perivascular fibrosis, but many tumors continue to have significant
vascularity on angiography after radiosurgery despite decreased growth. Furthermore,
unlike the vessels, the tumor (chief) cells are radioresistant and persist after
radiotherapy.\textsuperscript{20,29,30,42,43,46}

Recently, reports of the use of gamma knife and linear accelerator stereotactic
radiosurgery as a primary and secondary treatment modality for glomus jugulare tumors
have increased.\textsuperscript{10-12,14,15,26,28-31,37,42} Glomus jugulare tumors are well demarcated on MRI
and rarely invade the brain, which makes them ideal candidates for treatment with
radiosurgery because it allows a steep dose decrease at the margin.\textsuperscript{42} Compared with
conventional radiotherapy, radiosurgery involves a shorter treatment time, precise
stereotactic localization, and a small volume of irradiated normal tissue; thus, the
incidence of complications is lower.\textsuperscript{14,42} Proponents for the use of radiosurgery as a
primary modality argue that it has the potential to avoid the hospital costs and potential
post-operative morbidity associated with surgery, providing a more cost-effective
treatment.\textsuperscript{14,42} Radiosurgical treatment usually takes one day, rarely two days, compared
with 4-6 weeks for conventionally fractionated external beam radiation, and several weeks of post-operative recovery associated with surgical resection.\textsuperscript{14}

As more outcome data for radiosurgery become available, it is important to evaluate which treatment modality is associated with the best outcomes, lowest recurrences, and lowest complications. Several papers have compared conventional radiotherapy with surgery.\textsuperscript{7,10,48,49,51} Carrasco and Rosenman\textsuperscript{7} evaluated 24 series with a total of 582 patients and found that after surgery compared with radiotherapy as a primary treatment, 6\% versus 11\% of patients had residual tumors, 7\% versus 8\% had tumor recurrences, and the mortality was 2.5\% compared with 6\%. Conversely, Springate and colleagues in 1991\textsuperscript{48} reviewed the literature from 1965 to 1988 and found that the control rate for surgery alone was 86\% (394/405), whereas that for radiation alone was 93\% (182/195). In that report, the follow-ups for the surgery series were mostly greater than 7 years, but the duration of follow-up for the patients treated with only radiotherapy was not reported. To our knowledge, the outcomes of radiosurgery and surgery have not been directly compared.

The goal of this paper is to evaluate the most recent literature to determine which modality, surgery or radiosurgery, is the most effective at tumor control and safest. Additionally, the literature will be evaluated to determine whether individual tumor and patient characteristics, including age, degree of neurological impairment, growth rate, and tumor size, make one treatment modality more appropriate than the other.

**Methods**

The study involved a retrospective literature review of English language articles listed in MEDLINE that referenced the primary treatment of glomus jugulare tumors with
radiosurgery or surgery, with attention placed on the larger series and those published from 1994 to 2004. A total of 10 radiosurgical articles fit this criteria, although two of these were smaller series\textsuperscript{10,14} and their data were included in later studies.\textsuperscript{11,15} Therefore, 8 radiosurgery studies, including 142 patients, were evaluated for this study. Seven surgical articles met the criteria and they included 374 patients. All attempts were made to only include patient data from glomus jugulare tumors and to exclude data from glomus tympanicum tumors, glomus vagale tumors, or other paraganglia tumors. When a series included some patients with these other tumors, a reference was made (see Table 3, below). Of note, the radiosurgery series described all of their patients as having glomus jugulare tumors.

The following parameters were evaluated: tumor size, distribution of tumor extent using the staging systems (see below) of Fisch\textsuperscript{13} and Glasscock-Jackson,\textsuperscript{23} neurological outcome, change of tumor size for radiosurgery/percent of total resections for surgery, recurrences (radiographic or clinical), tumor control, need for further treatment, and complications.

Series that noted the Fisch or Glasscock-Jackson classification of the tumors are listed in Table 1 for comparison. The Fisch system recognizes five types of tumors: type A tumors are limited to the middle ear cleft, type B tumors are limited to the tympanomastoid area without infralabyrinthine compartment involvement, type C are tumors involving the infralabyrinthine compartment of the temporal bone and extending into the petrous apex, type D1 are tumors with an intracranial extension less than 2 cm in diameter, and type D2 are tumors with greater than 2-cm diameter intracranial extension.\textsuperscript{13} Variants of this Fisch classification were used by some of the series
reviewed in this paper. For example, Di refers to tumors with intradural extension, whereas De refers to those with extradural extension. For the Glasscock-Jackson classification, type I refers to a small tumor involving the jugular bulb, middle ear, and mastoid, type II is a tumor extending under the internal auditory canal, type III is a tumor extending into the petrous apex, and type IV is a tumor extending beyond the petrous apex and into the clivus or infratemporal fossa. Types II, III, or IV may have intracranial extension.

