Oncologic outcome in surgical management of jugular paraganglioma and factors influencing outcomes

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ABSTRACT: *Background.* The purpose of this study was to identify the factors that may influence the management outcome in patients with jugular paragangliomas.

Methods. The surgical records of 121 cases of jugular paraganglioma (Fisch classifications C and D) were reviewed.

Results. The average follow-up was 88 months. Intracranial extension (ICE; Fisch classification De and Di) constitutes 55.4% of the cases. Two cases had a malignant jugular paraganglioma. Complete tumor resection was achieved in 81.8% of the cases, and there was evidence of recurrence in 4.0% from this group. Surgical tumor control was achieved in 96% of cases. Perioperative complications consisted mainly of cerebrospinal fluid leakage in 1.6% of the cases. The lower cranial nerve (CN) was preserved in 63% of the patients mainly in the cases without ICE.

Conclusion. The infratemporal fossa approach type A allows for complete tumor resection with low perioperative morbidity and recurrence rates. The significant influential factors were the severity of ICE and internal carotid artery involvement. © 2012 Wiley Periodicals, Inc. *Head Neck* **00:000–000, 2012**

KEY WORDS: jugular paraganglioma, glomus jugulare tumors, surgical management, surgical control

INTRODUCTION

Jugular paragangliomas are rare benign neoplasms that occur in a deep-seated complex anatomic region of the lateral skull base. Jugular paraganglioma accounts for 0.6% of head and neck tumors and 80% of jugular foramen tumors.[1] They have an insidious growth pattern with destructive behavior and a tendency for bone and intracranial extension (ICE) via finger like projections, which may cause dysfunction of the facial and lower cranial nerves (CNs). The choice of management either with surgery or radiotherapy has been debated widely with the main aim being minimal management morbidity. Nowadays, the surgical resection of jugular paraganglioma is safe and excellent oncological control and minimal morbidity is achievable due to advancements in interventional neuroradiology and refinements in the microsurgical techniques. For these reasons, surgery remains the primary treatment of choice in many centers.[2–5] Although published evidence[6–9] seems to indicate that radiotherapy may be a valuable treatment modality, reported data do not justify its use as the primary mode of treatment for jugular paraganglioma. In fact, rather than eradication, mostly tumor stabilization was achieved via radiotherapy.

The oncological outcomes from surgical management of jugular paraganglioma have significantly improved in recent decades. The surgery oncological controls range from 72% to 98%[5,10–17] (Table 1) with low reported perioperative mortality and morbidity, such as cerebrospinal fluid (CSF) leaks. Tumors with intradural and circumferential internal carotid artery involvement, that were previously considered inoperable, are now technically resectable.[18,19] In this article, we present our experience with surgical treatment of jugular paraganglioma for the past 20 years and evaluate the factors that may influence the oncological outcomes in the surgical management of jugular paraganglioma. This study also aims to provide sufficient surgical outcome data to confirm the efficacy of surgical treatment of jugular paraganglioma.

MATERIALS AND METHODS

We reviewed a series of 156 cases of class C and D jugular paraganglioma (Fisch classification)[20] that underwent surgical treatment at the Gruppo Otologico between April 1988 and April 2011. Inclusion criteria were complete patient records and a minimum of 1-year follow-up. Thirty-five cases that had incomplete follow-up were excluded from this review. One hundred twenty-one cases met the criteria and were analyzed. All patients underwent preoperative catecholamine level investigation and

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TABLE 1. Reported series in the past 15 years on the surgical management outcome of jugular paraganglioma (class C and D).

Published article	Patient number	Mean follow-up duration in y (mo)	Tumor classification	Surgical approach	Total resection %	Recurrence rate %	Surgical control %*	Perioperative mortality	CSF leakage (%)	Postoperative new CND (%)
Tran Ba Huy et al[10]	47	5.5 (66)	Fisch	ITFA	70 (33 pts)	8.0 (2 pts)	93.9	1 pt	7 pts (14.9)	10 pts (22)
Al–Mefty et al[11]	28	3.2 (38)	Not mentioned	ITFA. ITFA + post-fossa cranio-orbitozygomatic + petrosectomy.	85.7 (24 pts)	8.3 (2 pts)	91.6	Nil	4 pts (14.3)	2 pts (7.1)
Ramina et al[5]	58	1987–2004, 17-y study duration†	Not mentioned	Craniocervical involving transmastoid + retrosigmoid.	77.5 (45 pts)	6.7 (3 pts)	93.3	4 pts	4 pts (6.9)	10 pts (17)
Suárez et al[12]	37	1977–2006, 29-y study duration†	Fisch	ITFA. Extended facial recess. Canal down transmastoid.	86.5 (32 pts)	28.1 (9 pts)	71.9	Nil	4 pts (10.8)	11 pts (29.7)
Pareschi et al[13]	37	4.9 y (59)	Fisch	ITFA. Petrosectomy.	96 (35 pts)	Nil	100	Nil	3 pts (8.1)	18 pts (50)
Papaspyrou et al[14]	52	9.3 y (112)	Not mentioned	No description	Not mentioned	19.2 (10 pts)	81.5	Nil	Nil	25 pts (48.1)
Kaylie et al[15]	202	4.5 y (54)	Not mentioned	No description	90 (181 pts)	6.0 (11 pts)	84.2	5 pts	12 pts (6)	121 pts (60)
Moe et al[16]	119	2.1 y (24–132)	Fisch	ITFA, pterosectomy transmastoid.	80.7 (96 pts)	1.0 (1 pts)	98.0	1 pt	14 pts (11)	(31 to 70)‡
Borba et al[17]	34	4.3 y (52)	Fisch	ITFA. ITFA + post-fossa.	91 (31 pts)	6.4 (2 pts)	93.5	1 pt	6 pts (17.6)	6 pts (17.6)
Present study	121	7.3 y (88) Min: 12 mo Max: 252 mo	Modified Fisch	ITFA alone (104 pts). ITFA combined with other (12 pts). Petrosectomy (5 pts).	81.8 (99 pts)	4.0 (4 pts)	96.0	Nil	2 pts (1.6)	19 pts (15.9)

