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The Role of Wait-and-Scan and the Efficacy of Radiotherapy in the Treatment of Temporal Bone Paragangliomas

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Objective: To define the role of wait-and-scan and radiotherapy (RT) in the treatment of temporal bone paragangliomas and to review the literature on the outcomes of RT as a treatment modality.

Materials and Methods: This was a retrospective and literature review. The records of 381 patients with 382 tumors between 1988 and 2012 were analyzed. Patients who were subjected to initial wait-and-scan or primary RT were analyzed for tumor response, facial, and lower cranial nerve status on follow-up (FU).

Results and Observations: None of the 145 patients (38%) with Class A and B tumors were subjected to wait-and-scan or RT and all were operated on. Of the 237 patients (62%) with Class C and D tumors, 47 (19.8%) were subjected to an initial wait-and-scan policy and 1 (0.4%) underwent primary RT. In 24 patients subjected to wait-and-scan with a FU of less than 3 years, tumor remained stable in 22 patients (92%). In 12 patients with a FU between 3 and 5 years, the tumor remained stable or regressed in 10 patients (83%). In 11 patients with a FU of more than 5 years, the tumor remained stable or regressed in 5 patients (45%). A literature review of the results of RT did not conclusively prove that it was effective as a primary modality of treatment for temporal bone paragangliomas.

Conclusion: In elderly patients with advanced tumors, a wait-and-scan approach is recommended, and RT is initiated only when fast-growing tumors are detected. There is insufficient evidence in literature to suggest that RT could be an effective alternative to surgery in Class C and D tumors. **Key Words:** Lower cranial nerve palsy—Radiotherapy—Stereotactic radiosurgery—Temporal bone paragangliomas—Tympanojugular paragangliomas—Tympanomastoid paragangliomas—Wait-and-scan.

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Temporal bone paragangliomas (TBPs), including tympanomastoid paragangliomas (TMPs; modified Fisch Class A and B) and tympanojugular paragangliomas (TJPs; modified Fisch Class C and D) (1,2), are benign tumors involving the middle ear cleft and the skull base for which 3 distinct treatment modalities are currently in practice: microsurgery, radiotherapy (RT), and wait-and-scan. In the past, RT was offered as the treatment of choice for Class C and D TJPs because they were deemed inoperable (3,4). Subsequently RT, especially stereotactic radiosurgery (SRS) gained ground as a primary treatment option that was an alternative to surgery in TBPs. However, advances in neuroradiology, microsurgery, intraoperative neuromonitoring, and neuroanesthesia of the skull base in the last few decades have made it possible to surgically remove even the most complex tumors in this area with minimal complications and morbidity. Meanwhile, the recognition of wait-and-scan as a separate treatment modality, exploiting the insidious nature of these tumors, has added another viable option in the management of TBPs, especially in elderly patients. In the wake of these developments, there is presently a need to redefine the roles of surgery, wait-and-scan, and RT in the treatment of TMPs.

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Although proponents of RT claim it to be an effective alternative to surgery (5–7), a review and analysis of literature proves that is indeed a premature conclusion because of a variety of considerations. First, RT does not completely eliminate the tumors but only achieves at maximum a tumor control or volume reduction of approximately 10% to 25% (7–13). This presents a risk of regrowth in this particular subset of tumors that are known to be locally aggressive, and the risk is more so in younger patients. Second, a review of literature shows that there is a lack of standardization when it comes to reporting results of conventional RT or SRS, and radiotherapists reporting on the successful results of RT often use many parameters of analysis that are either nonconsensual between radiotherapists themselves or are divergent from those used for reporting by the surgeons. For instance, reports on TBPs by radiotherapists do not classify tumors according to the Fisch classification, while preferring to report them based on tumor sizes. This leads to confusion in reporting outcomes and making comparisons between different modalities difficult. Finally, many studies on RT have limitations like short follow-up, nondetermination of the stability of tumors before irradiation, and a lack of clarity on the size or class of tumors that need to be irradiated. In this article, we performed a systematic review of literature on the outcomes of RT, drew out the limitations of RT as a primary treatment option in TBPs, and compared the outcomes of RT with the outcomes of our series of patients who were subjected to a wait-and-scan policy.

MATERIALS AND METHODS

The medical records of all patients diagnosed with TBPs between 1988 and 2012, at the Gruppo Otologico (Piacenza-Rome), Italy, were analyzed. Patients who were lost for follow-up and case sheets with incomplete records were excluded from the study. The TBPs were classified according to the modified Fisch classification (1,2). The age, sex, presenting complaints, clinical findings, side and site of the tumors and cranial nerve status were noted. The preoperative evaluation including audiogram, high-resolution computed tomography, magnetic resonance imaging (MRI) with gadolinium diethylenetriamine penta-acetic acid, and angiography were noted. The management policy for the treatment of all TBPs is presented elsewhere and in our textbook on skull base paragangliomas (14–18).