Results

Radiosurgery

Of the eight radiosurgery series evaluated (Table 2), 5 (62.5%) used gamma knife stereotactic radiosurgery and 3 (37.5%) used a frame-based LINAC system. One of the studies that used primarily LINAC treated four patients with Cyberknife. A total of 143 patients who were treated with radiosurgery were described. All patients received their treatments during the period from 1990 to 2001. Sixty-nine of 143 (48%) received radiosurgery as a primary treatment and 74 (52%) had undergone other therapies prior to radiosurgery. Across all of these studies, the mean age at treatment was 56.7 years (range 44 to 63.5 years) and the mean time of follow-up was 39.4 months (range 20 to 86.4 months).

The status of the tumor size following treatment was reported for 137 patients. The studies evaluated tumors after radiosurgery with axial, coronal, and sagittal MRIs to measure the largest dimensions of each tumor in the x-, y-, and z-axes. Any change in any dimension was scored as tumor growth or reduction. After treatment with
sereotapeutic radiosurgery, at latest follow-up, the tumor size decreased in 50 of 137
tumors (36.5%), and there was no change in tumor size in 84 of 137 (61.3%). There were
no cases of total elimination of the tumor. Only one study documented the timing of the
first appreciation of a decrease in tumor volume,30 and only one study reported on the
percent of tumor shrinkage.31 An observation of a decrease in tumor volume was
observed as early as 6 months after radiosurgery and the median time reported was 20
months.30 In Maarouf, et al.,31 tumor shrinkage ranged from 25 to 74% compared with
pre-radiosurgery scans in eight patients. Three patients (2.2%) had new tumor growth
after radiosurgery, which was observed at 6, 40, and 84 months.11,12 The cases of
recurrences are discussed further below.

Neurological outcome was reported for 141 patients. Neurological outcome was
determined by an objective change in patients’ physical exams when this information was
available, or if this information was not provided, it was based on changes in patients’
symptoms. An improvement was noted if a patient had one or more findings of resolution
or decreased intensity of tinnitus, vertigo, headaches, or hearing loss or if they had partial
recovery of a neurological deficit or cranial nerve function with improvements in speech,
swallowing, voice quality, or shoulder strength.

In 82 of 141 (58.2%) patients, the neurological exam remained stable, 55 of 141
(39%) patients had an improvement, and 4 of 141 (2.8%) patients had a permanent
worsening of their neurological exam after radiosurgery. One of these four patients with
a permanent worsening of their symptoms was later found to have metastatic disease.12
Improvements in hearing, tinnitus, or vertigo were first appreciated by some patients at 1
to 6 months, and most patients who noted improvement appreciated it by 12 months.26,26,30

Overall, neurological complications occurred in 12 of 141 patients (8.5%), although 9 of these cases (6.4%) were transient. In the report by Saringer and colleagues,42 two patients experienced transient facial or glossopharyngeal neuropathies due to delayed radiation injury, one at one month and the other at one year after radiosurgery. Both completely resolved within 6 months after treatment with steroids. In the study, the target volume and the administered dose were not associated with the incidence of cranial neuropathies.42 One patient in the study by Jordan, et al.,26 had immediate onset of severe vertigo after radiosurgery that resolved after 11 months. Two patients had inflammatory complications of the inner ear.30 Four other patients experienced transient worsening of their pre-existing cranial nerve deficits, tinnitus, or vertigo after radiosurgery that resolved without treatment.12,15,28

The rate of permanent deficits associated with radiosurgery was 3 of 141 patients (2.1%).12,30,31 Liscak and colleagues30 described two patients with permanent worsening. In one of these patients, facial nerve function deteriorated to House Brackmann grade II and hearing loss progressed to deafness over 12 months. The other patient’s facial nerve function deteriorated to a grade IV and vertigo worsened at six months. Maarouf and colleagues31 had one patient who developed facial weakness 6 months after radiosurgery. There was no mortality associated with the use of radiosurgery.