Abbreviations: CSF, cerebrospinal fluid; CND, cranial nerve deficit; ITFA, infratemporal-fossa type A.

*Surgical control $= \frac{(\text{Total resection cases} - \text{Recurrence cases})\ \%}{\text{Total resection cases}}$

†The authors did not describe the mean for follow-up duration.

‡The rates of lower cranial nerve preservation in this series were varied according to the specific cranial nerve.

TABLE 2. Cases presented with multicentric tumor.

Multicentricity	No. of cases (%)*	ICE, genetic mutation (%), malignant change
JP + CBT	8 cases (6.4)	ICE (3 cases) 2 cases positive-SDHB mutation
JP + VP	9 cases (7.2)	ICE (7 cases) None had genetic mutation
JP + VP + CBT	4 cases (3.3)	ICE (1 case) None had genetic mutation 1 malignant changed
Total	21 cases (16.9)	11 cases had ICE (10 cases presented with intradural extension)

Abbreviations: ICE, intracranial extension; JP, jugular paraganglioma; CBT, carotid body tumor; SDHB, succinate dehydrogenase subunit B; VP, vagal paraganglioma.
*The age range is between 17 and 62 years with a mean of about 42 years.

complete radioimaging evaluation. The imaging studies included high-resolution CT with bone windows, gadolinium-enhanced MRI, and 4-vessel angiography with manual cross-compression testing. The tumor classification was identified according to the radiological findings and was confirmed by the intraoperative findings.

Follow-up included clinical examination as well as high-resolution CT and MRI scans. The follow-up radiological evaluation was usually performed at 6 months and subsequently annually, unless otherwise indicated. The facial nerve function was recorded according to the House-Brackmann (H–B) grading system.[21] Facial nerve function was graded at each postoperative follow-up by a member of the operating team and the patient was photographed using the technique described in our previous article.[4] All of the cases underwent otoscopic, hearing, vocal cord, and lower CN assessment. The analyzed clinical data included the surgical procedure, tumor classification, intraoperative management of the facial nerve, preoperative and intraoperative management of the internal carotid artery (ICA), and the preoperative and postoperative lower CN function. We routinely used facial nerve monitoring in all our skull base operations.

All the cases underwent endovascular embolization between 2 to 4 days before surgery. Separate preoperative endovascular treatments, either with balloon occlusion or stent reinforcement, were carried out in the cases that had severe ICA encasement. The indication and methods of endovascular treatments have been discussed in the literature.[18] The majority of the tumors in our series were resected through the infratemporal fossa approach type A with the details of the surgical technique described elsewhere.[20,22] Supplementary surgical techniques were used in some of the cases, especially in staged surgical procedures. The resection of an intradural portion during the initial procedure is not advisable because connecting the subarachnoid space with the neck spaces would increase the risk of postoperative CSF leakage. Staged surgical resection was mainly used in cases that had tumor class Di2 (intradural tumor greater than 2 cm). The extradural tumors were removed first, and then, after at least 3 months, the intradural portion was removed, mainly through the petro-occipital transigmoid approach, with extension to the clivus when required.[22]

Statistical analysis

The statistical analysis was performed using IBM SPSS Statistics for Windows version 19 (SPSS, Chicago, IL). Data were described in mean and percentage. Differences between 2 categorical data were analyzed using the chi-square test or the Fischer exact test. Odds ratio with 95% confidence interval was calculated when relevant. The level of statistical significance was set at $p < .05$, 2-tailed.