Patients who were followed up with wait-and-scan or treated with RT were analyzed for tumor response, facial nerve (FN), and lower cranial nerve (LCN) status on follow-up. Patients in the wait-and-scan group were followed up at 6 months and then annually, unless otherwise indicated. The sizes of tumors were evaluated by MRI (1.5 T) by measuring their diameters in 2 perpendicular directions (mm). Growth of the tumor was determined by the increase in its greatest dimension on follow-up MRI studies. Tumors that grew at a rate of greater than 3 mm/yr were considered fast growing and any growth less than 3 mm was considered slow growing. Patients were referred for external beam RT between 1988 and 2008 and since then to gamma knife surgery. The FN function was recorded according to the House-Brackmann grading system (19) and graded at each follow-up (15).

A comprehensive search of the English-language literature was done to identify studies that collectively described outcomes for patients who underwent RT as a treatment modality for TBP tumors from January 1983 to January 2013. Reports where SRS was used were analyzed in a systematic review because SRS as a treatment option incorporates the benefits of RT with minimum adverse side effects and can be considered as representative of the studies on RT. Hence, the inclusion criteria were 1) reports that treated TMPs with SRS and 2) reports that included at a minimum of 10 cases. For each included study, data concerning the age of the patients, previous treatment, tumor class and volume, tumor response, neurological sequelae, follow-up, margin dose, and toxicity were collected.

RESULTS AND OBSERVATIONS

A total of 381 patients with 382 TBPs and were managed in our center between 1988 and 2012, after excluding 20 patients who were lost for follow-up (anytime during the postoperative period) or with incomplete records. This is the largest series at present in the English literature. Of these patients, 285 (74.6%) were females and 97 (25.4%) were males. Their ages ranged from 12 to 82 years, with a median of 52 years. Of all the tumors, 145 (38%) were classified as Class A (1, 2) and B (1, 2, and 3) TMPs and 237 (62%) were classified as Class C, D and V TJPs. Table 1 shows the distribution of tumors and the treatment modality in relation to age, laterality (unilateral or bilateral), and LCN palsy, which are important factors that need to be taken into account while deciding treatment modality.

Management of Tumors

None of the 145 patients with Class A (1, 2) and B (1, 2, 3) TMPs group were subjected to wait-and-scan or RT and all in the group underwent surgery. Of the 237 patients with Class C, D, and V TJPs, a total of 182 patients (76.8%) underwent surgery as the primary treatment modality, 47 patients (19.8%) were subjected to an initial wait-and-scan policy, and 1 patient (0.4%) underwent primary RT. Seven patients (3%) received secondary RT after surgery for residual tumors left behind near vital intracranial structures. Of them, 2 showed regressions, 4 were stable, and 1 patient was lost for follow-up 1 year after RT.

Results of Conservative Management

Forty-seven patients were subjected to wait-and-scan, of whom 32 (68.1%) were older than 65 years. The median age of the patients was 69 years. Of the 47 patients who were subjected to wait-and-scan, the results of 23 patients who had a follow-up longer than 3 years are presented in Table 2. The tumor size remained stable in 12 patients (52%), regressed in 3 patients (13%), and progressed in 8 patients (35%). Of the 8 progressions, 7 (88%) were slow-growing tumors and 1 (13%) was a fast-growing tumor. Pretreatment LCN deficits were seen in only 3 (13%) of the patients. Seven (30%) patients progressively developed new LCN deficits and only 1 (5%)

TABLE 1. *Age, laterality, and LCN palsy in relation to treatment policy in TBPs at the Gruppo Otologico*