In several series, patients underwent additional surgery (1 patient), embolization (4 patients), or further radiosurgery (5 patients) after their initial radiosurgery treatment, although in these cases, there was no evidence of radiographic or clinical recurrence at
the time of these treatments and many were treated for persistent complaints of tinnitus.\textsuperscript{10,11,30,31} After a mean follow-up of 39.4 months, three cases out of 137 patients (2.2\%) (with complete follow-up) had clinical or radiographic recurrences.\textsuperscript{11,12} One patient was treated with radiosurgery as a primary modality and had evidence of new disease at the field margin at 6 months after radiosurgery.\textsuperscript{12} The patient was treated with salvage radiotherapy and had no further disease progression or evidence of recurrence 21 months later. Another patient was treated for recurrent disease with radiosurgery and had a recurrence at 40 months after radiosurgery. She was subsequently found to have metastatic disease to her lymph nodes and further treatment was not performed.\textsuperscript{12} Finally, one patient who was treated with radiosurgery after a partial resection had a recurrence at 84 months that was thought to be due to under-treatment from the inability to identify the whole tumor on CT planning.\textsuperscript{11}

Although 69 of 143 patients underwent radiosurgery as a primary modality, very few series provided data on these patients separately.\textsuperscript{10,26} Typically, data were provided for all patients combined, and it was impossible to decipher the outcomes and complications in the patients receiving radiosurgery as a primary modality. In two series, Eustacchio, et al.,\textsuperscript{10} and Jordan, et al.,\textsuperscript{26} 8 patients received radiosurgery as a primary treatment; tumor size remained the same for six (75\%) and reduced for two (25\%), and the neurological outcome improved for four (50\%) and remained the same for four (50\%). Feigenberg and colleagues\textsuperscript{12} described a single patient who had a recurrence after radiosurgery as a primary treatment.

Radiosurgery was used as a secondary therapy in 74 of 143 patients (52\%). Of these patients, 60.3\% had surgery prior to radiosurgery, 15.1\% had radiation therapy, and
24.6% underwent embolization. Some of these patients had combinations of these treatments. Foote and coworkers\textsuperscript{15} found a reduction of tumor size after radiosurgery in 7 of 12 patients who had previously undergone surgery. Again, most series did not document separate data for the patients who underwent and failed other treatments prior to radiosurgery.

\textit{Surgery}

A total of 374 patients were treated with 384 surgical procedures in the 7 series (Table 3). All patients underwent surgery during the period from 1972 to 2000. Across all of these studies, the mean age at treatment was 47.3 years (range 41.7 to 49 years) and the mean time of follow-up was 49.2 months (range 37.2 to 58.8 months). Green, et al.,\textsuperscript{19} provided the only series with previously untreated glomus jugulare tumors. Between 7.7\% and 50\% of patients had previously undergone surgery and between 5.5\% and 18\% had previously undergone radiation treatment.\textsuperscript{24,35,36,52,53} Approximately 25\% of patients had pre-operative embolization,\textsuperscript{2,19,36,53} but in the study by Pareschi, et al., 100\% of patients had embolization.\textsuperscript{35} Tumors were approached via single operation\textsuperscript{2,19,24,35,52,53} or staged surgery.\textsuperscript{35,56} The approaches included lateral,\textsuperscript{24} posterolateral with posterior fossa craniectomy and infratemporal fossa approach,\textsuperscript{35,52} infratemporal fossa approach followed by petro-occipital trans-sigmoid approach (second stage),\textsuperscript{35} jugulopetrossectomy,\textsuperscript{35} transtemporal-infratemporal,\textsuperscript{36,53} subtemporal-infratemporal added to a transtemporal-infratemporal,\textsuperscript{36} transtemporal-infratemporal with a retrosigmoid craniectomy and/or extreme lateral transcondylar approach,\textsuperscript{36} infratentorial and posterior fossa,\textsuperscript{2} and intrabulbar dissection.\textsuperscript{2}
Its important to note that patients in two of these series\textsuperscript{2,36} had “complex glomus jugulare tumors” as described by Al-Mefty and Teixeira,\textsuperscript{2} that include tumors of giant size, multiple paragangliomas, malignancy, catecholamine secretion, previous treatment with adverse outcomes such as sacrifice of the internal carotid artery that make surgical intervention a higher risk, prior radiation, or adverse effects from embolization. The total resection of tumors in these series with challenging tumors was 83\% and 86\%.

