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Original Article

Head and Neck Paragangliomas: 16-year Single-center Experience and Mini Review on Diagnosis, Treatment, and Follow-up

Baş-boyun Paragangliomu: 16 Yıllık Tek Merkez Deneyimi ve Tanı, Tedavi, Takip için Kısa Derleme

Gokce AYDEMIR[1], Fazil Necdet ARDIC[1], Cuneyt Orhan KARA[1], Ferda BIR[2]

[1]Pamukkale University Faculty of Medicine, Department of Otorhinolaryngology and Head and Neck Surgery, Denizli, Türkiye
[2]Pamukkale University Faculty of Medicine, Department of Medical Pathology, Denizli, Türkiye

ABSTRACT

Objective: To investigate head and neck paraganglioma cases treated at a tertiary center from 2007 to 2023. The research includes a thorough examination of published studies that have focused on long-term outcomes. The additional goal is to contribute to the existing knowledge on head and neck paraganglioma, with a particular emphasis on refining diagnostic algorithms, treatment selection, and follow-up procedures.

Methods: A total of 44 patients were retrospectively analyzed, and 39 were included. Demographic information, symptoms, radiological examination results, types, stages, and postoperative complications were recorded. A review was conducted to select articles that reported single-center experiences with large cohorts, long follow-ups, and different treatment modalities since 2010.

Results: The mean age of the patients was 54 years, and the female/male ratio was 3.55:1. Among the 39 cases examined, 18 and 19 were identified as cervical paraganglioma and 19 as temporal bone paraganglioma. All patients initially underwent surgical resection. The mean follow-up duration was 5.42 years. Four residual cases and two recurrences were identified postoperatively, and a Gamma Knife was used as additional treatment. Subsequently, 17 articles were selected and summarized, and then a flowchart was prepared showing the possible options for diagnosis, treatment, and follow-up.

Conclusions: Preoperative staging is essential for surgical planning and predicting potential intraoperative complications. Based on our findings and review of the articles, we have prepared a flowchart that includes all possibilities depending on the tumor stage to help in the diagnosis, treatment, and follow-up of head and neck paragangliomas.

Keywords: Head and neck paraganglioma, surgery, radiation therapy, glomus tumors, staging paraganglioma

ÖZ

Amaç: Ana amacımız 2007 ile 2023 arasında bir üçüncü basamak merkezde tedavi edilen baş ve boyun paragangliomu olgularını araştırmaktır. Daha önce yayınlanmış tek merkezli ve uzun takip süreli çalışmaların detaylı bir şekilde incelenmesini içerir. İkincil amacımız, özellikle tanı algoritmasının, tedavi seçiminin ve takip prosedürlerinin geliştirilmesine odaklanmaktır.

Yöntemler: Kırk dört hasta retrospektif olarak analiz edildi. Otuz dokuz hasta çalışmaya dahil edildi. Demografik bilgiler, semptomlar, radyolojik muayeneler, paraganglioma tipleri, evreler ve ameliyat sonrası komplikasyonlar kaydedildi. 2010'dan bu yana yayınlanmış uzun takip süresi olan ve farklı tedavi yöntemlerini kullanan tek merkez deneyimlerini rapor eden makaleleri seçmek için bir literatür taraması da yapıldı.

Bulgular: Hastaların ortalama yaşı 54 ve kadın/erkek oranı 3,55:1 olarak bulundu. İncelenen 39 olgudan 18'i servikal paraganglioma ve 19'u temporal kemik paraganglioma olarak tanımlandı. Tüm olgular başlangıçta cerrahi rezeksiyon geçirdi. Ortalama takip süresi 5,42 yıl idi. Ameliyat sonrası dört kalıntı ve iki nüks tanımlandı ve ek tedavi olarak Gamma Knife kullanıldı. Daha sonra 17 makale seçildi ve özetlendi, ardından tanı, tedavi ve takip için bir akış şeması hazırlandı.

Sonuçlar: Preoperatif evreleme, cerrahi planlamada ve potansiyel intraoperatif komplikasyonları öngörmede esastır. Bulgularımıza ve makalelerin gözden geçirilmesine dayanarak, teşhis, tedavi ve baş boyun paragangliomalarının takibine yardımcı olmak için bütün olasılıkları ağırlıklandıran, tümör evresine bağlı bir akış şeması hazırladık.

Anahtar kelimeler: Baş boyun paragangliomu, cerrahi, radyaterapi, glomus tümörleri, paraganglioma evrelemesi

Address for Correspondence: Fazil Necdet Ardic, Pamukkale University Faculty of Medicine, Department of Otorhinolaryngology and Head and Neck Surgery, Denizli, Türkiye
E-mail: fnecdetardic@gmail.com **ORCID ID:** orcid.org/0000-0003-4230-3141

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INTRODUCTION

Paragangliomas (PGL) are neuroendocrine tumors that develop from neural crest cells in sympathetic or parasympathetic ganglia. These types of tumor are infrequent in the head and neck region, accounting for approximately 0.6% of all head and neck cancers[1]. In general, they are characterized by slow growth and a benign nature. However, a small proportion of cases exhibit malignant behavior and may metastasize. Although catecholamine secretion is uncommon, it can lead to troublesome complications if it is present. PGL can arise sporadically or be associated with a genetic syndrome. In familial PGL, a succinate dehydrogenase (*SDHx*) gene mutation is commonly identified as an underlying cause[2].

