



# Differential Diagnosis and Treatment Outcomes of Tumors at the Carotid Bifurcation

Jihee Kang<sup>1</sup>, Seon-Hee Heo<sup>2</sup>, Yang-Jin Park<sup>2</sup>, Dong-Ik Kim<sup>2</sup>, and Young-Wook Kim<sup>3</sup>

<sup>1</sup>Division of Vascular Surgery, Department of Surgery, Inha University Hospital, Inha University School of Medicine, Incheon,

<sup>2</sup>Division of Vascular Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul,

<sup>3</sup>Division of Vascular Surgery, Department of Surgery, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

**Purpose:** Primary tumor at the carotid bifurcation is uncommon, which includes paraganglioma, schwannoma, and lymphoma. Due to their rarity, characteristics of these tumors and problems related to their surgical treatment have not been well known. We tried to elucidate different clinical characteristics and surgical complications of these tumors.

**Materials and Methods:** We retrospectively reviewed 21 patients with carotid bifurcation tumor from the Vascular Surgery division of a Korean tertiary institution from 1995 to 2018. We investigated patients' demographics and clinical features, image characteristics, treatment details, and surgical outcomes.

**Results:** During the period from January 1995 to January 2018, we experienced surgical resections of 21 carotid bifurcation tumors which included 16 (76.2%) paragangliomas and 5 (23.8%) schwannomas. The most common clinical feature was a non-tender cervical mass. According to Shamblin classification, paragangliomas were classified into class II in 68.8% and class III in 25.0%. On the preoperative computed tomography images, all the paragangliomas showed characteristic splaying of the carotid bifurcation and hypervascularity of the tumors. On the contrary, all the schwannomas showed hypovascularity and splaying sign in 60%. Surgical complications related to cervical nerve injury developed in 50% and 60% of patients with Shamblin class III paraganglioma and schwannoma, respectively. During the mean follow-up period of 25 months (range, 1 to 163 months), distant metastases developed in 2 (12.5%) of paraganglioma patients.

**Conclusion:** Neurologic complications were more common after surgical resection of Shamblin class III paraganglioma and schwannoma. For patients with paraganglioma, postoperative periodic follow-up examination is advised to detect distant metastasis.

**Key Words:** Paraganglioma, Schwannoma, Carotid body tumor, Carotid bifurcation

Received April 23, 2020

Revised June 17, 2020

Accepted July 7, 2020

Published online August 6, 2020

**Corresponding author:** Young-Wook Kim

Division of Vascular Surgery, Department of Surgery, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29 Saemunan-ro, Jongno-gu, Seoul 03181, Korea

Tel: 82-2-2001-2569

Fax: 82-2-2011-2117

E-mail: ywkim52@gmail.com

<https://orcid.org/0000-0002-1106-3037>

Copyright © 2020, The Korean Society for Vascular Surgery

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Vasc Specialist Int 2020;36(3):128-135 • <https://doi.org/10.5758/vsi.200022>

## INTRODUCTION

Primary tumors such as paraganglioma, schwannoma, and lymphomas at the carotid bifurcation are uncommon.

Paraganglioma is the most common primary tumor at the carotid bifurcation which is often called carotid body tumor. It arises from the neural crest-derived chemoreceptor (carotid body) located at the medial wall of the carotid bi-

furcation [1].

Schwannoma is a type of neurogenic tumor derived from Schwann cells of the nerve sheath. The cervical schwannoma usually arises from the vagus nerve or cervical sympathetic chains [2].

Schwannoma is even rarer, but these two tumors have different clinical features as well as imaging characteristics, and carries different postoperative complications rates after surgical resection of the tumor. To predict outcomes of surgical treatment of the tumors, it needs to be differentiated preoperatively.

According to the Health Insurance Review and Assessment Service data, the incidence of paraganglioma is one (0.7 to 1.1) out of 500,000 in Korea over the past seven years (2012 to 2018) [3]. This is even lower than other studies reporting between 1/30,000 and 1/100,000 [4]. Due to rarity, it is hard to have sufficient experience of these tumors. In this report, we would like to share our experience on treatment of these tumors focusing on their different characteristics and postoperative complications.

## MATERIALS AND METHODS

After being approved by institutional review board (IRB) of Samsung Medical Center (IRB no. 2009-11-042), a retrospective study was conducted using database of patients who underwent surgical resection of tumors located at the carotid bifurcation between 1995 and 2018 in the vascular surgery division of a Korean tertiary medical center. Informed consent from individual patients was waived from IRB for this study. We retrospectively reviewed demographic, clinical features, and imaging studies of these patients.