Overall, total surgical resection on the first attempt was achieved in 254 of 288 surgeries (88.2\%), although this number excluded two series that did not provide enough information.\textsuperscript{35,52,53} Evaluating the series other than those with complex tumors, 85\% to 96\% of surgeries resulted in total resections.\textsuperscript{2,19,24,35,36,52,53} In a series by Jackson and colleagues,\textsuperscript{24} all subtotal resections (18 of 182, 10\%) were in class III or IV tumors and were planned based on pre-operative patient preference to preserve cranial nerves or the internal carotid artery or to perform palliative surgery in elderly patients. Most of the subtotal resections occurred in class D tumors, and some surgeons achieved 100\% total resections for class C tumors.\textsuperscript{35}

The surgical tumor control rate for the non-complex series ranged from 88.5\% to 94.5\%.\textsuperscript{19,24,36,53} Surgical control was defined as complete tumor elimination without any evidence of residual or recurrent disease throughout the follow-up period. For example, in the report by Green, et al.,\textsuperscript{19} two of eight patients with subtotally resected tumors underwent immediate repeat surgeries to remove the residual tumors, and thus, only 6 of 52 (11.5\%) patients remained with residual disease, and tumor control was 88.5\%. After repeat surgeries for residual or recurrent disease, the surgical control rate was 92\%. 
Cranial nerve (CN) preservation was most easily accomplished in smaller tumors and was as high as 80-95%. In one series, complete removal of a glomus jugulare tumor without cranial nerve resection or a new deficit occurred in 31% of patients. In this series, cranial nerves 9 through 12 had to be resected in 34.6% of cases, and this was mostly due to tumor involving the lower cranial nerves at the pars nervosa of the jugular bulb. In our review of the literature, one or more new cranial nerve deficits occurred in 22% to 59% of patients after surgery, whereas another review noted new CN 7, 9, or 10 dysfunction in 49% to 83% of patients. Jackson, et al., found that although it was necessary to sacrifice cranial nerves 7, 9, and 10 in 23%, 63%, and 59% of cases, respectively, preoperative deficits existed in 12%, 21%, and 31%, respectively. Several recent series noted new deficits in CN 7 in 4.4% to 11% of cases, in CN 9 in 26% to 42%, in CN 10 in 13% to 28%, in CN 11 in 25% to 26%, and in CN 12 in 5% to 21%.

Although almost all patients have facial weakness in the post-operative period after nerve transposition or nerve grafting, facial nerve functional outcomes are improving with the current advanced microsurgical techniques, use of facial nerve monitoring, and limiting of nerve transposition when possible. For example, Green and coworkers noted recovery of function of House grade I or II in 95% of patients on long-term follow-up, and Whitfield and colleagues noted that only 25% of patients had any facial nerve dysfunction on follow-up. Patel and coworkers maintained sensorineuronal hearing in 11 of 12 patients (91.7%).

The incidences of other morbidities or post-operative complications are listed in Table 4. The most common complications were cerebrospinal fluid (CSF)
leak (8.3%), aspiration (5.5%), wound infection/ischemia (5.5%), pneumonia (2.3%), and meningitis (2.1%). None of these complications resulted in long-term deficits or required re-hospitalization after initial discharge.

Adjunctive procedures were required in some patients after surgery and included vocal cord injection (10-25%), thyroplasty (8-10%), eyelid weights (percent not available), cricopharyngeal myotomy (4%), tracheostomy (0-5.4%), gastrostomy (4-5%), lateral tarsorrhaphy (20%), and nasogastric tube feeding (8-30%). Whitfield, et al., noted that patients with lower cranial nerve deficits in their series did well with the assistance of these adjunctive procedures; for example, five patients with dysphonia had a complete resolution after vocal cord injection or thyroplasty. Patel and coworkers had 10 patients with swallowing difficulties post-operatively, and symptoms resolved in 9 of these patients without the need for a feeding tube. Several authors noted that patients with pre-operative cranial nerve 9 and 10 deficits had an earlier and greater improvement in swallowing after surgery than patients without pre-operative deficits, and another paper reported that morbidity secondary to these cranial nerve deficits was greatly decreased by aggressive pre- and post-operative speech and swallowing therapy. Another group appreciated a decrease in the need for tracheostomy and gastrostomy tubes after surgery.

As mentioned above, the incidence of CSF leak was 8.3%, representing a significant complication associated with surgery for glomus jugulare tumors. The incidence of CSF leak ranged from 3.8 to 10% in most series, although in the two series with greater than 50% of re-surgeries, the incidence was 14.3-33.3%. The majority of CSF leaks resolved without the need for repeat surgical closure with
conservative management or the use of a lumbar drain. In the study by Whitfield and coworkers, two patients had to undergo additional surgery to repair CSF leaks. In one series, intracranial, transdural tumor extension was present in 36% of cases, and CSF was encountered in 64% of procedures. The risk of CSF leak was decreased with improvements in dural closure including reconstruction with a vascularized, local, regional or free flap, such as a temporoparietal fascia flap. With a good dural closure, one series appreciated a decrease in the incidence of CSF leak from 28% to 4.5%. Others lowered the risk of CSF leak for large intradural tumors by performing a staged procedures.