		<65 yr (n = 314)					>65 yr (n = 68)					
		Unilateral (n = 303)		Bilateral (n = 10)			Unilateral (n = 67)		Bilateral (n = 2)			
		No LCN palsy	LCN palsy	No LCN palsy	LCN palsy	Total	No LCN palsy	LCN palsy	No LCN palsy	LCN palsy	Total	Grand total (n = 382)
Class A and B[a] TMP	Surgery	120	—	—	—	120 (100%)	25	—	—	—	25 (100%)	145 (100%)
	Wait-and-scan	—	—	—	—	—	—	—	—	—	—	—
	RT	—	—	—	—	—	—	—	—	—	—	—
	Total (in A and B TJP)	120 (50%)	—	—	—	120 (100%)	25 (41.7%)	—	—	—	25 (100%)	145 (38%)
Class C, D, and V[a] TJP	Surgery	109	52	9	1	171 (88.1%)	5	5	1[b]	—	11 (25.6%)	182 (76.8%)
	Wait-and-scan	10	5	—	—	15 (7.7%)	29	2	—	—	31 (72.1%)	46 (19.4%)
	RT	—	—	—	1	1 (0.5%)		—	—	—	—	1 (0.4%)
	Wait-and-scan followed by RT	—	—	—	—	—	1	—	—	—	1 (2.3%)	1 (0.4%)
	Surgery followed by RT	1	6	—	—	7 (3.6%)	—	—	—	—	—	7 (3%)
	Total (in C and D TJP)	120 (50%)	63 (100%)	9 (100%)	2 (100%)	194 (61.8%)	35 (58.3%)	7 (100%)	1 (100%)	0	43 (63.2%)	237 (62%)
Grand total		240 (76.4%)	63 (20%)	9 (3%)	2 (0.6%)	314 (82.2%)	60 (88.2%)	7 (10.3%)	1 (1.5%)	0	68 (17.8%)	382 (100%)

[a]Modified Fisch classification.
[b]Partial resection.
LCN indicates lower cranial nerve; TJP, tympanojugular paraganglioma; TMP, tympanomastoid paraganglioma.

TABLE 2. *Outcomes of conservative management in Class C and D TBPs with follow-up longer than 3 years*

			Modified Fisch classification of TBPs		Tumor response				LCN status at presentation		LCN status during wait-and-scan			FN status at presentation		FN status during wait-and-scan		
							Progressed											
	No.	Age (yr)	C	D	Regressed	Stable	Fast	Slow	Deficits	No deficits	Stable	Worsened	New deficits	Deficits	No deficits	Stable	Worsened	FU (mo)
Wait-and-scan	23	69[a]	15 (65%)	8 (35%)	3 (13%)	12 (52%)	1 (4%)	7 (31%)	3 (13%)	20 (87%)	15 (65%)	1 (5%)	7 (30%)	2 (9%)	21 (91%)	23 (100%)	—	61[a]
RT	1	55	1 (100%)	—	—	1 (100%)	—	—	—	1 (100%)	—	—	—	—	1	—	—	48
Total	24		16 (67%)	8 (33%)	3 (13%)	13 (54%)	1 (4%)	7 (29%)	3 (13%)	21 (87%)	15 (65%)	1 (5%)	7 (30%)	2 (8%)	22 (92%)	23	—	

[a]Median.
C, D indicates classes of Fisch classification of TBPs; FN, facial nerve; FU, follow-up; LCN, lower cranial nerve; N, number; TBP, temporal bone paraganglioma.