PGL in the head and neck region can be classified into two anatomical categories: cervical PGL (carotid body and vagal) and temporal bone (tympanomastoid and tympanojuguler). The most common locations for head and neck PGL are the following: the carotid bifurcation (known as glomus carotid body), the superior vagal ganglion (known as glomus tympanojugular), the middle ear promontories (involving the auricular branch of the 10th cranial nerve, also known as Arnold's nerve, and the tympanic branch of the 9th cranial nerve, known as Jacobson's nerve, forming glomus tympanomastoid), and the inferior vagal ganglion (known as glomus vagale)[1,3]. In addition to the locations mentioned above, PGL rarely occur in the nasal cavity, orbit, oropharynx, and larynx[4].

Given their proximity to critical structures, deciding whether to prioritize preserving these structures or pursuing complete tumor removal can be a challenge for both patients and physicians. Treatment options, such as surgery, radiation therapy, a combination of both, and regular follow-up, are suggested. While there are consensus statements regarding the treatment of PGL, it is important to consider that each patient possesses unique characteristics that can influence the outcome of treatment[5].

Our aim was to thoroughly examine head and neck PGL treated at our medical center from 2007 to 2023 and to compare them with previously published studies that concentrated on the long-term outcomes of individual medical centers. Our additional goal is to improve our understanding of these cases, with a particular focus on refining the diagnosis, treatment selection, and follow-up algorithm.

MATERIALS and METHODS

This single-center retrospective study was conducted following the guidelines established in the Declaration of Helsinki and was approved by the Pamukkale University Non-Interventional Clinical Research Ethics Committee (no.: E-60116787-020-380730, date: 14.06.2023). All patients gave their written consent, including data usage before treatment. It is retrospectively registered on clinical trials.com (NCT05942482). This retrospective analysis examined data from 44 patients who underwent head and neck surgeries by the same surgical team at university hospital between 2007 and 2023, and a histopathological diagnosis of PGL. Five patients were excluded from the study due to limitations in accessing their data, leaving a total of 39 patients with a minimum follow-up period of 6 months who were included in the analysis.

The study recorded various demographic data, including age, sex, and any relevant medical history. Patients' complaints reported at the time of admission were documented along with the results of preoperative radiological examinations, such as contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), and angiography. Pure tone audiometry results were also noted to assess any hearing-related issues.

The stages were determined by radiological examination and surgical notes. The surgical techniques were also recorded. The Shamblin classification system was used for carotid body PGL[6]. For vagal PGL, the staging system defined by Browne et al.[7] based on the relationship between the tumor and the jugular foramen was used. On the other hand, the modified Fisch classification was used to stage temporal bone PGL[8]. Postoperative complications after surgery and any recurrent PGL observed during follow-up were documented.

During the review phase, we conducted a comprehensive literature search and focused on articles presenting large series from single centers newer than 2010. Because they represented highly experienced centers. Subsequently, we extracted key data points, including age and sex distribution, familial, multiple, and functional case numbers, selected interventions, embolization options, complications, follow-up duration, residual or recurrence rates, and second-line treatments. These data were sourced from text, tables, and graphs.

Statistical Analysis

Descriptive analyses were performed to summarize the data. The results are reported as mean ± standard deviation, median, number, and percentage (%). The analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY).

RESULTS

The mean age of the patients was 54 years (range 18-79 years), and the female/male ratio was 3.55:1. Among the 39 cases examined, 18 were cervical, 19 were temporal, 1 was paranasal, and 1 was metastatic. The detailed classification and treatment results are shown in Figure 1. The mean follow-up duration was 5.42 years.

All cases, except metastatic PGL, demonstrated a non-functional and benign nature, accounting for 97.4% of the cases. In the 24 hour urine samples, only three individuals exhibited a slight elevation in vanillylmandelic acid levels. These PGL were also classified as nonfunctional. The most common complaint in patients with cervical PGL was the presence of a neck mass. Transcervical surgery was performed on all patients, leading to a successful total excision of the masses. Of the 18 lesions, 14 were carotid body tumors. No recurrence was observed in any of the patients with carotid body PGL cases (Figure 2). The probability of postoperative nerve palsy increased with increasing stage.

Patients with vagal PGL were classified into three stages according to the relative position of the tumor to the jugular foramen (Figure 3). Half of our four cases of vagal PGL (50%) were classified as stage 1, while the