Overall, there were 5 deaths relating to surgery out of 374 patients for a total mortality rate of 1.3%. The mortality rate after surgery ranged from 0 to 4.1%. Deaths occurred from stroke caused by internal carotid artery injury (2 patients), intracerebral hemorrhage (1 patient), and pulmonary emboli (2 patients). The incidence of stroke, hemorrhage, or pulmonary emboli was low at 1.6%, 1.6%, and 0.8%, respectively (Table 4).

Recurrence of glomus jugulare tumors after surgery occurred in 12 of 360 cases (3.3%). The range in these series was 0 to 5.5%. The mean time of recurrence was 82.8 months. Of benign glomus jugulare tumors, recurrences occurred at a range of 25 to 273 months. Al-Mefty and Teixeira described a patient in whom they achieved a total resection of a very extensive and malignant glomus jugulare tumor after radiation failure, and the tumor recurred four months later. In the report by Jackson, et al., 9 of 18 subtotally resected tumors recurred; five of these cases
were treated with a total resection, two were observed, one underwent radiotherapy, and one was left untreated.

Pareschi and coworkers\(^3\) noted that 84% of their patients were sent home within 14 days of surgery, and another two studies had a mean hospital stay of 10 days.\(^1\),\(^5\) Green and colleagues\(^1\) noted that 85% of patients were able to fully resume all preoperative activities and take care of themselves. Another study found that all patients who were independent prior to surgery continued to be independent.\(^3\) In another series, 70% of patients subjectively noted that they had an excellent functional outcome.\(^5\)

**Discussion**

Since the original description of glomus jugulare tumors in the 1940s, there has been considerable controversy regarding the best management of this tumor. In the past, observation, surgery, and radiotherapy were all used as primary treatments for glomus jugulare. One factor that makes selecting the appropriate treatment difficult is the variable growth rate and clinical course of the tumors. Although the majority are benign and slow growing, they are locally invasive and, if left untreated, they have the potential to progress to cause considerable cranial nerve and brain stem injury in some patients. In the past, the main arguments against surgical intervention were the high percentage of incomplete resections and, more importantly, the high rates of morbidity and mortality. Surgeons, however, argued that this modality was the only one to obtain a complete removal of the tumor. Radiotherapy was criticized for the high exposure of normal neural tissue and bone to radiation resulting in considerable radiation-induced
complications. Additional criticisms included the delay in the treatments effect and the fact that residual tumor remained after a successful intervention.

Our review demonstrates that the treatment of glomus jugulare tumors is now safer and more efficacious than it has ever been. This improvement is most likely due to considerable advances in surgery and in the delivery of radiation via stereotactic radiosurgery. In the surgical literature we reviewed, we found that 88.2% of tumors were totally resected on the first surgery with a surgical control rate of 92.1%. Cranial nerve preservation improved, the incidence of CSF leak decreased, recurrences occurred in only 3.1% of patients, and mortality was 1.3%. Among radiosurgical studies, 36.5% patients had tumors decrease in size, 61.3% of tumors stayed the same size, all patients (100%) had residual tumors, 39.0% of patients had subjective or objective improvements, recurrences occurred in 2.1%, morbidity was 8.5%, and there was 0% mortality. Interestingly, the question of whether one defines treatment success as a cure via total elimination of tumor (surgery definition) or growth inhibition (radiosurgery definition) remains, and therefore, makes it difficult to compare these modalities.

The radiosurgery and surgery groups in this review were similar. The average patient age in the surgery series was 47.3 compared with 56.7 in the radiosurgery series. The surgery patients were followed for 49.2 months and the radiosurgery patients for 39.4 months. It is significant to note that whereas all of the radiosurgery patients were treated in 1990 or later, many of the surgery patients were treated in the 1970s and 1980s, and therefore, the overall results for the more recently treated surgical patients may be even better than reported in this review. It is difficult to make any comparison or draw any conclusion about the sizes or classifications of the tumors from these two groups.
because of the variability in the way the data were reported. In addition, the current classification systems do not account for various important surgical factors such as brain stem compression, degree of vascular involvement, or extreme size.\textsuperscript{36}