For preoperative work up for the carotid bifurcation tumor, contrast-enhanced computed tomography (CT) was ordered routinely. Then, magnetic resonance imaging (MRI) and transfemoral carotid angiography were selectively performed for further differential diagnosis and preoperative tumor embolization. Preoperative assessment of 24-hour urine metanephrine and normetanephrine level using high performance/pressure liquid chromatography method was selectively performed for patients with hypertension or bilateral lesions to rule out functioning paraganglioma. Genetic analyses for mutation of succinate dehydrogenase (SDH) subunits were also selectively performed for paraganglioma patients with metastasis or tumor recurrence after surgical excision, bilateral tumors, and presence of family history. Making a definitive diagnosis depended on histologic examination of the surgical specimen.

For the tumor embolization, a transfemoral catheter was introduced to the ipsilateral carotid artery and cyanoacrylate glue (N-butyl cyanoacrylate; Codman Neurovascular,

Inc., Raynham, MA, USA) was injected into the branches of the external carotid artery (e.g., ascending pharyngeal or superior thyroid artery).

During the removal of the tumor, incision and dissection similarly followed procedural steps practiced in carotid endarterectomy. We tried to keep the precise surgical plane to avoid tumor bleeding or carotid injury, as well as to achieve early division of feeding vessels to reduce the amount of bleeding. We preferred using a bipolar electrocoagulator to prevent adjacent nerve injury. For patients with a high-lying tumor, we performed surgery with otolaryngologists. They exposed a high-lying tumor with mobilization of the parotid gland.

Postoperatively, neurologic examination was routinely performed to detect injury of hypoglossal, vagus, recurrent laryngeal, mandibular branch of the facial nerves, or cervical sympathetic ganglions.

Categorical variables were expressed in number and percentage, and continuous variables were expressed in mean value±standard deviation.

**Table 1.** Demographic, clinical, and imaging characteristics (n=21)

Feature	Pathology of the tumor	
	Paraganglioma	Schwannoma
Number	16 (76.2)	5 (23.8)
Female	11 (68.8)	0
Age (y)	42.6±14.8	39.6±11.8
Site of tumor		
Right	9 (56.3)	3 (60.0)
Left	5 (31.3)	2 (40.0)
Bilateral	2 (12.5)	0
Clinical presentations		
Non-tender neck mass	14 (87.5)	5 (100.0)
Neck pain or discomfort	3 (18.8)	0
Otalgia	1 (6.3)	0
Headache	1 (6.3)	1 (20.0)
Dysphagia and hoarseness	1 (6.3)	0
CT findings		
Splay of carotid bifurcation	16 (100.0)	3 (60.0)
Medial deviation of ICA	4 (25.0)	0
Hypervascular tumor	16 (100.0)	0
Hypovascular tumor	0	5 (100.0) <sup>a</sup>
Shamblin classification:		
Class I	1 (6.3)	NA
Class II	11 (68.8)	
Class III	4 (25.0)	

Values are presented as number (%) or mean±standard deviation. CT, computed tomography; ICA, internal carotid artery; NA, not applicable.

<sup>a</sup>Among 5 patients with schwannoma, 2 (40.0%) patients showed regional contrast enhancement within the tumor.

## RESULTS

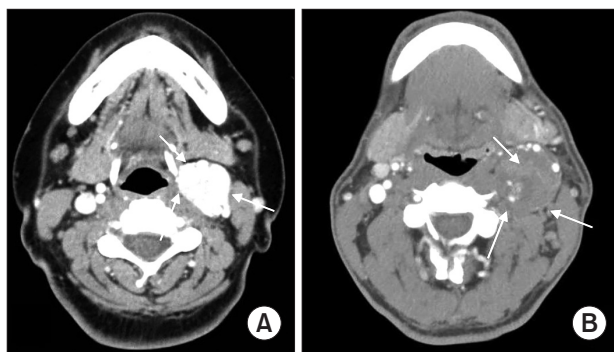
During the period from January 1995 to January 2018, we experienced surgical resections of 22 carotid bifurcation tumors including 16 (72.7%) paragangliomas, 5 (22.7%) schwannomas, and 1 (4.5%) leiomyosarcoma. Among them, we included 16 paragangliomas and five schwannomas to compare clinical characteristics and treatment outcomes. The demographic and clinical features of the patients are summarized in Table 1.