RESULTS

There were 121 cases (41 male and 80 female patients). The patients' ages ranged from 16 to 75 years, with a mean of 47 years. Our patient follow-up had a mean duration of 88 months (range, 12–252 months). Sixty-six of these tumors (54.5%) were on the left side and 54 on the right side (44.6%). One of the cases (0.9%) had bilateral jugular paraganglioma but 1 side was treated elsewhere. The most common otologic presenting symptoms were hearing loss in 87 cases (72%) and pulsatile tinnitus in 82 cases (68%). Hoarseness was the most common nonotologic presenting symptom, seen in 30 cases (25%). Twenty-one of the cases (17.4%) presented with multicentric tumors. The multicentric cases are summarized in Table 2. Eleven of the multicentric cases (52.4%) presented with ICE. However, statistically (Table 3), multicentricity did not significantly affect the surgical management outcome (chi-square = 0.541; df = 1; $p = .462$).

TABLE 3. Surgical management outcome in relation with tumor characteristics.

	Total		Subtotal				
	No. of patients	%	No. of patients	%	Chi-square	df	*p* value
Tumor extension							
ICE	50	50.50	17	77.30	5.219	1	.022
ECE	49	49.50	5	22.70			
Multicentric tumor							
Yes	16	16.16	5	22.70	0.541	1	.462
No	83	83.84	17	77.30			
Endovascular ICA management							
Yes	12	12.12	10	45.45	13.440	1	<.001
No	87	87.88	12	54.55			

Abbreviations: ICE, intracranial extension; ECE, extracapsular extension; ICA, internal carotid artery.

TABLE 4. Tumor classification (Fisch).

Fisch class	No. of ECE (%)*	No. of ICE (%)†			
		De1	De2	Di1	Di2
C1	15 (12.4)	0	0	2 (1.6)	0
C2	37 (30.6)	13 (10.7)	0	17 (14.0)	3 (2.5)
C3	2 (1.6)	6 (4.9)	2 (1.6)	11 (9.1)	10 (8.3)
C4	0	0	1 (0.8)	1 (0.8)	1 (0.8)
Total	54 (44.6)	22 (18.3) (extradural)		45 (37.1) (intradural)	

Abbreviations: ECE, extracranial extension; ICE, intracranial extension; C1, no invasion of carotid; destruction of jugular bulb/foramen; C2, invasion of vertical carotid canal between foramen and bend; C3, invasion along horizontal carotid canal; C4, invasion of foramen lacerum and along carotid into cavernous sinus; De1, intracranial/extradural extension up to 2-cm dural displacement; De2, intracranial/extradural extension more than 2-cm dural displacement; Di1, intracranial/intradural extension up to 2-cm; Di2, intracranial/intradural extension more than 2-cm.

* The age range is between 17 and 75 years with a mean of about 47 years.

† The age range is between 16 and 68 years with a mean of about 45 years.

Malignant jugular paraganglioma was observed in 2 cases, with the first patient, aged 26 years, presenting with ipsilateral cervical lymph nodes metastases. Genetic studies showed a mutation in succinate dehydrogenase subunit B. The second patient, aged 46 years, had multicentric paragangliomas but genetic analysis did not show any mutation. There were no cases with catecholamine-secreting tumors.

Fisch classification and tumor growth pattern

The frequency of tumor extension by Fisch's classification is depicted (Table 4). This was confirmed from radiological and intraoperative findings. Sixty-seven cases (55.4%) had ICE. Forty-four of the 67 cases (36.5%) had intradural extension and 23 (18.9%) had extradural extension. Fifty-four of cases (44.6%) had extracranial extension. The percentage of intracranial involvement increased in proportion to tumor growth (Table 5; chi-square = 35.815; df = 3; $p < 0.001$, p trend $< .001$).

Surgical approaches

One hundred four of the tumors (86.1%) were resected via the infratemporal fossa approach type A. In 12 cases (9.8%), the tumors were approached through a combination between infratemporal fossa approach type A and other surgical approaches, in order to have adequate surgical access for tumor removal. In view of the patients' age and wishes in 5 cases (4.1%), the tumors were removed via a petrosectomy approach. Complete tumor resection was achieved in 99 cases (81.8%). In 22 cases (18.2%), the tumors could not be removed completely. The tumors needed to be dissected from the ICA in 83 cases (68.6%). Twenty-two of these 83 cases underwent endovascular treatment of the ICA. Endovascular stent reinforcement was carried out in 15 of the 22 cases. Seven cases underwent permanent balloon occlusion. No complications occurred during endovascular treatment or during surgery in these cases. Planned 2-stage surgery was performed in 17 cases (14%). Twelve of the 17 cases (70.5%) had more than a 2-cm intradural tumor extension. Five of the 17 cases (29.5%) had less than a 2-cm intradural extension. The average duration between the first and second surgeries was 10 months, with a range of 3 to 21 months. Eight cases underwent the petro-occipital transigmoid approach for their second-stage surgery. The modified transcochlear approach was performed in 5 cases.[23] Translabyrinthine approach was performed in 2 cases. Two cases underwent transotic[20] and extreme lateral approach,[24,25] respectively. Ten of the 17 patients (58.8%) undergoing staged surgery had carotid artery management by either stenting (5 cases) or balloon occlusion (5 cases). In 1 case, the intradural portion was unresectable because it was attached to the vertebral and basilar arteries, and the procedure was abandoned. The tumor was controlled with gamma knife surgery.