Nonetheless, the data support the fact that the recurrence after either treatment is very low and is similar at 3 or 4 years after treatment, regardless of how one defines control. It will be interesting to have more long-term studies to see how recurrence rates compare at 10 and 20 years, because surgery and radiosurgery now have such promising results. Many authors argue that the true test of a cure cannot be confirmed until observation of at least 10 or 20 years.\textsuperscript{30} Liscak et al.,\textsuperscript{30} warn that a five-year follow-up cannot be considered adequate to judge the success of the treatment. It is well known that tumor cells persist after radiation therapy, and therefore, it will be very important to see whether radiosurgery patients, who all have persistent tumors despite growth stabilization or reduction, have increased recurrences compared with surgery at 10 and 20 years. For example, the radiosurgery study with the longest follow-up (mean 7 years)\textsuperscript{11} had a recurrence at seven years. A study that treated patients exclusively with radiation therapy found that the tumor control rate was 90\% at 10 years, but 73\% at 25 years.\textsuperscript{39}

No mortality was associated with radiosurgery and the mortality secondary to surgery was just above 1\%. The biggest difference between surgery and radiosurgery is the morbidity. Although it is easy to compute the morbidity associated with radiosurgery (8.5\%), it is difficult to establish the short- and long-term morbidity in the surgical patient. The surgical patient is faced with many possible complications (\textbf{Table 4}). Furthermore, although it is safe to say that greater than 8.5\% of the surgical group will have a new cranial nerve deficit after surgery for larger tumors, the impact of this new
deficit on a patient’s long-term outcome is difficult to interpret in the surgical papers. Long-term cranial nerve functional outcomes in patients with new deficits (aside from the facial nerve) were not commonly reported in the surgical series. The surgical series did note that when cranial nerve dysfunction occurred, the use of adjunctive procedures and rehabilitation resulted in less associated morbidity from this new deficit, and that many patients eventually improved to preoperative status. Proponents of radiosurgery as a primary modality argue that it has the potential to avoid the hospital costs and potential post-operative morbidity associated with surgery, providing a more cost-effective treatment. As mentioned earlier, radiosurgical treatment usually takes one day, rarely two days, compared with an average 10-day hospital stay after surgery and possibly more if rehabilitation is needed.

Surgery remains the treatment of choice in a healthy patient who desires an immediate cure of disease with a total resection. Al-Mefty and Teixeira have shown that even the most complex glomus jugulare tumors can be totally resected with minimal complications. Other strong indications for surgery are invalidating cranial nerve palsies, tumors that are too large for radiosurgery, tumors causing vascular insufficiency due to major arterial encasement, or tumors that have significant intracranial extension and are life threatening. Obviously, resection is more difficult in cases with brain-stem compression or major encasement of arteries by tumor and, if a complete resection cannot be guaranteed or if there is a high risk of neurological deficits or morbidity with a radical resection, then a subtotal resection can be performed with the goal to debulk the tumor and prevent further neurological compromise. After a subtotal resection, stereotactic radiosurgery is a safe and effective option to treat residual tumor. Finally,
patients with advanced age or significant comorbidities may elect to undergo radiosurgery as a primary treatment modality.\textsuperscript{10} The same guideline applies to cases of recurrent glomus jugulare tumors.

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References


TABLE 1  Fisch and Glasscock/Jackson tumor classification for glomus jugulare tumors treated with radiosurgery or surgery*

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<tr>
<th>Series</th>
<th>Fisch\textsuperscript{13}</th>
<th>Glasscock/Jackson\textsuperscript{23}</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiosurgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eustacchio (1999)</td>
<td>2 C1, 1 C2, 5 D1, 2 D2</td>
<td>3 II, 4 III, 3 IV</td>
</tr>
<tr>
<td>Eustacchio (2002)</td>
<td>4C2, 12 D1, 3 D2</td>
<td>7 II, 6 III, 6 IV</td>
</tr>
<tr>
<td>Saringer (2001)</td>
<td>8 De1, 1 De2, 4 Di1</td>
<td>NA</td>
</tr>
<tr>
<td>Jordan (2000)</td>
<td>3 B, 3 C1, 1 D1, 1?</td>
<td>NA</td>
</tr>
<tr>
<td>Maarouf (2003)</td>
<td>1C, 11D1 or D2</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jackson (2001)</td>
<td>NA</td>
<td>27 I, 26 II, 44 III, 29 IV</td>
</tr>
<tr>
<td>Pareschi (2003)</td>
<td>25 C, 8 D1, 4 D2</td>
<td>NA</td>
</tr>
<tr>
<td>Whitfield (1996)</td>
<td>4B, 5C, 6D</td>
<td>NA</td>
</tr>
<tr>
<td>Patel (1994)</td>
<td>1B, 11 C or D</td>
<td>4 II, 1 III, 7 IV</td>
</tr>
</tbody>
</table>

NA, not available.