The mean ages of the patients were  $42.6 \pm 14.8$  and  $39.6 \pm 11.8$  years in paraganglioma and schwannoma, respectively. There was female predilection (68.8%) in patients

with paraganglioma. Paragangliomas were bilateral in two (12.5%) patients. However, we could not find any family history.

The most common clinical feature was a non-tender cervical mass in both paraganglioma and schwannoma. In patients with Shamblin class III paraganglioma, one patient complained of headache and dizziness, and another patient presented with dysphagia and hoarseness at the initial presentation. In the later patient, vocal cord palsy was confirmed on preoperative laryngoscopic examination.

On preoperative contrast-enhanced CT images, all the

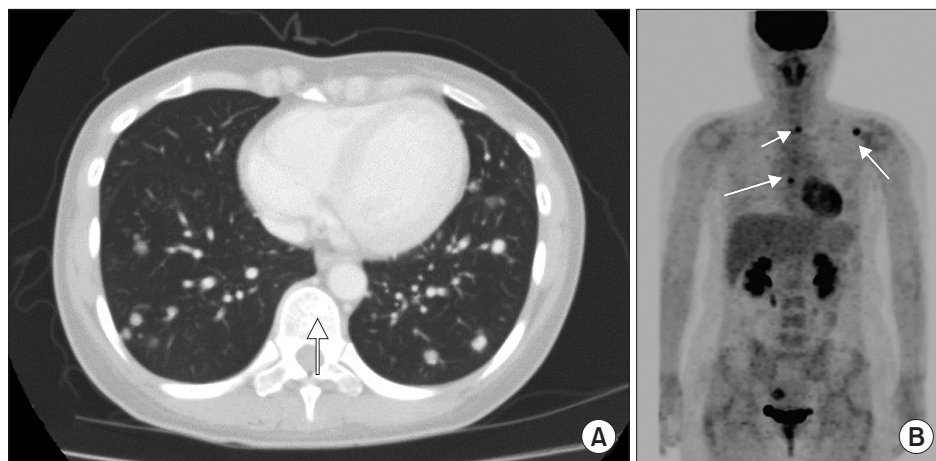


**Fig. 1.** Axial view of the contrast-enhanced computed tomography images of carotid bifurcation tumors. (A) Shamblin class III paraganglioma (arrows) at the left carotid bifurcation which shows hypervascularity and splaying of the carotid bifurcation. (B) Schwannoma (arrows) at the left carotid bifurcation which shows hypovascularity and antero-lateral deviation of the internal carotid artery.

**Table 2.** Details of surgical procedure

	Pathology of the tumor	
	Paraganglioma (n=16)	Schwannoma (n=5)
Preoperative tumor embolization <sup>a</sup>	5 (31.3)	NA
Carotid reconstruction		
Patch angioplasty	0	0
Interposition graft	1	0
Cranial nerve sacrifice	2 (12.5)	0
IJV resection	1 (6.3)	0
Use of carotid shunt	1 (6.3)	0
Joint operation with ENT surgeon	2 (12.5)	0
Operation time (min)	$179.6 \pm 86.4$	$112.2 \pm 17.6$

Values are presented as number (%) or mean  $\pm$  standard deviation. NA, not applicable; IJV, internal jugular vein; ENT, ear nose throat. <sup>a</sup>Catheter tumor embolization was performed by injection of cyanoacrylate glue into the tumor via branches of the external carotid artery (e.g., ascending pharyngeal or superior thyroid artery) before mean 2.5 days (range, 1 to 5) of surgical excision of the tumor.



**Fig. 2.** Images of metastatic paragangliomas. (A) An axial computed tomography image of 19-year-old female patient shows multiple lung nodules and osteoblastic lesion (arrow) of the thoracic spine at 12 years after surgical excision of paraganglioma. (B) An 18 fluorodeoxyglucose positron emission tomography image shows multiple bone metastases (arrows) in a 41-year-old female patient at 5 months after surgical excision of the cervical paraganglioma.

paragangliomas showed characteristic widening or splaying of the carotid bifurcation and hypervascularity of the tumors (Fig. 1A, 4A). Schwannomas showed splaying sign and displacement of ipsilateral internal carotid arteries posterolaterally or anterolaterally in 60% (Fig. 1B). On the contrary to the paragangliomas, schwannomas showed hypovascularity but with regional contrast enhancement in 40% (Fig. 1B).