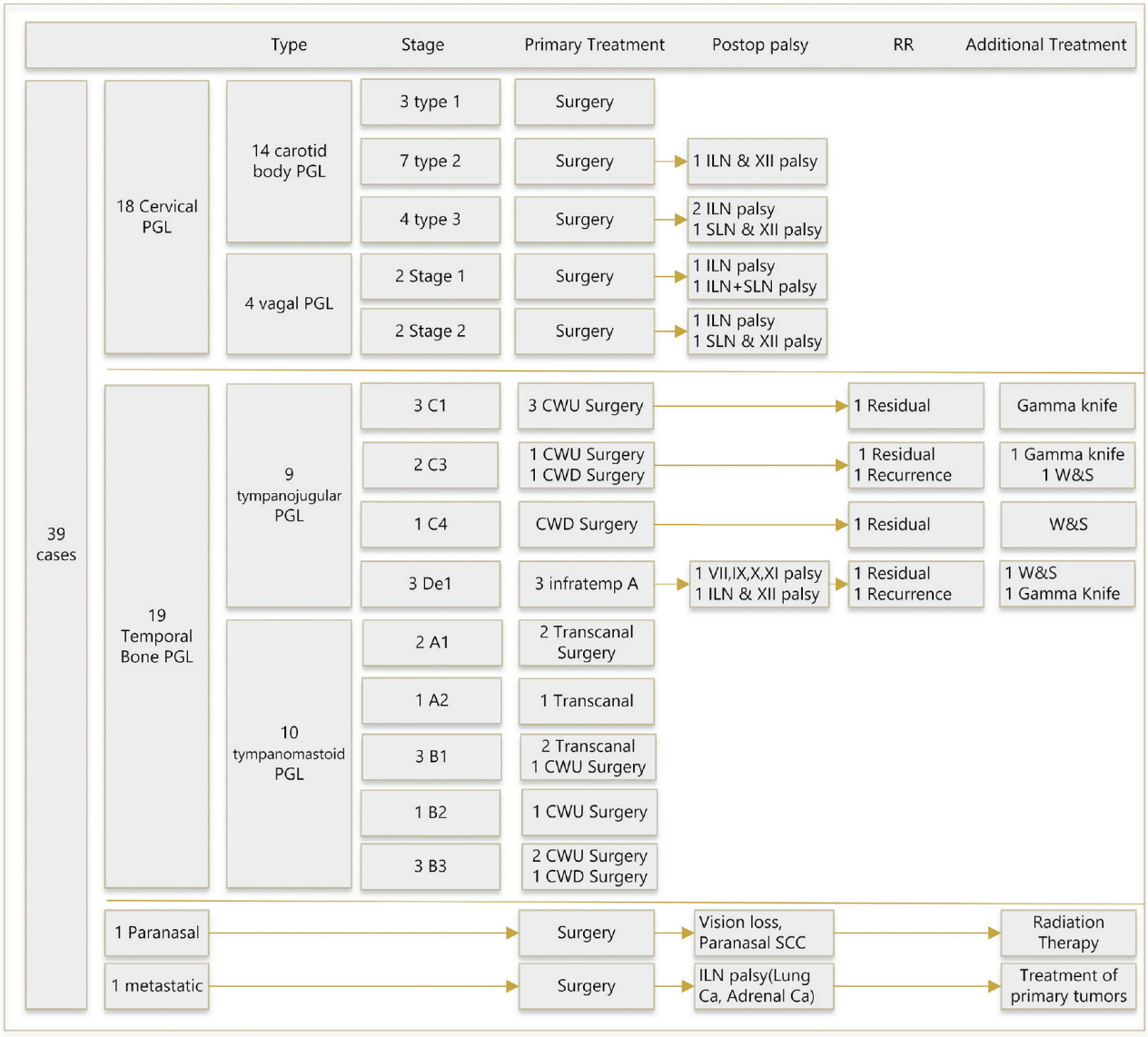

Figure 1. Our case summaries: Staging of PGL subtypes, surgical method, postoperative outcome.
CN paralysis. CN: Cranial nerve, PGL: Paragangliomas, CWU: Canal wall up, CWD: Canal wall down, RR: Residual/recurrence, SLN: Superior laryngeal nerve, ILN: Inferior laryngeal nerve, Ca: Cancer

remaining half (50%) were classified as stage 2. Hearing loss and pulsatile tinnitus were identified as the most common complaints in cases of temporal bone PGL. Detailed information about temporal bone PGL is presented in Figure 1.

Another PGL case involved a patient who underwent orbital exenteration and maxillectomy due to paranasal sinus squamous cell carcinoma. Interestingly, an incidental PGL was detected during the histopathological examination of the orbital tissue. In the second case, the patient was diagnosed with adrenal gland and lung cancers. Additionally, a metastatic PGL was discovered on histopathological examination, prompting us to perform surgery due to the presence of a neck mass.

Subsequently, 17 articles with extensive cohorts and long follow-up durations were selected. These studies included various treatment modalities, such as surgery, surgery combined with radiation therapy, radiation therapy alone, and a wait-and-scan policy. The data collected from these articles are presented in Table 1. Initially, information about the diagnosis was collected and subsequently merged. The focus then shifted to the preferred interventions and their outcomes. This information was used to design a diagnostic and therapeutic flowchart (Figure 4).

DISCUSSION

In this study, we conducted a retrospective review of 39 cases treated in our clinic. The average duration

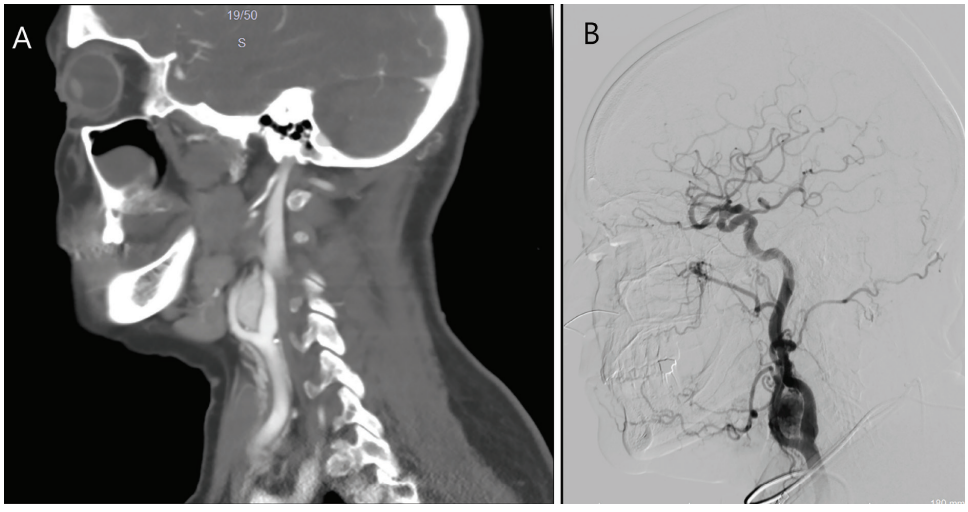

Figure 2. A 64-year-old woman with right Shamlin type 2 glomus caroticum [CT angiography, sagittal view **(A)**, conventional carotid angiography **(B)**].