*Not all studies provided this information.
### TABLE 2  Patient information and outcomes after radiosurgical treatment of glomus jugulare tumors

<table>
<thead>
<tr>
<th>Series</th>
<th>Treatment</th>
<th>Mean Age (years)</th>
<th>Follow-up (months)</th>
<th>Volume (cm³)</th>
<th>Number of Patients</th>
<th>Long-term neurologic outcome</th>
<th>% patients clinically improved</th>
<th>Change size</th>
<th>% patients reduced tumor size</th>
<th>Recurrence (%)</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eustacchio (1999)</td>
<td>GK</td>
<td>52.4</td>
<td>37.6</td>
<td>6.4</td>
<td>10 (4P,6S)</td>
<td>5U, 5I</td>
<td>50</td>
<td>6s, 4r</td>
<td>40</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Eustacchio (2002)^a</td>
<td>GK</td>
<td>56</td>
<td>86.4</td>
<td>5.2</td>
<td>19 (10P,9S)</td>
<td>8U,10I, 1L</td>
<td>53</td>
<td>11s, 7r, 1i</td>
<td>37</td>
<td>1/18 (5.6)</td>
<td>0</td>
</tr>
<tr>
<td>Saringer (2001)</td>
<td>GK</td>
<td>63.5</td>
<td>50.4</td>
<td>9.0</td>
<td>13 (4P,9S)</td>
<td>6U, 6I, 1L</td>
<td>50</td>
<td>10s, 3r</td>
<td>23</td>
<td>0</td>
<td>2t</td>
</tr>
<tr>
<td>Foote (1997)</td>
<td>GK</td>
<td>67</td>
<td>20</td>
<td>8.6</td>
<td>9 (5P,4S)</td>
<td>2U, 7I</td>
<td>78</td>
<td>8s, 1r</td>
<td>11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Foote (2002)^b</td>
<td>GK</td>
<td>62.5</td>
<td>37</td>
<td>10.4</td>
<td>25 (12P, 13S)</td>
<td>10U,15I</td>
<td>60</td>
<td>17s, 8r</td>
<td>32</td>
<td>0</td>
<td>1t</td>
</tr>
<tr>
<td>Liscak (1999)</td>
<td>GK</td>
<td>54</td>
<td>24</td>
<td>5.7</td>
<td>52 (24P,28S)</td>
<td>35U, 15I, 2W</td>
<td>29</td>
<td>28s, 19r, 5L</td>
<td>40</td>
<td>0</td>
<td>3t, 2p</td>
</tr>
<tr>
<td>Jordan (2000)</td>
<td>GK</td>
<td>61.9</td>
<td>27</td>
<td>9.8</td>
<td>8 (5P,3S)</td>
<td>4U, 4I, 1W</td>
<td>50</td>
<td>3s, 4r, 1L</td>
<td>57</td>
<td>0</td>
<td>1t</td>
</tr>
<tr>
<td>Maarouf (2003)</td>
<td>LIN</td>
<td>59</td>
<td>48</td>
<td>12.2</td>
<td>12 (6P,6S)</td>
<td>8U, 3I, 1W</td>
<td>25</td>
<td>4s, 8r</td>
<td>67</td>
<td>0</td>
<td>1p</td>
</tr>
<tr>
<td>Lim (2003)</td>
<td>CK/LIN</td>
<td>44</td>
<td>26</td>
<td>NA</td>
<td>9 (4P,5S)</td>
<td>9U</td>
<td>0</td>
<td>8s, 1r</td>
<td>11</td>
<td>0</td>
<td>1t</td>
</tr>
<tr>
<td>Feigenberg (2002)</td>
<td>LIN</td>
<td>49</td>
<td>27</td>
<td>10.8</td>
<td>5 (4P, 1S)</td>
<td>2U, 2I, 1W</td>
<td>40</td>
<td>3s, 2i</td>
<td>0</td>
<td>2/5 (40)</td>
<td>1t</td>
</tr>
</tbody>
</table>

GK, gamma knife; LIN, linear accelerator; CK, Cyberknife; P, primary treatment; S, secondary treatment; U, unchanged; I, improved; W, worse; L, lost to follow-up; s, same; r, reduced; i, increased; t, transient; p, permanent.