Perioperative complications

All the cases underwent preoperative embolization. The procedure was uneventful except in 1 case, which developed an H–B grade IV facial nerve paresis. Perioperative mortality was not encountered in the present series. The most frequent perioperative complication was CSF leakage, which occurred in 2 cases (1.6%). In the first case, there was intradural extension and the CSF leak occurred after the first-stage surgery. In the second case, the histopathology showed a malignancy, and the CSF leak developed after second-stage surgery. In both cases, the CSF leak required surgical closure where the area was intersewn with a muscle plug.

Cranial nerve status

The preoperative and postoperative CN status is depicted in Table 6. Sixty of the cases (49.6%) presented

TABLE 5. Association of Intracranial extension and extracapsular extension with Fisch class and lower cranial nerve deficit involvement.

	ICE		ECE				
	No. of patients	%	No. of patients	%	Chi-square	df	*p* value
Fisch class							
C1	2	11.8	15	88.2	35.815	3	< .001*
C2	33	47.2	37	52.8			
C3	29	93.5	2	6.5			
C4	3	100.0	0	0			
Lower CND							
Yes	22	40.7	38	56.7	3.053	1	.081
No	32	59.3	29	43.3			

Abbreviations: ICE, intracranial extension; ECE, extracranial extension; CND, cranial nerve deficit.

* Fisher exact test.

TABLE 6. Cranial nerve function in preoperative, postoperative, and number of cases that developed new cranial nerve deficit.

	Number of cases with CNDs (%)		
CN	Preoperative	Postoperative*	Postoperative new CND, mean 15.9[†]
IV	2 (1.6)	1 (0.8)	Nil
V	1 (0.8)	Nil	Nil
VI	3 (2.4)	2 (1.6)	Nil
VII[‡]	17 (14.9)	41 (33.9)	24 (19.0)
IX	36 (29.8)	66 (54.5)	30 (24.7)
X	39 (32.2)	57 (47.1)	18 (15.0)
XI	24 (19.7)	36 (29.7)	12 (10.0)
XII	24 (19.8)	37 (30.6)	13 (10.8)

Abbreviations: CN, cranial nerve; CND, cranial nerve deficit.
* At least 1-year follow-up after primary surgical intervention.
[†] For lower cranial nerves the overall new postoperative deficits were seen in 15.1% of cases.
[‡] The facial nerve status was House–Brackman (H–B) grade II to VI.

preoperatively with at least 1 lower CN deficit. The majority of these cases (63.3%) had ICE and 36.7% did not have ICE. Although there was a higher percentage of lower CN deficit among cases with ICE compared to extracapsular extension (ECE), the difference was not statistically significant (Table 5; $p = .08$; odds ratio = 1.9; 95% confidence interval = 0.9–3.9). The most commonly involved CN was IX (28.8%) and X (31.2%). Intraoperatively, the lower CN could be preserved anatomically in 78 cases (63%). Cases without ICE had the greatest potential for functional lower CN preservation. The lower CN could be preserved anatomically in 25 of the 67 (37.3%) cases that had ICE. Postoperative follow-up of at least 1 year showed that the most common new CN deficit was seen in IX CN (24.1%), followed by X CN (14.5%), XII CN (10.4%), and XI CN (9.6%). The 43 cases (64%) with ICE demonstrated some degree of functional deficit. Eighteen of them had normal lower CN function preoperatively. In these cases, their lower CN were sacrificed due to tumor invasion particularly at the level of intradural. In 7 cases without intradural extension, the medial wall of the jugular bulb was preserved during surgery. All of these cases had good postoperative lower CN function. Three cases had varying degrees of aspiration, which resolved with conservative management except in 1 case which required a feeding jejunostomy. A medialization thyroplasty was performed in 4 cases (3.3%) that had persistent dysphonia or aspiration symptoms. The surgical intervention was performed at least 6 months after tumor extirpation. Eighty-four cases underwent permanent anterior transposition of the facial nerve. One-year after primary surgery, we observed 59.6% of them had good functional recovery (H–B grade I and II).

Surgical oncologic outcomes

Of the 121 cases in this series, 99 (81.8%) underwent gross total tumor resection. From this number, 4 cases (4%) developed tumor recurrence. The age of patients who had recurrence ranged from 26 to 40 years, with a mean age of 32.5 years. Two cases had recurrence 3 years after surgery, 1 case 5 years after surgery and another 6 years after surgery. Three of the recurrent cases were class C2, whereas the remaining recurrent case was a C3Di2 tumor. Ninety-five cases (78.5%) showed no evidence of tumor recurrence from clinical or radiologic investigations at a mean follow-up of 88 months (7.3 years). The surgical tumor control was achieved in 96% of the total resection cases. Twenty-two cases (18.2%) underwent subtotal resection. Eleven of these cases had carotid artery management either by stenting (7 cases) or balloon occlusion (4 cases). Statistical analysis has shown that the percentage of endovascular ICA management was significantly higher in cases that underwent subtotal tumor resection (Table 3; 45.45% vs 12.12%; chi-square = 13.440; df = 1; $p < .001$). Nineteen of these 22 cases of the residual tumor were intracranial involving the cavernous sinus, foramen magnum, posterior fossa dura, prepontine cistern, and the vertebral and basilar artery. For extracranial residual tumors, partial resection was performed in 2 cases due to significant cardiac comorbidities. In 1 case, the extracranial residual tumor was attached to a dominant sigmoid sinus. There was significantly higher ICE among those who had subtotal resection (Table 3; 77.3% vs 50.5%; chi-square = 5.219; df = 1; $p = .02$).