TABLE 3. *Review of results of radiosurgery for TBPs*

Authors, year of report	No. of patients	Age[a] (yr)	Patients with prior treatment, n (%)		Class of TBPs	Tumor volume[a] (cm^3)	Tumor response			Neurological deficit[b]		FU[a] (mo)	Margin dose[a] (Gy)	Toxicity
			Surgery/ embolization	RS			Regression (%)	Stable (%)	Progression (%)	Improved (%)	Worsened (%)			
Liscak et al. (20) 1999	52	54	24 (46%)	5 (10%)	B/C/D	5.7	19 (40%)	28 (60%)	—	15 (29%)	3 (6%)	24	10–30	None
Eustacchio et al. (21) 1999	10	56	6 (60%)	—	C, D	6.4	4 (40%)	6 (60%)	—	5	—	37.6	12–20	None
Saringer et al. (22) 2001	13	67	9 (69%)	2 (15%)	D	8.7	3 (23%)	10 (77%)	—	6 (46%)	—	60	9–14	Headache
Foote et al. (23) 2002	25	62.5	12 (48%)	—	NA	10.4	8 (32%)	17 (68%)	—	—	—	35	12–18	Vertigo
Maarouf et al. (24) 2003	12	59	6 (50%)	—	C, D	12.2	8 (67%)	4 (33%)	—	4 (80%)	—	48	15–20	NA
Pollock (25) 2004	42	NA	23 (55%)	—	NA	13.2	12 (31%)	26 (67%)	1 (2%)	NA	3 (NA)	44	12–18	HL, headache, vomiting
Varma et al. (26) 2006	17	63.5	6 (35%)	—	NA	6.9	8 (47%)	5 (29%)	4 (24%)	NA	NA	44.5	13–18	HL
Gerosa et al. (27) 2006	20	56	8 (40%)	3 (15%)	C/D	7	9 (45%)	11 (55%)	—	5 (26%)	2 (11%)	50.85	15–24	HL
Feigl and Horstmann (9) 2006	12	51.7	5 (42%)	—	GJ	9.4	12 (100%)	—	—	—	—	33	14–20	HL
Bitaraf et al. (28) 2006	16	46.5	10 (63%)	2 (13%)	C/D	9.8	6 (43%)[c]	8 (57%)	—	10 (63%)	—	18.5	14–20	—
Lim et al. (29) 2007	13	52	4 (31%)	—	NA	3	2 (15%)	11 (85%)	—	—	2 (15%)	41	14–27	NA
Sharma et al. (30) 2008	24	46.6	9 (38%)	1 (4%)	GJ	8.7	7[d] (70%)	3 (30%)	—	NA	NA	24	12–20	None
Ganz and Abdelkarim (31) 2009	14	—	—	—	D	14.2	8 (57%)	6 (43%)	—	Yes (NA)	—	28	12–16	NA
Genc et al. (32) 2010	18	51	11 (61%)	—	NA	5.5	17 (94%)	—	1 (6%)	6 (35%)	1 (6%)	52.7	13–20	Aspiration pneumonia
Wegner et al. (33) 2010	18	60	8 (44%)	3 (17%)	—	5.8	1 (6%)	17 (94%)	—	2 (40%)	—	22.5	12–18	None
Chen et al. (10) 2010	15	60	4 (27%)	—	C/D	4.1	7 (47%)	5 (33%)	3 (20%)	—	—	35	14.6	HL, dizziness, headache
Lee et al. (34) 2010	14	42.3	3 (21%)	2 (14%)	GT/GJ	9.5	14 (100%)	—	—	9 (64%)	2 (14%)	40.3	12–15	HL
Lieberson et al. (8) 2012	38	59	10 (28%)	—	NA	4.6	19 (50%)	19 (50%)	—	6 (24%)	2 (8%)	57.6	18–36	Vertigo, second surgery
Kunzel et al. (35) 2012	22	70	—	—	B, C, D	NA	7 (30%)	15 (70%)	—	—	—	37.5	32–54	Dyspnea, tracheostomy

[a]Median or mean as reported by the authors.
[b]Percentages calculated against number of patients with preoperative deficits.
[c]FU in only 14 patients
[d]FU in only 10 patients.

A, B, C, D indicates class of TBP according to Fish classification; FU, follow-up; GJ, glomus jugulare; GT, glomus tympanicum; Gy, gray; HL, hearing loss; n, number; NA, not available; RS, radiosurgery; Surg, surgery; TBP, temporal bone paraganglioma.

of the old deficits worsened. The FN was affected in 2 patients (9%) before treatment, and all patients maintained stable FN status postoperatively. One patient in the wait-and-scan group who was older than 65 years received secondary SRS after being diagnosed with a fast-growing tumor.

One patient who underwent primary SRS had a bilateral Class C TJP. This patient had been previously operated upon on 1 side after which he developed LCN palsy and ipsilateral cophosis. A decision was taken to irradiate the contralateral tumor. But after the full course of RT, the patient lost hearing on the irradiated side as well, becoming bilaterally deaf. He was then rehabilitated successfully with a cochlear implant on the irradiated side.

Systematic Literature Review of Outcomes of RT

We reviewed 45 reports in the English literature where RT was used as a treatment option for TBPs. Of them, 22 reports where SRS was used to treat patients were analyzed in a systematic review. Of the 22 reports, 3 reports with a study population of less than 10 patients were excluded, and the remaining 19 studies are summarized in Table 3. The total number of patients in all reports put together were 393. Of the 357 patients in whom the data were available, 158 (56%) underwent previous surgery or embolization. Of the 19 series, 9 (47%) were classified TBPs according to the modified Fisch classification. Tumor volumes ranged from 3 to 14.2 cm^3, with 9 reports (47%) reporting tumor sizes below 7 cm^3. Of the 368 patients in whom follow-up data were available, tumor control (regression and stable tumors after SRS) was reported in 359 patients (98%). About 100% tumor control was reported in 15 (79%) of the 19 series. The follow-up of the reports ranged from 22.5 to 60 months. Nine reports (47.4%) had a follow-up less than 3 years, 9 (47.4%) had a follow-up between 3 and 5 years, and only 1 (5.2%) had a 5-year follow-up. Side effects of RT were reported in 11 reports (58%).