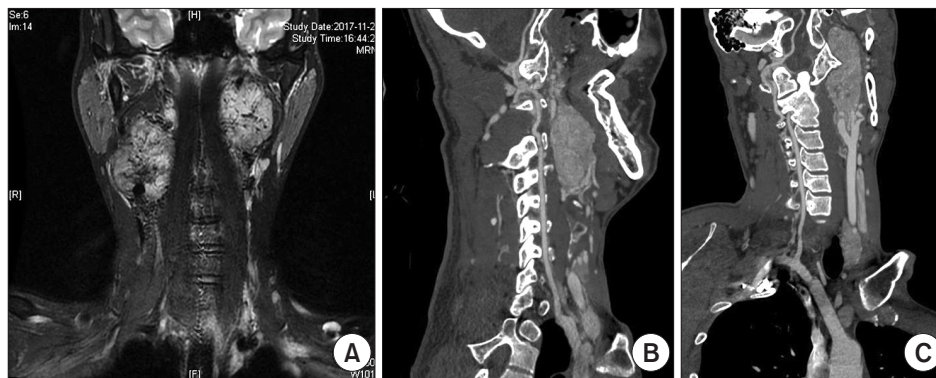
Preoperative 24-hour urine metanephrine and normetanephrine levels were measured in 10 hypertensive patients which revealed no abnormality in this series. Genetic analyses for mutation of SDH subunits were conducted in two female patients with metastatic paraganglioma (Fig. 2), which resulted in SDH subunits B (SDHB) mutation in one patient.

Surgical procedures are summarized in Table 2. Preoperative tumor embolization was performed for 5 (31.3%) paraganglioma patients at mean 2.5 days (range, 1 to 5)

before surgical excision of the tumor. There was no complication related to preoperative tumor embolization in our series.

One patient with Shamblin class III paraganglioma required a segmental resection of the internal carotid artery (ICA) along with the tumor, which required carotid shunting and ICA reconstruction with autogenous vein graft. For two patients with high-lying paraganglioma (Fig. 3), we performed surgery with assistance of otolaryngologist.

As shown in Table 3, all complications related to cervical nerve injury developed in patients with Shamblin class III paraganglioma (n=2) or schwannoma (n=3). One patient with paraganglioma had ipsilateral lower lip drooping, but the other patient had Horner syndrome, dysphagia, and hoarseness. Among three patients with schwannoma, one patient experienced first bite syndrome and Horner syndrome, and another patient had only first bite syndrome, while the other patient had hoarseness and dysphasia.



**Fig. 3.** High-lying bilateral cervical paragangliomas in a 19-year-old male patient. (A) Magnetic resonance imaging shows bilateral high-lying cervical tumors suggestive of paraganglioma which shows characteristic feature of "salt and pepper" appearance. (B) A sagittal view of contrast-enhanced computed tomography (CT) shows the right carotid body tumor. (C) A sagittal view of contrast-enhanced CT shows the left carotid body tumor extending to the skull base.

**Table 3.** Postoperative complications (mean follow-up duration: 25 months, median 1.3 months, range 1 to 163 months)

Complications	Shamblin class of paraganglioma			Schwannoma (n=5)
	I (n=1)	II (n=11)	III (n=4)	
None	1 (100.0)	11 (100.0)	2 (50.0)	2 (40.0)
Early postoperative				
Dysphagia	0	0	1	1
Hoarseness	0	0	1	1
First bite syndrome <sup>a</sup>	0	0	0	2
Horner syndrome	0	0	1	1
Ipsilateral lower lip drooping	0	0	1	0
Late postoperative				
Distant metastasis <sup>b</sup>		1 (9.1)	1 (25.0)	0

<sup>a</sup>First bite syndrome denotes postoperative symptom of an acute and intense pain in the ipsilateral parotid region occurred with the first bite of each meal. <sup>b</sup>Distant metastases were detected in 2 paraganglioma patients at 12 years and 5 months each after the primary surgical resection.



There was no stroke postoperatively.

During the follow-up period of 25 months (mean: range, 1 to 163 months), distant metastases occurred in two patients with paraganglioma. In a 19-year-old patient of Shamblin class III, paraganglioma developed back pain at 12 years after the surgery. The imaging studies revealed recurrent mass extending to the skull base and distant metastases to the lung and spine (Fig. 2A). In the other 41-year-old patient of Shamblin class II paraganglioma, multiple bone metastases to the spines and scapula were detected at 5 months after primary surgery (Fig. 2B).