The 2 cases that had malignancy presented with recurrence and regrowth of the disease at the primary site at 3

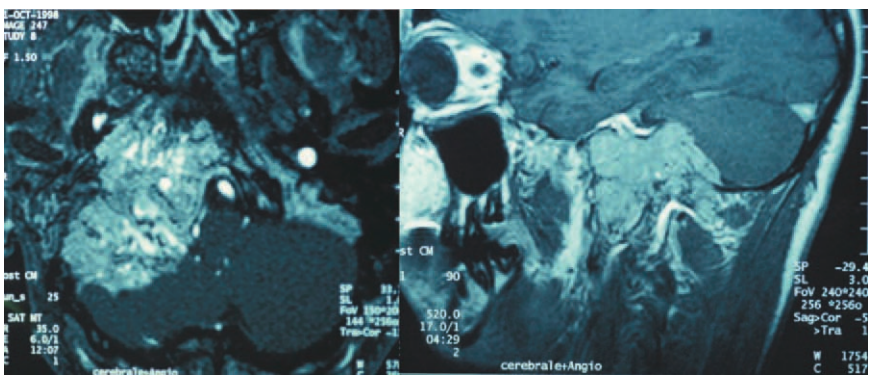

FIGURE 1. Axial and sagittal MR images of the patient who passed away 10 years after his primary surgery illustrating that the progressive tumor regrowth leads to compression of the brain stem and right cerebellum.

TABLE 7. Surgical oncologic outcomes and summary of subsequent treatment in the subtotal resection and recurrence cases.

	Total resection (No: 99 cases) (81.8%)	Subtotal resection (No: 22 cases) (18.2%)*		Recurrence after total resection (No: 4 cases) (4.0%)
Mean age	48.0 y	47.8 y		32.5 y
Oncologic outcome (mean follow-up: 88 mo)	Tumor free: 95 cases	Tumors were stable: 12 cases (watchful & rescan)†	Mean for the occurrences mo of tumor recurrence: 51 mo (4.3 y)	Tumors were stable: 2 cases (watchful & rescan)
	Recurrence: 4 cases	Tumors regrowth: 5 cases		Reoperated: 1 case (stable)‖
	Surgical tumor control: 96%	4 cases underwent gamma knife surgery/RT (stable)‡		Intratumoral embolization: 1 case (stable)
		1 case underwent multiple embolization§		

Abbreviation: RT, radiotherapy.
* Five of the residual cases were lost during the follow-up.
† Five of the residual cases, the tumors undergo spontaneous regression through routine MRI investigation after 5 years follow-up.
‡ One of them was the malignant changed case, had persistent presence of tumor at cavernous sinus despite of revision surgery.
§ This patient died 10 years after his primary surgery.
‖ The case had malignant changed, achieved complete removal in revision surgery.

and 5 years, respectively. The first patient, aged 26, developed recurrence in the internal acoustic canal and the tumor was resected via combined infratemporal fossa approach type A and translabyrinthine approach. The second patient, aged 46, had regrowth of the residual tumor at the cavernous sinus and was subjected to gamma knife surgery. One of the residual cases died 10 years after his primary surgery due to regrowth of the residual disease despite 5 episodes of intratumoral embolization (Figure 1). The summary for these oncological outcomes is described in Table 7.

DISCUSSION

Jugular paragangliomas are slow-growing tumors arising from paraganglia cells located within the adventitia of the jugular bulb and along the Jacobson's and Arnold's nerves, connected to venous channels.[26,27] They tend to grow along the planes of least resistance by following preexisting pathways in the skull base (ie, fissures, air cell tracts, vascular channels, and nerve foramina).[28,29] These hypervascular tumors often develop unnoticed, resulting in a delay in the diagnosis.

In previously published series, it has been reported that jugular paragangliomas are diagnosed predominantly in the fifth to sixth decades of life.[5,30] However, in our present series, the majority of the tumors occurred in the fourth decade of life, with a female-to-male ratio of 2:1. It has also been reported that catecholamine-secreting tumors occur symptomatically in 1% to 3% of cases.[31,32] Although we did not encounter such cases in the present series, the preoperative screening for catecholamine-secreting tumors was routinely performed in all patients to avoid intraoperative anesthetic complications.