Comparison of Our Wait-and-Scan Results With Reports of RT

We divided our patients subjected to wait-and-scan into 3 groups based on follow-up, namely, less than 36 months, between 36 and 60 months, and more than 60 months, and compared them with reports of RT with a similar grouping (Table 4). This showed that when the follow-up was less than 60 months, the results were almost similar between wait-and-scan and RT. Only when the follow-up extended for more than 60 months did the RT group show better tumor control.

DISCUSSION

Because of the indolent growth pattern of HNPs, the natural course of the disease is of foremost importance when considering treatment strategies (36). Wait-and-scan

TABLE 4. *Comparison of outcomes of our series of wait-and-scan with outcomes of RT*

Authors, year of report	FU^ (mo)	No. of patients	Tumor response		
			Regression (%)	Stable (%)	Progression (%)
<36 mo FU					
Bitaraf et al. (28) 2006	18.5	16	6[a] (43%)	8 (57%)	—
Wegner et al. (33) 2010	22.5	18	1 (6%)	17 (94%)	—
Liscak et al. (20) 1999	24	52	19 (40%)	28 (60%)	—
Sharma et al. (30) 2008	24	24	7[b] (70%)	3 (30%)	—
Ganz and Abdelkarim (31) 2009	28	14	8 (57%)	6 (43%)	—
Feigl and Horstmann (9) 2006	33	12	12 (100%)	—	—
Foote et al. (23) 2002	35	25	8 (32%)	17 (68%)	—
Chen et al. (10) 2010	35	15	7 (47%)	5 (33%)	3 (20%)
Our series of wait-and-scan	24[a]	24	—	22 (92%)	2 (8%)
		36–60 mo FU			
Kunzel et al. (35) 2012	37.5	22	7 (30%)	15 (70%)	—
Eustacchio et al. (21) 1999	37.6	10	4 (40%)	6 (60%)	—
Lee et al. (34) 2010	40.3	14	14 (100%)	—	—
Lim et al. (29) 2007	41	13	2 (15%)	11 (85%)	—
Pollock (25) 2004	44	42	12 (31%)	26 (67%)	1 (2%)
Varma et al. (26) 2006	44.5	17	8 (47%)	5 (29%)	4 (24%)
Maarouf et al. (24) 2003	48	12	8 (67%)	4 (33%)	—
Gerosa et al. (27) 2006	50.85	20	9 (45%)	11 (55%)	—
Genc et al. (32) 2010	52.7	18	17 (94%)	—	1 (6%)
Lieberson et al. (8) 2012	57.6	38	19 (50%)	19 (50%)	—
Our series of wait-and-scan	48[a]	12	1 (8%)	9 (75%)	2 (17%)
		>60 mo FU			
Saringer et al. (22) 2001	60	13	3 (23%)	10 (77%)	—
Our series of wait-and-scan	84[c]	11	2 (18%)	3 (27%)	6 (55%)

[a]FU in only 14 patients.
[b]FU in only 10 patients.
[c]Follow-up in median.
FU indicates follow-up.

is an established treatment policy in the management of TBPs, which is tactically applied to specific situations taking advantage of the fact that these tumors are slow growing. In some scenarios, this may be a primary modality in itself or may lead to surgery or RT based on the rate of tumor growth. On the other hand, the indications for the use of RT in the treatment of TBPs are a matter of raging debate (30,37).

The Advent of Skull Base Surgery

The evolution and ongoing refinements in surgery and neuroradiology of the skull base in the last decade have been impressive wherein new surgical techniques and preoperative vascular management of skull base tumors have been defined and perfected. With the development of infratemporal fossa approaches (38) for skull base tumors and the transcondylar–transtubercular extensions (39), it is now possible to envision and precisely remove even large tumors in this area with minimal morbidity and mortality. Preoperative intravascular neuroradiological interventions like preoperative balloon occlusion and protective stenting (of the internal carotid artery and/or the vertebral artery) have helped eliminate the potential risks associated with arterial involvement, which is often the case in TBPs (17,18,40).

Limitations of RT

Because TBPs are benign but locally aggressive, tumor eradication should be the single most important objective of treatment followed by preservation of the FN and LCN and functions. Hence, it is important to reevaluate the role of RT in the present context where the indications for surgery and wait-and-scan have expanded. There are important differences in the treatment goals when choosing radiation over surgery for TBPs. Surgery offers a chance at a cure if gross total resection is obtained. Radiation does not cause eradication of TBPs but only results in a stable tumor or small decrease in its volume. The risk of touting SRS as the preferred treatment is that the available evidence does not show that SRS meets the treatment goal of long-term local tumor control (41). An analysis of reports in Table 3 raises several issues that question the efficacy of RT as a primary treatment for TBPs, which are discussed below.