CT: Computed tomography

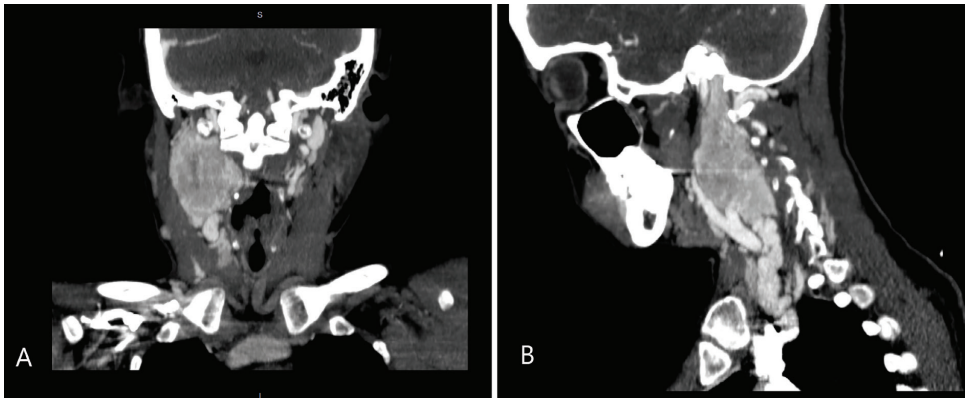

Figure 3. A 41-year-old woman with right stage 2 vagal glomus [CT angiography, coronal view **(A)**, and sagittal view **(B)**].

CT: Computed tomography

Table 1. The summary of cohorts from single center studies.

	Type	mAge	F:M	Fml	Mtpl	Func	Emb
Aydemir et al. (our series)	14 carotid	57.21	7:1	0	0	0	None
	4 vagal	55.75	1:1	0	0	0	None
	9 jugular	56	3.5:1	0	11%	0	100%
	10 tympanic	47.16	10:0	0	0	0	None
Rijken et al.[9] 2019	17 carotid	45.3	2.12:1	43%	54%	30%[c]	-
	10 vagal						-
	25 jugular						-
	15 tympanic						-
Ferrante et al.[17] 2015	44 carotid	55	3.71:1	20%	16%	-	50%
Merzouqi et al.[12] 2021	10 carotid	56.67	2.3:1	-	50%	10%	6%
	5 vagal	58.4	5:0		0	0	0
	6 jugular	54.72	2.7:1	-	0	0	50%
	5 tympanic					0	0
Nicoli et al.[13] 2017	18 jugular	55	2.6:1	-	-	-	44%
	18 tympanic			-	-	-	-
Castelhano et al.[10] 2022	24 carotid	56.5	1.92:1	37.5%	20.5%	14%	64.4%[c]
	22 vagal					16%	
	31 jugular					10%	
	9 tympanic						
Yildiz et al.[14] 2021	41 jugular	56	3.21:1	-			51%[c]
	18 tympanic					-	31%[c]
Valero et al.[20] 2020	68 carotid	49.1	1.51:1	14.6%	11.7%	1%[g]	6.8%
	24 vagal	52.9	2.5:1				30%
	8 jugular						
	2 tympanic						
Smith et al.[15] 2017	61 carotid	54	1.58:1	84%[f]	12.4%	-	51%[c]
	20 vagal	47.7	1:1.33			0	100%[c]
	41 jugular	52.5	2.72:1			16%	68%[c]
	22 tympanic	60.3	6.3:1			-	-
Jackson et al.[31] 2001	152 jugular	41	2.59:1	-	9%	9.7%	-
	27 vagal						
	3 carotid						
Anderson et al.[24] 2020	25 jugular	55	2:1	13.3%		-	23%
	3 carotid						
	1 tympanic						
	1 glomus vagale						

Table 1. Continued

	Intervention	Complication[a]	FU	Rce/Rsd	Second line[b]
Aydemir et al. (our series)	100% Srg	28% CNP	6.42	0	-
	100% Srg	100% CNP	4.62	0	-
	100% Srg	22% CNP	5.1	66%	50% GK, 50% W&S
	100% Srg	0	4.3	0	-
Rijken et al.[9] 2019	53% Srg, 47% W&S	?	11.2	11%[c]	?
	40% Srg, 10% RTA, 50% W&S	?	7.2	33%[c]	?
	32% Srg, 12% RTA, 48% W&S, 8% Srg + ART	?	8.7	36%[d]	?
	67% Srg, 33% W&S	?	3.1	0	-
Ferrante et al.[17] 2015	100% Srg	6.7% CNP, 2% bleeding	-	2%	100% Srg
Merzouqi et al.[12] 2021	100% Srg	10% CNP	3.6	10%	100% RTA
	100% Srg	100% CNP	2.4	0	-
	50% Srg, 50% RTA	36% CNP[e]	3.95	0	-
	100% Srg	-			-
Nicoli et al.[13] 2017	94% Srg, 6% RTA	53% CNP[c], 2% bleeding	6.1	60%[c]	22% Srg, 11% Srg + RTA, 55% RTA
		11% CNP		22%	25% Srg, 25% RTA, 50% Srg + ART
Castelhano et al.[10] 2022	66.3% Srg, 29.4% RTA, 4.4% W&S	33% CNP	7.6	52%[c]	32% W&S, 3.5% Srg, 50% RTA
		100% CNP			
		40% CNP			
		-			
Yildiz et al.[14] 2021	36% Srg, 34% Srg, 34% Srg + RTA, 24% RTA, 2.5% W&S, 2.5% none	23%[c] CNP, 3% bleeding	10.3	34%	50% RTA, 35% Srg
	88% Srg, 5% RTA, 5% W&S	0		5%	?
Valero et al.[20] 2020	16.2% W&S, 82.4% Srg + ART, 1.5% RTA	5.9% CNP	2	10.6%	18% Srg
	25.7% W&S, 54.3% Srg + ART, 20% RTA	71.4% CNP	4		
Smith et al.[15] 2017	80.3% Srg, 23% W&S	40.8%[c] CNP	1.58	3%	100% Srg
	52% Srg, 9.5% RTA, 38% W&S	100%[c] CNP	2	9.5%	50% Srg
	39% Srg, 26.8% RTA, 24.3% W&S	56%[c] CNP	3.84	36.5%	60% RTA
	86% Srg, 13.6% W&S	-	2	-	-
Jackson et al.[31] 2001	100% Srg	69% CNP	4.5	14.8%	22% Srg, 7% W&S, 3.5% RTA, 66% None[i]
		100% CNP			
		67% CNP			
Anderson et al.[24] 2020	20% ART, 20% salvage, 60% RTA (36.7% Srg before)	16.6% CNP	4.16	0	-