The Glasscock–Jackson[33] and Fisch[20] classifications are commonly used in describing tumor extension. We prefer the Fisch classification because as it is closely related to surgical management and morbidity. Due to the tumor's complex and intimate relationship with important neurovascular structures, a wide access is mandatory to facilitate complete tumor resection while preserving the important structures, when possible. For this, we believe the infratemporal fossa approach type A is sufficient and is a widely accepted surgical approach. By utilizing the infratemporal fossa approach type A, the surgical tumor control ranged from 72% to 100% (Table 1). Jugular paragangliomas that extend intracranially represent a treatment challenge, which requires an appropriate management approach. For the intradural portion, the tumors were removed via staged surgical procedures to avoid a potentially catastrophic communication between the subarachnoid and neck spaces, leading to CSF leaks.[4,34,35] In our present series, there were no additional deficits or morbidities related to these approaches.

The incidence of ICE in jugular paraganglioma has been reported to range from 36% to 72%.[16,36,37] In our present series, ICE constitutes 55.4% of cases. The intracranial involvement correlates well with the advancing tumor stage. The severity of ICE also significantly influences the surgical outcome in the present series. Successful surgical management in jugular paraganglioma requires understanding its growth pattern and behavior. In the present series, we found that the frequency of intracranial involvement was higher in class C2 and C3 tumors. As the tumor progresses from these 2 stages, it grows intracranially more commonly along the lower CN rather than along the ICA and extends toward the prepontine cistern, foramen magnum, and vertebral and basilar artery. This observation is particularly helpful and valuable for radioimaging studies and surgical planning strategies.

Although the ICA is no longer a limiting factor in jugular paraganglioma surgery, in the present series, the severity of its invasion by the tumor is significantly related to the surgical oncologic outcome. Therefore, accurate preoperative radioimaging evaluation of the extent of ICA invasion by the tumor is necessary in order to achieve a favorable surgical outcome. Three of our recurrent cases (75%) were in class C2, and 1 of them had malignancy. In these cases, even though during surgery the tumor could be resected completely from the ICA, there may be microscopic deposits left around the wall of the artery. Oncologically, the best solution to achieve favorable surgical outcome in ICA involvement by paraganglioma is arterial resection and this should be carefully and accurately assessed by radioimaging investigation.

Our results support the observation that advancing tumor stage and preoperative lower CN function influence the prospect of postoperative functional lower CN

preservation. Sixty of the cases (49.6%) presented preoperatively with at least 1 lower CN deficit. In our present series, the majority of the preoperative CN deficit (63.3%) were developed in the tumors with ICE, reflecting a tendency for late manifestation of lower CN deficit, usually after ICE has already occurred.

The intrabulbar tumor removal technique, described first by Gejrot[38] and reproposed later by Al–Mefty and Teixeira,[11] consists of preservation of the anteromedial wall of the jugular bulb and internal jugular vein, in order to preserve the lower CN function. This intrabulbar removal technique is possible whenever the tumor does not breach the wall of the jugular bulb and is suitable for jugular paragangliomas without ICE. In our present series, we have observed that in jugular paraganglioma with ICE, the tumor capsule was densely adherent to the lower CN, making the preservation of the nerves almost impossible. Makek et al[39] demonstrated neurological infiltration of CNs by paragangliomas and the degree of infiltration increased with the size of the tumor, progressively involving further the perineurium and then endoneurium.[39] This explains and justifies the need for the lower CN resection along with the tumor for a complete tumor removal, especially in cases that have ICE with risk of recurrence.

For the cases that have evidence of preoperative lower CN dysfunction, total resection of the involved lower CN is recommended. Hoarseness, aspiration, and dysphagia are the recognized clinical features resulting from the lower CN dysfunction. In persistent postoperative lower CN dysfunction with poor compensation, rehabilitative surgical procedures, such as vocal cord medialization and cricopharyngeal myotomy, are recommended after at least 6 months.[40] In the present series, most of the cases with lower CN dysfunction regained satisfactory neurological compensation and only 4 cases (3.3%) needed surgical rehabilitation to overcome their prolonged lower CN dysfunction.

Jugular paraganglioma can exhibit malignant transformation and metastasize. In our present series, the incidence of malignancy was 1.6%, with 36 being the average age at presentation. The diagnosis of malignant transformation requires a high index of suspicion. Regional lymphadenopathy could be an indication of this malignant transformation. Cervical lymph node metastasis occurred in 1 of the cases. The primary treatment for malignancy should be complete tumor resection along with the ipsilateral lymphatic tissues. Postoperative radiotherapy may be indicated in cases of positive surgical margins or residual tumors. It has been reported that the 5-year survival rate for regionally confined malignant paragangliomas was 76.8%.[41]