For the treatment of metastatic paraganglioma of the younger patient, targeted radiation therapy with  $^{131}\text{I}$ -MIBG (metaiodobenzylguanidine) was performed twice. After then, other metastatic nodules developed in the right breast at seven months after the therapy. We performed partial mastectomy and confirmed that it was metastatic paraganglioma. Five years later, follow-up imaging studies showed progressive metastases to the lungs and spine again, palliative radiotherapy was performed. On the follow-up visit a year after the radiotherapy, there was no evidence of recurrence. Her gene study did not show mutation of the SDH subunits.

The 41-year-old patient developed tenderness over the left shoulder at 5 months after primary surgery of the Shamblin class II paraganglioma. Imaging study revealed multiple bone metastases to the left scapula and thoracic vertebra (Fig. 2B), and we confirmed metastatic paraganglioma through bone biopsy. Her gene study revealed SDHB mutation, thus familial evaluation was recommended. She underwent radiotherapy to the metastatic bone lesions,

and there was no recurrence developed during 60-month follow-up.

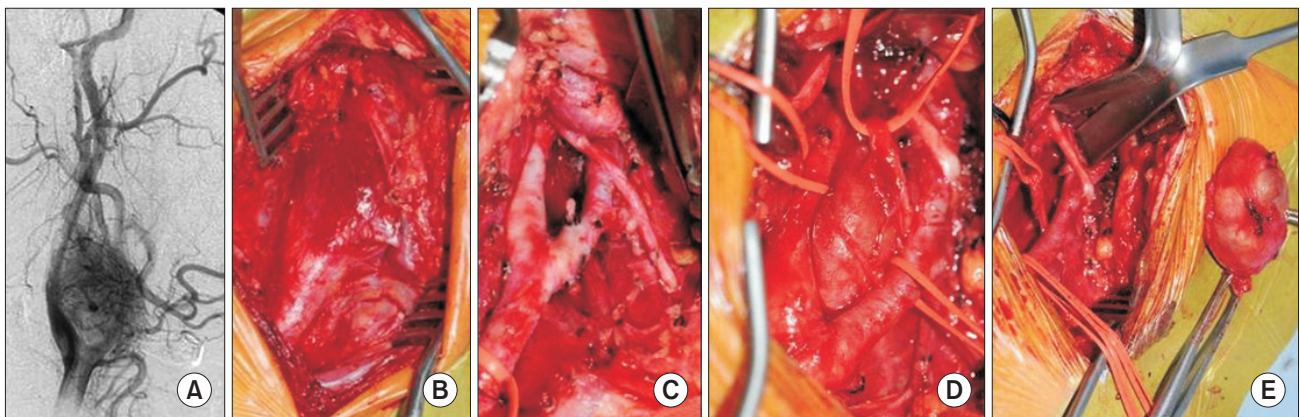
## DISCUSSION

Paraganglioma arising from the carotid body is an asymptomatic and slow growing tumor, which accounts for 60% to 70% of head and neck paragangliomas [5].

The most common reason to seek medical attention is a non-tender, palpable neck mass at the carotid triangle of the neck [5]. The majority of cervical paragangliomas are nonfunctioning, while less than 5% of the cervical paragangliomas are functioning with secretion of the catecholamine from the tumor [6].

An etiology of paraganglioma has not been well known, however, exposure to chronic hypoxia or germ line mutation of SDH subunits are accepted as one of the etiology [7]. The mutation of SDH is known to activate chronic hypoxia pathways in the cells then induces paraganglioma from the carotid body [8]. Whether which one comes first, chronic hypoxia seemed to play an important role in pathogenesis of paraganglioma of the carotid body.

In 1971, Shamblin et al. [9] classified paraganglioma into three categories; class I, tumor localized at the carotid bifurcation not adherent to the arteries; class II, tumor adherent or partially surrounding carotid arteries; and class III, tumor encasing carotid artery. The classification was designed to predict technical difficulty during surgical excision of the tumor, in other words, to predict likelihood of occurrence of the cervical nerves or carotid artery damage during the operation.



**Fig. 4.** (A-C) A paraganglioma at the carotid bifurcation in a 31-year-old male patient. (A) Preoperative carotid angiography showing a hypervascular tumor at the carotid bifurcation which splays the internal and external carotid arteries. (B) Surgical findings of a hypervascular paraganglioma adherent to the carotid arteries. (C) A photograph of the surgical field after removal of the paraganglioma which shows the well-preserved hypoglossal nerve. (D, E) A schwannoma at the carotid bifurcation in a 38-year-old male patient (D) A photograph of the surgical field before tumor resection shows clear demarcation between the tumor and carotid arteries. (E) After tumor resection, tumor is well encapsulated unlike that of paraganglioma.