Table 1. Continued

	Type	mAge	F:M	Fml	Mtpl	Func	Emb
Alvarez-Morujo et al.[11] 2016	24 multicentric (37 carotid, 10 vagal, 13 jugular)	40.4	1:1	70.8%	100%	0	-
Dorobisz et al.[19] 2016	47 carotid	45	1:1.5	-	4%	-	-
Prasad et al.[16] 2016	236 jugular	46.7	1:1.06		14.6%	0	99%
Smee et al.[21] 2015	27 jugular 7 tympanic 9 cervical	54	1.78:1	20%	16%	-	-
Hong et al.[25] 2021	4 tympanic 21 jugular 3 carotid	50	1.07:1		7%	14%	
Gilbo et al.[26] 2014	131	55	2:1		15%		
Carlson et al.[27] 2015	16 jugular	64.2	4:1	-	20%	-	-
Langerman et al.[28] 2012	28 carotid 19 vagal	56	2.30:1	19%	25%		

Table 1. Continued

	Intervention	Complication[a]	FU	Rce/Rsd	Second line[b]
Alvarez-Morujo et al.[11] 2016	36 Srg (21 carotid, 9 jugular, 6 vagal) 9 RTA (1 carotid, 6 jugular, 2 vagal) 12 W&S (10 carotid, 1 jugular, 1 vagal)	83% CNP	3	20.8%	20% Srg, 80% RTA
Dorobıscz et al.[19] 2016	100% Srg	42% vascular work, 10% CNP	?	0	-
Prasad et al.[16] 2016	66.9% single-stage Srg, 11.4% two-stage Srg, 19.4% W&S, 0.4% RTA	23.2%[b] new facial 36%[b] new IX 32.9%[b] new X 48%[b] new XI 20%[b] new XII	3.8	12.4%[c]	30.4% RTA, 69.6% W&S
Smee et al.[21] 2015	23% Srg + RT (9% ART, 4.5% SRS, 7% SRT)	2% CNP	3.5	50%[c]	?
	77% RT (20% SRS, 38.6% SRT, 25% RTA)			0	
Hong et al.[25] 2021	10% adjuvant SRT 42% salvage SRT 48% primer SRT	3% facial palsy 3% cerebellar necrosis	5.25	59% PR 3% PRG	?
Gilbo et al.[26] 2014	55% RTA, 9% SRT, 36% IMRT, (14% treated before)	0	11.5	3.8%	20% RTA, 20% Srg, 20% Srg +ART, 40% None
Carlson et al.[27] 2015	100% W&S	38% hearing loss, 12.5% bloody otorhea, 37% CNP	6.85	33%	20% Srg, 20% RTA, 60% None
Langerman et al.[28] 2012	100% W&S	42% stable, 38% grew little, 20% reduced	5	0	-

Fml: Familial, Mtpl: Multiple, Embo: Embolization, FU: Mean follow-up (years), Rce: Recurrence, Rsd: Residual, mAge: Mean age in years, Srg: Surgery, GK: Gamma Knife, W&S: Wait and scan, RTA: Radiotherapy alone, ART: Adjuvant radiotherapy, SRS: Stereotactic radiosurgery, SRT: Stereotactic radiotherapy, PR: Partial response, PRG: Progressive, IMRT: Intensity-modulated radiation therapy. [a]New complications after intervention, [b]Ratio of treatment preference in residual and recurrent tumors, [c]Only in the surgery group, [d]Only in treated group, [e]Tumors that extended to the skull base were not included in this series, [f]Only 53 patients had genetic tests, 41 was positive