The choices of treatment for the residual and recurrent jugular paragangliomas are usually individualized. The available treatment modalities include surgery, radiotherapy, intratumoral embolization, and observation only. We agree with Fayad et al[42] that the aim of treatment for these 2 tumor categories is to gain control of growth and prevent further neurological deficits. In the present study of 22 residual cases, tumor regrowth was observed in 5 cases (23%). Four of them underwent radiotherapy and intratumoral embolization was performed in the remaining 1 case. Twelve stable residual tumors in the present study underwent surveillance only. Five of these 12 cases had spontaneous regression through routine MRI and or high-resolution CT investigation after 5-year follow-up. The reported rates of regrowth from the remnant tumor ranged from 17% to 27%.[10,43]

Adopting an observation attitude in asymptomatic jugular paragangliomas seems a reasonable approach especially for patients who are medically unfit for surgery or of an advanced age. In our institution, there were 21 such patients who underwent conservative management and we did not observe any changes in the size of their tumor during follow-up (unpublished data). Long-term tumor control rates remain to be established. Due to the slow growth of paragangliomas, it is difficult to draw any conclusion about prognosis after relatively short follow-up periods. In the present series, 1 of the residual cases succumbed to tumor regrowth 10 years after primary surgery. Based on this observation, and on the indolent nature of the tumor, it is reasonable that the postoperative follow-up for jugular paragangliomas should be extended to at least 10 years after the primary surgery.

CONCLUSION

Jugular paraganglioma may present in a variety of manners. Ideally, the tumor should be surgically treated in the early stages, in order to have a favorable oncological outcome. Recurrence and malignancy tend to develop in a younger group of patients. In our present series, jugular paragangliomas have shown a predictable pattern of ICE along the lower CN. The surgical oncologic outcomes were significantly related to the severity of ICE and ICA involvement by the tumor. These are the crucial factors to be adequately assessed preoperatively, in order to achieve an encouraging surgical outcome with minimal morbidity. Future studies should shed light into the molecular bases of paragangliomas, with particular regard to the biological factors that stimulate tumor growth, formation of feeding vessels, and metastatic progression. Then novel tumor classifications and therapies based on these factors will improve the management of patients with jugular paraganglioma.

REFERENCES

1. Batsakis JG. Paraganglioma of the head and neck. In: Batsakis JG, editor. Tumours of the head and neck: clinical and pathological considerations. 2nd ed. Baltimore: Williams and Wilkins; 1979. pp 369–380.
2. Jackson CG. Surgery for benign tumors of the temporal bone. In: Glasscock ME III, Gulya AJ, editors. Surgery of the ear. Hamilton, Ontario: BC Decker; 2003. pp 714–742.
3. Fayad JN, Keles B, Brackmann DE. Jugular foramen tumors: clinical characteristics and treatment outcomes. *Otol Neurotol* 2010;31:299–305.
4. Sanna M, Jain Y, De Donato G, Rohit MS, Lauda L, Taibah A. Management of jugular paragangliomas: the Gruppo Otologico experience. *Otol Neurotol* 2004;25:797–804.
5. Ramina R, Maniglia JJ, Fernandes YB, et al. Jugular foramen tumors: diagnosis and treatment. *Neurosurg Focus* 2004;17:E5.
6. Chen PG, Nguyen JH, Payne SC, Sheehan JP, Hashisaki GT. Treatment of glomus jugulare tumors with gamma knife radiosurgery. *Laryngoscope* 2010;120:1856–1862.
7. Maarouf M, Voges J, Landwehr P, et al. Stereotactic linear accelerater-based radiosurgery for the treatment of patients with glomus jugulare tumors. *Cancer* 2003;97:1093–1098.
8. Eustacchio S, Trummer M, Unger F, Schröttner O, Sutter B, Pendl G. The role of gamma knife radiosurgery in the management of glomus jugular tumours. *Acta Neurochir Suppl* 2002;84:91–97.
9. Krych AJ, Foote RL, Brown PD, Garces YI, Link MJ. Long-term results of irradiation for paraganglioma. *Int J Radiat Oncol Biol Phys* 2006;65:1063–1066.