During the operation of carotid paraganglioma, keeping dissection plane at the subadventitial layer of the carotid bifurcation has been emphasized (Fig. 4B) [10]. The other important point is early division of the feeding vessels to the tumor to reduce the amount of tumor bleeding. Paragangliomas usually receive their blood supply from the branches of external carotid artery, most commonly from the ascending pharyngeal branch [11]. Some authors have asserted the importance of preoperative tumor embolization to reduce intraoperative bleeding and to allow easier dissection during the removal of the hypervascular tumor [12,13]. However, there has been controversy over the risk versus benefit of preoperative tumor embolization. Some authors reported stroke or retinal artery occlusion after embolization [14,15]. A recent meta-analysis regarding the tumor embolization reported that there was no significant difference in the postoperative re-exploration rate due to neck hematoma between embolization and no-embolization groups [11]. About 20% of our patients underwent preoperative tumor embolization in the earlier part of the study period. There was no complication related to preoperative tumor embolization in our patients. However, we do not currently perform preoperative tumor embolization considering risk-benefit of it.

Among our patients, one patient with Shamblin class III paraganglioma underwent carotid artery reconstruction with interposition graft. For those whose ICA is expected to be permanently ligated, balloon test occlusion (BTO) can be performed preoperatively to estimate the risk of stroke after permanent occlusion of an ICA. However, considering the test related complications including permanent neurologic deficit [16] and the absence of a universally accepted method to monitor the BTO [17], we do not conduct BTO in our institution.

Two main difficulties in surgery of carotid bifurcation tumor are risk of injuries to the carotid artery and cervical nerves (Fig. 4C). Carotid injury during the tumor resection may cause stroke or cervical nerve damage by obscuring the surgical field. In our series, ICA reconstruction was required in one patient with Shamblin class III paraganglioma.

A recent European meta-analysis reported that procedural risks of paraganglioma surgery are much higher than that of carotid endarterectomy in terms of cranial nerve injury (25%) [11]. Although we did not experience postoperative stroke, 30-day stroke rate has been reported up to 3.5% after cervical paraganglioma surgery [11]. In the study of Gwon et al. [18], they reported 23% of postoperative stroke rate. They mentioned that the postoperative stroke rate was associated with higher Shamblin classification along with ICA manipulation including repair of injury. We also had ICA reconstruction in one patient, but it was a planned

procedure, in contrast to that unplanned ICA manipulation which occurred in 35% of the patients in the previous study.

Schwannomas arising from the vagus nerve or cervical sympathetic chains may present as a carotid bifurcation tumor. Its true incidence has not been well known. Unlike paragangliomas, cervical schwannomas are hypovascular on contrast-enhanced CT images [19]. On MRI, they often show hypointense and hyperintense on the T1 and T2-weighted images [20], respectively. Schwannomas arising from the vagus nerve tend to displace the internal jugular vein and ICA posteriorly without splaying carotid bifurcation, and schwannoma originated from the sympathetic chain may displace the vessels slightly posterolaterally [21]. We felt that dissection is somewhat easier in schwannoma than that of paraganglioma due to less adherences to the carotid arteries (Fig. 4D), better encapsulation of the tumor (Fig. 4E), and less bleeding during the tumor resection. Recurrence has been known to be extremely rare after complete removal of the cervical schwannoma [22]. However, we found that postoperative neurologic complications were more frequent in schwannoma compared to in paraganglioma. First bite syndrome denotes postoperative symptom of acute and intense pain in the ipsilateral parotid region which occurs with the first bite of each meal and usually persists for less than one minute [23]. It is typically seen after parapharyngeal or deep parotid space surgery [23]. We experienced this complication in two patients with schwannoma. Though intra-parotid injection of botulinum toxin A has been recommended to treat it [24], the symptoms were resolved spontaneously by pain medication in our patients.

Preoperative measurement of urine catecholamine metabolites (metanephrine and normetanephrine) is required to avoid unexpected intraoperative hypertensive crisis in patients with functioning paraganglioma. Presence of preoperative symptoms such as fluctuating hypertension, facial blushing, or palpitation can be a clinical clue to identify functioning paraganglioma [25], and are indicated for urine test. However, the incidence of functioning paraganglioma has been reported to be very low in head and neck paragangliomas [26].

We experienced malignant paraganglioma in two (12.5%) patients. In a comparative study of malignant head and neck paragangliomas, they reported that younger mean age at the time of diagnosis (38 years in their study), hormone-secreting tumors, and multifocal tumors constitute risk factors for malignancy [27]. Genetic component also has been known as an important risk factor for malignant paraganglioma; SDHB mutation is associated with metastatic disease at an early age [28].