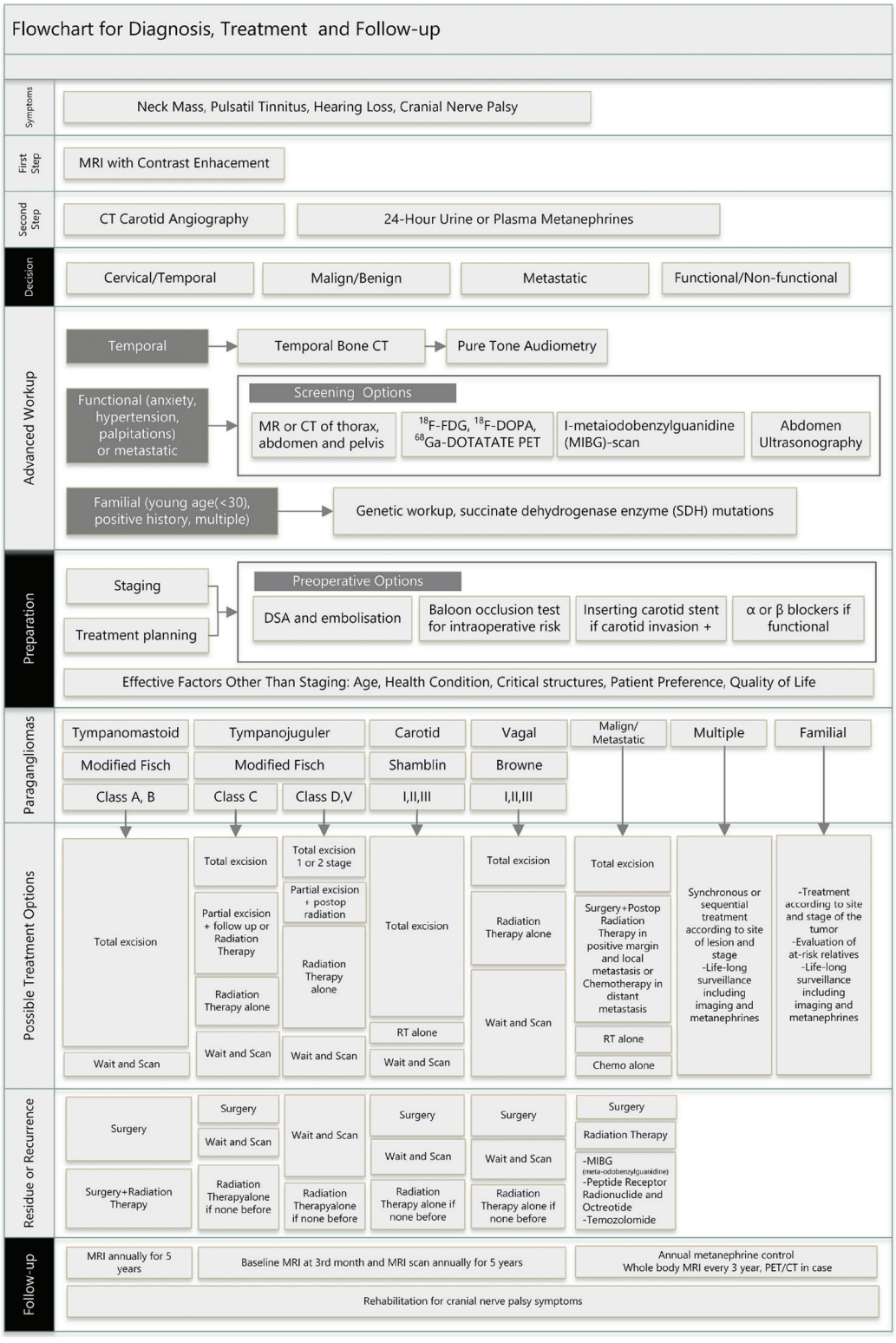

Figure 4. We combined all algorithms and the preferences of experienced centers in a simple flowchart. Our flowchart shows the possible treatment options. The size of the rectangles in the flowchart represents the power of the recommendations.

CT: Computed tomography, MRI: Magnetic resonance imaging, F-FDG: F-fluorodeoxyglucose, F-DOPA: F-deoxyphenyl-alanine, DSA: Digital subtraction angiography, RT: Radiotheraphy, PET/CT: Positron emission theraphy/computed tomography

of follow-up was 5.42 years. The main issues observed were cranial nerve palsy in cervical PGLs and residual/recurrence rates in tympanojugular PGLs. Diagnostic tools were generally sufficient and easily accessible, except for genetic testing, which was not as readily available. In our clinic, radiation therapy or Gamma Knife treatment was the secondary treatment. Most patients did not show signs of disease, whereas those with residual/recurrence lived with stable disease and underwent regular follow-up visits.

However, regardless of treatment, head and neck PGL can significantly affect quality of life. Hence, determining the treatment method is a challenging decision for doctors and patients. We selected 17 articles reporting single-center experiences with different treatment modalities (Table 1). Imaging techniques such as contrast-enhanced CT, MRI, and angiography were common. In addition, all functional tests were performed routinely. However, genetic studies were limited[9-11]. Staging procedures were performed for all cases, with a consensus among the authors on using the Fisch classification for temporal bone PGLs and the Shamblin classification for carotid PGLs. However, there was no unanimous decision on vagal PGLs.

The diversity of treatment modalities represents the initial step. Surgery was the predominant choice among the selected articles, possibly influenced by our selection bias. Surgical intervention for head and neck PGL presents distinct challenges because of their proximity to critical vascular structures and cranial nerves. To mitigate excessive bleeding and minimize brain tissue damage, certain patients favored alternative approaches, such as embolization, carotid stenting, and balloon occlusion tests. Embolization was predominantly preferred for tympanojugular PGL like us[10,12-16], but some authors also opted for this method for carotid and vagal PGLs[15,17]. In a retrospective study by Han et al.[18], a comparison was made between patients who underwent preoperative embolization and those who did not. The study did not reveal any differences in stroke rate, recurrence, cranial nerve injury, operation duration, and blood loss[18]. In our clinic, the balloon occlusion test, which provides vital information about the collateral circulation of brain vessels, was routinely used for cervical and tympanojugular PGLs.

The success of the surgical approach hinges on the utilization of meticulous techniques and the promotion of close collaboration among the surgical team. Although employing sophisticated methods and experienced surgeons may not always be possible, complete tumor removal may not always be possible, depending on tumor size, location, involvement of neighboring structures, and potential risks to vital components[11,16,19]. Alternative treatment options, such as partial resection or adjuvant therapy, may be considered in such cases. In addition to subtotal excision, radiotherapy, particularly Gamma Knife, plays a crucial role in the effective treatment of tumors, especially in stage 3-4 glomus tympanojugular tumors[9,14,20,21]. In our patient cohort, a considerable proportion (66.7%) of advanced-stage (class C-D) temporal bone PGL cases experienced recurrence over time, despite the absence of visible residual tumor during initial treatment or when residual tissue was deliberately retained during surgery to avoid potential complications. Recurrence of early-stage (class A-B) TBP was observed at a rate of 11.1%.