Mechanism of Action Remains Unclear

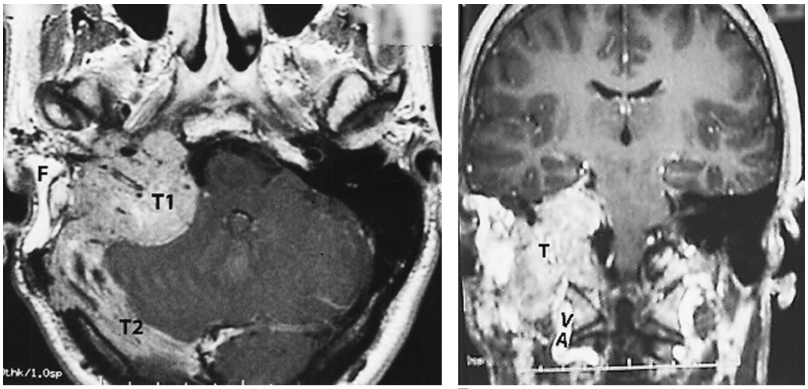
The mechanism by which RT seems to inhibit the growth of the tumor is unknown and remains unclear (5,42). Studies on the effect of radiation on TBPs showed that the histologically chief cells were radio resistant and therefore were not destroyed by radiation (43–45). While some authors have attributed the reduction in tumor volume seen after RT to fibrosis around the supplying vessels leading to obliterative endarteritis (30), certain other authors have shown that vascularization of the tumors remained almost unchanged after radiation (45,46). Sen et al. (44), in their study, could not find any histopathological changes that were attributable to RT.

There is evidence emerging that head and neck paraganglioma cells could be provided with molecular mechanisms allowing adaptive tolerance of radiation damage. We recently demonstrated that NOTCH signaling, a fundamental molecular pathway implicated in stem cells maintenance, organogenesis, and carcinogenesis, is commonly activated in head and neck paragangliomas (47). This could have therapeutic implications because it has been shown that NOTCH signaling promotes radioresistance in glioma cells (48). Moreover, microRNAs that we found to be significantly downregulated in head and neck paragangliomas, such as mir-34b/c and miR-200c (47), were shown to enhance radiosensitivity by promoting radiation-induced apoptosis in various cancer classes (49–51).

Lack of Standardization

The definition of local control or tumor stability varies from author to author, and in many cases, it is vaguely described as good local control or is not defined at all (9,10,23,25,36). Several studies have reported local tumor control to be as high as 100%, which is, however, not based on consensual definitions of tumor control (9,24,33,52), making any meaningful comparison difficult. There is also a lack of consensus on the indications and contraindications of RT. Some authors have reported the use of RT for tumors less than 1 cm (23,27,33,53), whereas some others reserve it for larger tumors (24,25,31). In Table 3, the median or mean tumor volumes in the reports ranged from 3 cm^3 (approximately 1.45 cm in the greatest dimension in each dimension) to 14.2 cm^3 (approximately 2.45 cm in the greatest dimension in each dimension), with only 4 series reporting tumor sizes of greater than 10 cm^3. These small tumors may have been resected safely by microsurgery, providing the benefit of disease eradication for the patient. In contrast, the more difficult tumors that we encountered in our surgical experience were very large tumors with volumes reaching up to 250 cm^3 (Figs. 1 and 2). Moreover, regarding the timing of RT, some studies have evaluated its use as a primary treatment modality (8,10), whereas some others as a secondary modality after surgery or embolization (7,9,30,54). Bitaraf et al. (28) have reported that all the patients in whom they documented a decrease in the size of the tumor were from the subset of patients in whom previous microsurgery had been performed and no decrease in tumor size was observed in patients where SRS was the primary treatment. Table 3 shows that, in almost all the reports, a section of patients (21%–69%) had received previous treatment interventions. In the partially resected tumors, the regression reported after RT could be attributed to the partial devascularization of tumors after surgery or embolization.

There are other factors that make examining results of RT difficult. For instance, contraindications for RS as reported by various authors are large tumor (while some do not define ''large,'' others define it as 30 mm) (11,13, 31,51,55), tumor invading bone (9), tumor extension below the skull base and into the neck (6,56), and encasement of the vessels (5). All the above-mentioned



A B

FIG. 1. Preoperative magnetic resonance image (axial [*A*] and coronal [*B*]) showing massive class C and D tympanojugular paraganglioma. F indicates fat that was used to close the mastoid after a previous incomplete excision done elsewhere; T1, extension of the tumor into the cerebellopontine angle; T2, extension of the tumor into the confluence of the sinuses; VA, vertebral artery.