Malignant paraganglioma is diagnosed by histologic

confirmation of metastasis to non-neuroendocrine tissues such as regional lymph nodes, lung, liver, bone, or skin [29]. For detection of metastatic paraganglioma, MIBG scan can be used. An overall sensitivity of MIBG to detect functioning paraganglioma has been reported up to 90% to 95% and specificity up to 99% [30]. We did not perform MIBG scan as a routine diagnostic study.

There is a general agreement that surgical removal is the treatment of choice for patients with carotid bifurcation tumors when it is feasible. However, operation may be quite challenging in particular for the patients with cephalad extension of the tumor. For those patients, joint operation with otolaryngeal surgeon was helpful in dissection of the high-lying tumor through proximal extension of skin incision and mobilization of the parotid gland. In patients with very high-lying tumor close to the jugular foramen, radiation therapy is recommended rather than surgical treatment [13].

As described before, cervical nerve injuries seemed more likely to be associated with Shamblyn class III paragangliomas and schwannomas. To avoid those complications, surgical treatment in earlier stage of the tumor is recommended.

Although this study is limited due to a small number of patients, differential diagnosis can prepare surgeons to predict possible intraoperative difficulties, possible postoperative complications, and disease course of these rare conditions.

## CONCLUSION

In conclusion, for patients with carotid bifurcation tumor, early and correct diagnosis can be made preoperative-

ly with contrast-enhanced CT or MRI. Various neurologic complications developed more frequently after surgical resection of Shamblyn class III paraganglioma or schwannoma. Although the incidence of metastatic paraganglioma was not high, we recommend postoperative periodic surveillance for prompt detection of possible distance metastasis.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

## ORCID

Jihee Kang

<https://orcid.org/0000-0002-6463-9458>

Seon-Hee Heo

<https://orcid.org/0000-0002-0250-2229>

Yang-Jin Park

<https://orcid.org/0000-0001-8433-2202>

Dong-Ik Kim

<https://orcid.org/0000-0001-6984-5982>

Young-Wook Kim

<https://orcid.org/0000-0002-1106-3037>

## AUTHOR CONTRIBUTIONS

Concept and design: JK, YWK. Analysis and interpretation: JK, YWK. Data collection: JK. Writing the article: JK. Critical revision of the article: YWK, YJP. Final approval of the article: JK, SHH, YJP, DIK, YWK. Statistical analysis: JK, SHH. Obtained funding: none. Overall responsibility: YWK.

## REFERENCES

- 1) Torrealba JI, Valdés F, Krämer AH, Mertens R, Bergoeing M, Mariné L. Management of carotid bifurcation tumors: 30-year experience. *Ann Vasc Surg* 2016;34:200-205.
- 2) Sargar K. Parapharyngeal neck schwannomas with unusual vascular displacement. *Case Rep Med* 2013;2013:563019.
- 3) von Meijenfeldt GC, Vainas T, Mistrionis GA, Gans SL, Zeebregts CJ, van der Laan MJ. Accuracy of routine endoscopy diagnosing Colonic ischaemia after abdominal aortic aneurysm repair: a meta-analysis. *Eur J Vasc Endovasc Surg* 2018;56:22-30.
- 4) Sajid MS, Hamilton G, Baker DM; Joint Vascular Research Group. A multi-center review of carotid body tumour management. *Eur J Vasc Endovasc Surg* 2007;34:127-130.
- 5) Darouassi Y, Alaoui M, Mliha Touati M, Al Maghraoui O, En-Nouali A, Bouaity B, et al. Carotid body tumors: a case series and review of the literature. *Ann Vasc Surg* 2017;43:265-271.
- 6) van Duinen N, Steenvoorden D, Kema IP, Jansen JC, Vriends AH, Bayley JP, et al. Increased urinary excretion of 3-methoxytyramine in patients with head and neck paragangliomas. *J Clin Endocrinol Metab* 2010;95:209-214.
- 7) Knight TT Jr, Gonzalez JA, Rary JM, Rush DS. Current concepts for the surgical management of carotid body tumor. *Am J Surg* 2006;191:104-110.
- 8) Baysal BE. Clinical and molecular progress in hereditary paraganglioma. *J Med Genet* 2008;45:689-694.