In 2018, Jansen et al.[22] proposed a combined radiation therapy and surgery for stage 3-4 tumors. They found the highest local control rate (100%) in TBP when combined therapy consisting of tumor debulking and postoperative radiotheraphy was performed. This approach aims to maximize treatment effectiveness by harnessing the benefits of radiation therapy and surgical intervention, particularly for advanced-stage tumors. Additionally, another study reported a tumor control rate of 84% in C1- 4 tumors after radiation therapy, while tumor control ranged from 80% to 95% after surgery within the same Fisch class group[23]. Yildiz et al.[14] also supported this approach, emphasizing the importance of total excision surgery for stage 1-2 temporal PGL and advocating a combination treatment approach with subtotal excision for stage 3-4 patients. In 88% of all Fisch A and B tumors that underwent surgical resection, successful tumor control was achieved. However, this percentage decreased to 83% for surgically resected Fisch C and D tumors, particularly in larger tumor sizes[14]. However, some authors preferred radiotherapy as the primary modality and reported high success rates[24-26].

The wait-and-scan approach was also reported as feasible in selected patients[27,28]. Carlson et al.[27] reported that the most common indications were advanced age (73%), patient preference (73%), and contralateral skull base or cervical lesions (13%) for this approach.

Suárez et al.[29] mentioned that the risk of vascular injury is low when using the transcervical approach for PGL surgery. However, the risk of vagus nerve damage is relatively high. They found that the vagus nerve was functionally preserved in only 4.3% of surgically treated patients[29]. The Shamblin classification can be modified to include the assessment of the vagal ganglia and jugular foramen. This modification allows a more comprehensive evaluation of the extent and involvement of vagus nerve

structures. In our study, we observed postoperative recurrent nerve paralysis in four patients with vagal PGL.

Glomus caroticum was the most common type of head and neck paraganglioma, which is consistent with previous findings in the literature[20,28]. We encountered inferior laryngeal nerve palsy (28.6%) and hypoglossal nerve palsy (14.3%) in high-grade patients. In one patient, arterial anastomosis was performed via cardiovascular surgery because of rupture of the internal carotid artery caused by tumor invasion.

Smith et al.[15] proposed an algorithm based on their experience with 194 patients. Hu and Persky[30] also published an algorithmic approach to head-neck PGLs based on a literature review. Published algorithms ended with a certain decision. However, many experienced centers use different approaches. We combined all algorithms and preferences of experienced centers with large cohorts into a simple flowchart[9-17,19-21,24-28,31]. Our flowchart shows the possible treatment options. The size of the rectangles in the flowchart represents the power of the recommendations by experienced centers (Figure 4).

Our study has several limitations, notably the small sample size and retrospective design, which may introduce biases and constraints in data collection. Additionally, the selection of articles predominantly focusing on surgery reflects our preference. More research is warranted to establish stronger evidence for managing head and neck paraganglioma. This future investigation should consider larger sample sizes, employ prospective designs, conduct a comprehensive evaluation of various treatment modalities according to tumor stage, and, importantly, use quality of life questionnaires.

CONCLUSION

The location primarily dictates the clinical presentation of paraganglioma. As the stages progress, there is an increased risk of postoperative complications and the possibility of residual tumors. Therefore, preoperative staging is essential in surgical planning to predict potential intraoperative complications. We strongly believe in considering the patient's quality of life when selecting a treatment modality. Based on our findings and review of the articles, we have decided to alter our approach and have proposed an algorithm for diagnosis, treatment, and follow-up that takes into account tumor staging.

Ethics

Ethics Committee Approval: Approval was granted by the Pamukkale University Non-Interventional Clinical Research Ethics Committee (no.: E-60116787-020-380730, date: 14.06.2023).

Informed Consent: All patients gave their written consent, including data usage before treatment.

Author Contributions

Surgical and Medical Practices: G.A., F.N.A., C.O.K., F.B., Concept: G.A., F.N.A., C.O.K., F.B., Design: G.A., F.N.A., C.O.K., F.B., Data Collection and/or Processing: G.A., F.N.A., Analysis and/or Interpretation: G.A., F.N.A., Literature Search: G.A., F.N.A., C.O.K., F.B., Writing: G.A., F.N.A., C.O.K., F.B.