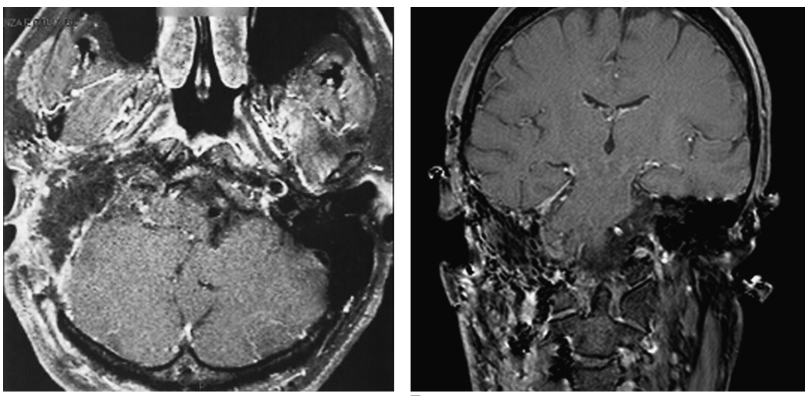
contraindications for RT are the very characteristics of the Class C, D, and V TJP.

Nondetermination of the Stability of Tumors

Many authors have irradiated patients without determining the stability of the tumors, that is, whether tumors were ''not growing,'' ''slow growing,'' or ''fast growing'' (12,21,54,57). It is well established that TBPs are indolent tumors, and there have been reports of TBPs that have remained inactive for many years (58,59). The stability of the tumors is an important factor that needs to be ascertained by wait-and-scan before opting for RT. Without this it is not logical to attribute the local control of tumor to RT itself because some of the tumors that are ''controlled'' by RT might actually be tumors that are inherently slow growing or not growing at all. In our series of wait-and-scan with a follow-up of 3 years and longer, 65% of the tumors were either stable or regressed (Table 2). In Table 4, the reported tumor stability or regression after RT in studies with follow-up longer than 3 years, ranges from 76% to 100%. Comparing the two it can therefore be assumed that the actual benefit of RT could be only in the remaining 15% to 39% of the population. This, according to us, is an important observation, and this may be corroborated when more reports are published regarding tumor response in a wait-and-scan policy.

Paucity of Long-term Follow-up

A review of the literature on treatment of TBPs with RT reveals that the lack of long-term follow-up after RT and selecting a small study population are significant shortcomings (7,21,25,56,60). Although some of the earlier studies reporting on outcomes with conventional RT have reported a follow-up longer than 5 years (3,55,57,61), this modality has now been abandoned in most centers in favor of the more effective SRS. However, studies reporting on SRS have reported short median follow-ups, sometimes even less than 3 years (7,9,21,60). In Table 4, 8 reports had a follow-up less than 3 years, 10 had a follow-up between 3 and 5 years, and only 1 had a follow-up 5 years. Table 4 shows that outcomes of wait-and-scan are corresponding to the outcomes of RT when the follow-up is less than 5 years. Because tumor is never completely eliminated after RT, the risk of recurrence after many years remains, especially so in TBPs, as they are inherently slow growing. This really requires long-term



A B

FIG. 2. Postoperative magnetic resonance image (axial [*A*] and coronal [*B*]) showing complete tumor eradication after a 3-stage surgery.

follow-up of at least 5 to 10 years. There are multiple reports that demonstrated tumor regrowth after many years of conventional RT or SRS (57,61–63), sometimes even after high doses (3). A longer-term study revealed that tumor control rates dropped to 75% at 10 years and 15% demonstrated new deficits (including hearing loss, facial numbness, vocal cord paralysis, and imbalance) (25). It is premature and indeed perilous to conclude that RT achieves good tumor control on the basis of studies with a short follow-up. Presently, we believe that this is a singular limitation in the study on RT for TBPs, and hence, the role of RT as a primary modality in the treatment of TJPs must be held reserve until more studies with longer follow-up substantiate such claims.

Neurological Deficiencies and Side Effects

It has been well documented that RT cannot protect the nerves against the infiltration by TJP (64) and that it is also not possible to avoid irradiating of cranial nerves in and around the tumors (8). While many studies report an improvement in LCN function after RT, there have also been reports of an increase in LCN deficits or worsening of deficits after treatment (35,65). Progression in glomus tumors can be so slow that ongoing neurologic deficits may undergo simultaneous compensation or go unnoticed by the patient (66). There are many articles that point toward the fact that the improvement in LCN deficits can be attributed to compensation mechanism by contralateral nerves (15,66–68), which usually takes place a few weeks after the palsy occurs, especially in younger patients (1,69). In our series, we had 2 patients in the wait-and-scan group who compensated well after an LCN palsy because the slow growth of the tumor allowed the patient to adapt to the deficits. Most authors in our review have reported improvement in LCN palsy not by objective clinical investigations but by symptomatology, which could be hiding the fact that such improvements could be due to adaptation (3,21,31,56).