10. Tran Ba Huy P, Chao PZ, Benmansour F, George B. Long-term oncological results in 47 cases of jugular paraganglioma surgery with special emphasis on the facial nerve issue. *J Laryngol Otol* 2001;115:981–987.
11. Al–Mefty O, Teixeira A. Complex tumors of the glomus jugulare: criteria, treatment, and outcome. *J Neurosurg* 2002;97:1356–1366.
12. Suárez C, Sevilla MA, Llorente JL. Temporal paragangliomas. *Eur Arch Otorhinolaryngol* 2007;264:719–731.
13. Pareschi R, Righini S, Destito D, Raucci AF, Colombo S. Surgery of glomus jugulare tumors. *Skull Base* 2003;13:149–157.
14. Papaspyrou K, Mann WJ, Amedee RG. Management of head and neck paragangliomas: review of 120 patients. *Head Neck* 2009;31:381–387.
15. Kaylie DM, O'Malley M, Aulino JM, Jackson CG. Neurotologic surgery for glomus tumors. *Otolaryngol Clin North Am* 2007;40:625–649.
16. Moe KS, Li D, Linder TE, Schmid S, Fisch U. An update on the surgical treatment of temporal bone paraganglioma. *Skull Base Surg* 1999;9:185–194.
17. Borba LA, Araújo JC, de Oliveira JG, et al. Surgical management of glomus jugulare tumors: a proposal for approach selection based on tumor relationships with the facial nerve. *J Neurosurg* 2010;112:88–98.
18. Sanna M, Piazza P, De Donato G, Menozzi R, Falcioni M. Combined endovascular-surgical management of the internal carotid artery in complex tympanojugular paragangliomas. *Skull Base* 2009;19:26–42.
19. Sanna M, Shin SH, De Donato G, et al. Management of complex tympanojugular paragangliomas including endovascular intervention. *Laryngoscope* 2011;121:1372–1382.
20. Fisch U, Mattox D, editors. Microsurgery of the skull base. Stuttgart, Germany: Georg Thieme Verlag; 1988.
21. House JW, Brackmann DE. Facial nerve grading system. *Otolaryngol Head Neck Surg* 1985;93:146–147.
22. Sanna M, Saleh E, Khrais T, et al. Atlas of microsurgery of the lateral skull base. 2nd ed. Stuttgart, Germany: Georg Thieme Verlag; 2008.
23. Sanna M, Mazzoni A. The modified transcochlear approach to the tumors of the petroclival area and prepontine cistern. Third annual meeting of the North American Skull Base Society. Acapulco, Mexico; February 15–20, 1992.
24. Sanna M, Mazzoni A, Saleh EA, Taibah AK, Russo A. Lateral approaches to the median skull base through the petrous bone: the system of the modified transcochlear approach. *J Laryngol Otol* 1994;108:1036–1044.
25. Sen CN, Sekhar LN. An extreme lateral approach to intradural lesions of the cervical spine and foramen magnum. *Neurosurgery* 1990;27:197–204.
26. Ernest EL. Paragangliomas. In: Mills SE, Carter D, Sternberg SS, editors. Sternberg's diagnostic surgical pathology. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2010. pp 587–610.
27. Rhoton AL Jr. Jugular foramen. *Neurosurgery* 2000;47(3 Suppl): S267–S285.
28. Spector GJ, Maisel RH, Ogura JH. Glomus tumors in the middle ear. I. An analysis of 46 patients. *Laryngoscope* 1973;83:1652–1672.
29. Chakeres DW, LaMasters DL. Paragangliomas of the temporal bone: high-resolution CT studies. *Radiology* 1984;150:749–753.
30. Heth J. The basic science of glomus jugulare tumors. *Neurosurg Focus* 2004;17:E2.
31. Groblewski JC, Thekdi A, Carrau RL. Secreting vagal paraganglioma. *Am J Otolaryngol* 2004;25:295–300.
32. Schwaber MK, Glasscock ME, Nissen AJ, Jackson CG, Smith PG. Diagnosis and management of catecholamine secreting glomus tumors. *Laryngoscope* 1984;94:1008–1015.
33. Jackson CG, Glasscock ME III, Harris PF. Glomus tumors. Diagnosis, classification, and management of large lesions. *Arch Otolaryngol* 1982; 108:401–410.
34. Fisch U, Fagan P, Valavanis A. The infratemporal fossa approach for the lateral skull base. *Otolaryngol Clin North Am* 1984;17:513–552.
35. Jackson CG. Glomus tympanicum and glomus jugulare tumors. *Otolaryngol Clin North Am* 2001;34:941–970.
36. Jackson CG, McGrew BM, Forest JA, Netterville JL, Hampf CF, Glasscock ME III. Lateral skull base surgery for glomus tumors: long-term control. *Otol Neurotol* 2001;22:377–382.
37. Green JD Jr, Brackmann DE, Nguyen CD, Arriaga MA, Telischi FF, De la Cruz A. Surgical management of previously untreated glomus jugulare tumors. *Laryngoscope* 1994;104(8 Pt 1):917–921.
38. Gejrot T. Surgical treatment of glomus jugulare tumours with special reference to the diagnostic value of retrograde jugulorography. *Acta Otolaryngol* 1965;60:150–168.
39. Makek M, Franklin DJ, Zhao JC, Fisch U. Neural infiltration of glomus temporale tumors. *Am J Otol* 1990;11:1–5.
40. Cheesman AD, Kelly AM. Rehabilitation after treatment for jugular foramen lesions. *Skull Base* 2009;19:99–108.
41. Lee JH, Barich F, Karnell LH, et al. National cancer data base report on malignant paragangliomas of the head and neck. *Cancer* 2002;94: 730–737.
42. Fayad JN, Schwartz MS, Brackmann DE. Treatment of recurrent and residual glomus jugulare tumors. *Skull Base* 2009;19:92–98.
43. Briner HR, Linder TE, Pauw B, Fisch U. Long-term results of surgery for temporal bone paragangliomas. *Laryngoscope* 1999;109: 577–583.