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REFERENCES

1. Sandow L, Thawani R, Kim MS, Heinrich MC. Paraganglioma of the Head and Neck: A Review. Endocr Pract. 2023;29:141-7.
2. Muth A, Crona J, Gimm O, et al. Genetic testing and surveillance guidelines in hereditary pheochromocytoma and paraganglioma. J Intern Med. 2019;285:187-204.
3. Tokgöz SA, Saylam G, Bayır Ö, et al. Glomus tumors of the head and neck: thirteen years' institutional experience and management. Acta Otolaryngol. 2019;139:930-3.
4. Mete O, Wenig BM. Update from the 5th Edition of the World Health Organization Classification of Head and Neck Tumors: Overview of the 2022 WHO Classification of Head and Neck Neuroendocrine Neoplasms. Head Neck Pathol. 2022;16:123-42.
5. Lloyd S, Obholzer R, Tysome J; BSBS Consensus Group. British Skull Base Society Clinical Consensus Document on Management of Head and Neck Paragangliomas. Otolaryngol Head Neck Surg. 2020;163:400-9.
6. Shamblin WR, ReMine WH, Sheps SG, Harrison EG Jr. Carotid body tumor (chemodectoma). Clinicopathologic analysis of ninety cases. Am J Surg. 1971;122:732-9.
7. Browne JD, Fisch U, Valavanis A. Surgical therapy of glomus vagale tumors. Skull Base Surg. 1993;3:182-92.
8. Shin SH, Sivalingam S, De Donato G, Falcioni M, Piazza P, Sanna M. Vertebral artery involvement by tympanojugular paragangliomas: management and outcomes with a proposed addition to the fisch classification. Audiol Neurootol. 2012;17:92-104.
9. Rijken JA, de Vos B, van Hest LP, et al. Evolving management strategies in head and neck paragangliomas: A single-centre experience with 147 patients over a 60-year period. Clin Otolaryngol. 2019;44:836-41.
10. Castelhano L, Correia F, Donato S, Ferreira L, Montalvão P, Magalhães M. Paragangliomas da Cabeça e Pescoço: A Experiência de um Centro Oncológico do Sul da Europa. Acta Med Port. 2022;35:789-97.
11. Álvarez-Morujo RJ, Ruiz MÁ, Serafini DP, Delgado IL, Friedlander E, Yurrita BS. Management of multicentric paragangliomas: Review of 24 patients with 60 tumors. Head Neck. 2016;38:267-76.

12. Merzouqi B, El Bouhmadi K, Oukesou Y, et al. Head and neck paragangliomas: Ten years of experience in a third health center. A cohort study. Ann Med Surg (Lond). 2021;66:102412.
13. Nicoli TK, Sinkkonen ST, Anttila T, Mäkitie A, Jero J. Jugulotympanic paragangliomas in southern Finland: a 40-year experience suggests individualized surgical management. Eur Arch Otorhinolaryngol. 2017;274:389-97.
14. Yildiz E, Dahm V, Gstoettner W, et al. Long-Term Outcome and Comparison of Treatment Modalities of Temporal Bone Paragangliomas. Cancers (Basel). 2021;13:5083.
15. Smith JD, Harvey RN, Darr OA, et al. Head and neck paragangliomas: A two-decade institutional experience and algorithm for management. Laryngoscope Investig Otolaryngol. 2017;2:380.
16. Prasad SC, Mimoune HA, Khardaly M, Piazza P, Russo A, Sanna M. Strategies and long-term outcomes in the surgical management of tympanojugular paragangliomas. Head Neck. 2016;38:871-85.
17. Ferrante AM, Boscarino G, Crea MA, Minelli F, Snider F. Cervical paragangliomas: single centre experience with 44 cases. Acta Otorhinolaryngol Ital. 2015;35:88-92.
18. Han T, Pu J, Tang H, et al. Retrospective, multicenter study of surgical treatment for carotid body tumors with or without preoperative embolization. Front Oncol. 2023;13:1123430.
19. Dorobisz K, Dorobisz T, Temporale H, et al. Diagnostic and Therapeutic Difficulties in Carotid Body Paragangliomas, Based on Clinical Experience and a Review of the Literature. Adv Clin Exp Med. 2016;25:1173-7.
20. Valero C, Ganly I, Shah JP. Head and neck paragangliomas: 30-year experience. Head Neck 2020;42:2486-95.
21. Smee RI, Jayasekara J, Williams JR, Hanna C. Paragangliomas: presentation and management by radiotherapy at the Prince of Wales Hospital. J Med Imaging Radiat Oncol. 2015;59:229-35.
22. Jansen TTG, Kaanders JHAM, Beute GN, Timmers HJLM, Marres HAM, Kunst HPM. Surgery, radiotherapy or a combined modality for jugulotympanic paraganglioma of Fisch class C and D. Clin Otolaryngol. 2018;43:1566-72.
23. Jansen TTG, Timmers HJLM, Marres HAM, Kaanders JHAM, Kunst HPM. Results of a systematic literature review of treatment modalities for jugulotympanic paraganglioma, stratified per Fisch class. Clin Otolaryngol. 2018;43:652-61.
24. Anderson JL, Khattab MH, Anderson C, et al. Long-term Outcomes for the Treatment of Paragangliomas in the Upfront, Adjuvant, and Salvage Settings With Stereotactic Radiosurgery and Intensity-modulated Radiotherapy. Otol Neurotol. 2020;41:133-40.
25. Hong S, Kagawa K, Sato K, Ichi S. The Long-Term Outcome of CyberKnife-Based Stereotactic Radiotherapy for Head and Neck Paragangliomas: A Single-Center Experience. World Neurosurg. 2021;155:382-90.
26. Gilbo P, Morris CG, Amdur RJ, et al. Radiotherapy for benign head and neck paragangliomas: a 45-year experience. Cancer. 2014;120:3738-43.
27. Carlson ML, Sweeney AD, Wanna GB, Netterville JL, Haynes DS. Natural history of glomus jugulare: a review of 16 tumors managed with primary observation. Otolaryngol Head Neck Surg. 2015;152:98-105.
28. Langerman A, Athavale SM, Rangarajan SV, Sinard RJ, Netterville JL. Natural history of cervical paragangliomas: outcomes of observation of 43 patients. Arch Otolaryngol Head Neck Surg. 2012;138:341-5.
29. Suárez C, Rodrigo JP, Bödeker CC, et al. Jugular and vagal paragangliomas: Systematic study of management with surgery and radiotherapy. Head Neck. 2013;35:1195-204.
30. Hu K, Persky MS. Treatment of Head and Neck Paragangliomas. Cancer Control. 2016;23:228-41.
31. Jackson CG, McGrew BM, Forest JA, Netterville JL, Hampf CF, Glasscock ME 3rd. Lateral skull base surgery for glomus tumors: long-term control. Otol Neurotol. 2001;22:377-82.