Radiotherapy is not without side effects, and although the side effects of RT have been largely reduced by RS, they still occur. They include FN and LCN palsies (24,54), trigeminal neuralgia (30), hearing loss, vertigo, headache (70–72), and rarely malignant transformation (73). It can be noted that, in Table 3, 14 (74%) of 19 series reported side effects. Six (32%) of them reported a hearing loss on the irradiated side.

Economic Benefits

The economic benefits of RT like 1-day hospitalization and non-interruption of work for the patient are other factors considered in deciding the treatment modality (5,7,23,74). While this may be true, it must only be a secondary thought to the fact that the benefit of RT in controlling the disease has been proven in the first place.

Indications for Wait-and-Scan and RT

There is now a consensus that there are no indications for a patient to be managed with wait-and-scan or RT in Class A and B TMPs (66,75). Almost all tumors in this category can be surgically excised with excellent prognosis. In our series, surgery was the treatment of choice in all 145 (100%) patients with Class A and B TJPs, with only 1 patient (0.7%) developing a recurrence (76). Our results have been corroborated by other studies that show excellent postoperative outcomes (66,75,77). In Class C, D, and V TJPs too, surgery is the treatment of choice in patients younger than 65 years. In young patients, primary RT or wait-and-scan cannot be considered an option because the tumor remains after treatment, and hence, the potential threat of regrowth remains throughout the patients' longer life span compared to the older patients. Such patients will have to bear the emotional anguish of lifelong follow-up. It will also be difficult to manage any regrowth during the later years. Hence, we recommend surgery for this subset of patients. In case of LCN involvement, our experience has shown that total resection of such tumors with subsequent loss of LCN function on

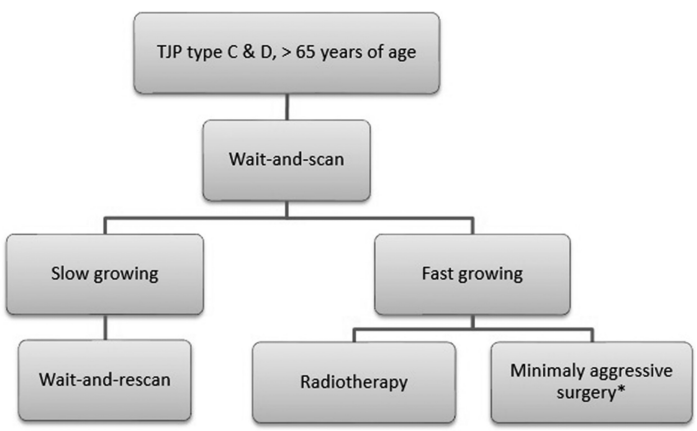


FIG. 3. Algorithm for the management of elderly patients in Class C, D, and V tympanojugular paragangliomas.

1 side was well compensated by the opposite nerves in the younger patients. However, we admit that this fact is based entirely on clinical observation and subjective patient feedback and that this has not been determined by Quality of Life questionnaire–based studies. In this situation, subtotal resections followed by RT or wait-and-scan can be considered as an alternative. However, 2 issues need to be addressed before adopting this policy. First, it has to be seen whether RT is effective for (residual) tumors and if wait-and-scan could replace RT. Second, the fate of such residual tumors over a long-term also remains to be determined.

In patients older than 65 years, as per the algorithm in Figure 3, we recommend that such patients be subjected to a wait-and-scan policy to determine the stability of the tumors. Surgery is not an option in them because of the deterioration in the general surgical condition in such patients. Patients must be referred to RT only when a fast-growing tumor is determined in the wait-and-scan period. Radiotherapy can also be a primary treatment option in patients with comorbid conditions, poor general medical conditions, and other factors that pose a risk to surgery.

CONCLUSION

The main goal of treatment of TBPs is total tumor eradication with minimal damage to the FN and LCNs, and this can only be achieved by surgery. In the era of modern skull base surgery, the application of RT in Class A and B TMPs is unjustified because all tumors can be removed completely with surgery with very low rates of complications. There is insufficient evidence in the literature to suggest that RT could be an effective alternative to surgery as a primary treatment modality even in Class C and D TJPs. In elderly patients with Class C and D TJPs, a wait-and-scan approach is recommended. Radiotherapy is initiated in case of fast-growing tumors after wait-and-scan and in certain other specific circumstances.

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