Data in bold were not included in the overall review because these results were included in the larger series by the same primary author.

a Series included the ten patients from Eustacchio, 1999

b Series included the nine patients from Foote, 1997.
### TABLE 3 Patient information and outcomes after surgical treatment of glomus jugulare tumors

<table>
<thead>
<tr>
<th>Series</th>
<th>Most used approach</th>
<th>Patients</th>
<th>Surgeries</th>
<th>Mean age (years)</th>
<th>Follow-up (months)</th>
<th>Total resection (%)</th>
<th>Recurrence (%)</th>
<th>Time to recurrence (months)</th>
<th>CSF leak (%)</th>
<th>New cranial nerve deficit (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jackson (2001) ^a</td>
<td>Lateral</td>
<td>176</td>
<td>182</td>
<td>49</td>
<td>54</td>
<td>158/176 (90)</td>
<td>9/164 (5.5)</td>
<td>Mean, 98</td>
<td>4.5</td>
<td>59</td>
<td>3/176 (1.7%)</td>
</tr>
<tr>
<td>Watkins (1994) ^b</td>
<td>Posterolateral</td>
<td>49</td>
<td>50</td>
<td>41.7</td>
<td>40.8</td>
<td>NA</td>
<td>0/47</td>
<td>NA</td>
<td>NA</td>
<td>57</td>
<td>2/49 (4.1%)</td>
</tr>
<tr>
<td>Pareschi (2003)</td>
<td>Infratemporal</td>
<td>37</td>
<td>37</td>
<td>NA</td>
<td>58.8</td>
<td>(96)</td>
<td>0/37 (0)</td>
<td>8.1</td>
<td>NA</td>
<td>0/37 (0)</td>
<td></td>
</tr>
<tr>
<td>Green (1994)</td>
<td>Infratemporal</td>
<td>52</td>
<td>54</td>
<td>47.7</td>
<td>47</td>
<td>44/52 (85)</td>
<td>0/52 (0)</td>
<td>3.8</td>
<td>NA</td>
<td>0/52 (0)</td>
<td></td>
</tr>
<tr>
<td>Whitfield (1996) ^c</td>
<td>Transtemporal-Infratemporal</td>
<td>20</td>
<td>20</td>
<td>47</td>
<td>37.2</td>
<td>18/20 (90)</td>
<td>1/20 (5.0)</td>
<td>48</td>
<td>10</td>
<td>NA</td>
<td>0/20 (0)</td>
</tr>
<tr>
<td>Patel (1994) ^d</td>
<td>Transtemporal-Infratemporal</td>
<td>12</td>
<td>13</td>
<td>45.7</td>
<td>44</td>
<td>10/12 (83)</td>
<td>0/12 (0)</td>
<td>33.3</td>
<td>NA</td>
<td>0/12 (0)</td>
<td></td>
</tr>
<tr>
<td>Al-Mefty (2002) ^e</td>
<td>Infratentorial/posterior fossa or intrabulbar</td>
<td>28</td>
<td>28</td>
<td>47</td>
<td>38</td>
<td>24/28 (86)</td>
<td>2/28 (7.1)</td>
<td>4^e and 60</td>
<td>NA</td>
<td>0/28 (0)</td>
<td></td>
</tr>
</tbody>
</table>

NA, not available.

^a Series included 27 glomus vagale tumors and 3 carotid body tumors.

^b Two additional patients died, but they had carotid body tumors.

^c Series included 5 glomus vagale tumors.

^d Series included complex glomus jugulare tumors.

^e Recurrence occurred at 4 months in a patient with a malignant glomus jugulare tumor.
**TABLE 4 Complications after 384 surgeries for glomus jugulare tumor**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF leak</td>
<td>32</td>
<td>8.3</td>
</tr>
<tr>
<td>Aspiration</td>
<td>21</td>
<td>5.5</td>
</tr>
<tr>
<td>Wound infection/ischemia</td>
<td>21</td>
<td>5.5</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>9</td>
<td>2.3</td>
</tr>
<tr>
<td>Meningitis</td>
<td>8</td>
<td>2.1</td>
</tr>
<tr>
<td>Ileus</td>
<td>6</td>
<td>1.6</td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>6</td>
<td>1.6</td>
</tr>
<tr>
<td>Stroke</td>
<td>6</td>
<td>1.6</td>
</tr>
<tr>
<td>External ear infection</td>
<td>5</td>
<td>1.3</td>
</tr>
<tr>
<td>Tympanic membrane perforation</td>
<td>4</td>
<td>1.0</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>3</td>
<td>.8</td>
</tr>
<tr>
<td>Worsened ataxia</td>
<td>3</td>
<td>.8</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>3</td>
<td>.8</td>
</tr>
<tr>
<td>Osteomyelitis temporal bone</td>
<td>2</td>
<td>.5</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>2</td>
<td>.5</td>
</tr>
<tr>
<td>Seroma</td>
<td>2</td>
<td>.5</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>1</td>
<td>.3</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
<td>.3</td>
</tr>
<tr>
<td>Tracheitis</td>
<td>1</td>
<td>.3</td>
</tr>
</tbody>
</table>