- 9) Shamblyn WR, ReMine WH, Sheps SG, Harrison EG Jr. Carotid body tumor (chemodectoma). Clinicopathologic analysis of ninety cases. *Am J Surg* 1971;122:732-739.
- 10) Prabakaran S, Subburayulu AS, Ravikumar PT. Surgical excision of carotid body tumor through modified approach—a case report. *J Maxillofac Oral Surg* 2016;15:251-255.
- 11) Robertson V, Poli F, Hobson B, Saratzis A, Ross Naylor A. A systematic review and meta-analysis of the presentation and surgical management of patients with carotid body tumours. *Eur J Vasc Endovasc Surg* 2019;57:477-486.
- 12) Davidovic LB, Djukic VB, Vasic DM, Sindjelic RP, Duvnjak SN. Diagnosis and treatment of carotid body paraganglioma: 21 years of experience at a clinical center of Serbia. *World J Surg Oncol* 2005;3:10.
- 13) Dupin C, Lang P, Dessard-Diana B, Simon JM, Cuenca X, Mazon JJ, et al. Treatment of head and neck paragangliomas with external beam radiation therapy. *Int J Radiat Oncol Biol Phys* 2014;89:353-359.
- 14) Rangel CM, Jaramillo S, Varón CL, Prada AM. Iatrogenic central retinal artery occlusion after carotid body tumor embolization and excision. *GMS Ophthalmol Cases* 2017;7:Doc09.
- 15) Lazzaro MA, Badruddin A, Zaidat OO, Darkhabani Z, Pandya DJ, Lynch JR. Endovascular embolization of head and neck tumors. *Front Neurol* 2011;2:64.
- 16) American Society of Interventional and Therapeutic Neuroradiology. Carotid artery balloon test occlusion. *AJNR Am J Neuroradiol* 2001;22(8 Suppl):S8-S9.
- 17) Galego O, Nunes C, Morais R, Sargento-Freitas J, Sales F, Machado E. Monitoring balloon test occlusion of the internal carotid artery with transcranial Doppler. A case report and literature review. *Neuroradiol J* 2014;27:115-119.
- 18) Gwon JG, Kwon TW, Kim H, Cho YP. Risk factors for stroke during surgery for carotid body tumors. *World J Surg* 2011;35:2154-2158.
- 19) Anil G, Tan TY. Imaging characteristics of schwannoma of the cervical sympathetic chain: a review of 12 cases. *AJNR Am J Neuroradiol* 2010;31:1408-1412.
- 20) Weber AL, Montandon C, Robson CD. Neurogenic tumors of the neck. *Radiol Clin North Am* 2000;38:1077-1090.
- 21) Saito DM, Glastonbury CM, El-Sayed IH, Eisele DW. Parapharyngeal space schwannomas: preoperative imaging determination of the nerve of origin. *Arch Otolaryngol Head Neck Surg* 2007;133:662-667.
- 22) Mikaelian DO, Holmes WF, Simonian SK. Parapharyngeal schwannomas. *Otolaryngol Head Neck Surg* 1981;89:77-81.
- 23) Chiu AG, Cohen JI, Burningham AR, Andersen PE, Davidson BJ. First bite syndrome: a complication of surgery involving the parapharyngeal space. *Head Neck* 2002;24:996-999.
- 24) Ghosh A, Mirza N. First bite syndrome: our experience with intraparotid injections with botulinum toxin type A. *Laryngoscope* 2016;126:104-107.
- 25) Wang SH, Chiu KM, Cheng PW. Bilateral carotid body paragangliomas. *CMAJ* 2011;183:E606.
- 26) Milardovic R, Corssmit EP, Stokkel M. Value of 123I-MIBG scintigraphy in paraganglioma. *Neuroendocrinology* 2010;91:94-100.
- 27) Mediouni A, Ammari S, Wassef M, Gimenez-Roqueplo AP, Laredo JD, Duet M, et al. Malignant head/neck paragangliomas. Comparative study. *Eur Ann Otorhinolaryngol Head Neck Dis* 2014;131:159-166.
- 28) King KS, Prodanov T, Kantorovich V, Fojo T, Hewitt JK, Zacharin M, et al. Metastatic pheochromocytoma/paraganglioma related to primary tumor development in childhood or adolescence: significant link to SDHB mutations. *J Clin Oncol* 2011;29:4137-4142.
- 29) Wang SJ, Wang MB, Barauskas TM, Calcaterra TC. Surgical management of carotid body tumors. *Otolaryngol Head Neck Surg* 2000;123:202-206.
- 30) Brink I, Hoegerle S, Klisch J, Bley TA. Imaging of pheochromocytoma and paraganglioma. *Fam Cancer* 2005;4:61-68.