SHORT COMMUNICATION

UDC: 616-066-089-06-084::617.51/.53
DOI: https://doi.org/10.2298/VSP190809121S

Therapeutic role of selective preoperative embolization in patients with paragangliomas of head and neck

Terapijska uloga selektivne preoperativne embolizacije kod bolesnika sa paragangliomima glave i vrata

[1]Igor Sekulić*, [1]Aleksandar Jovanovski*, Dejan Kostić*†, Srboljub Stošić†‡, Jelena Bošković-Sekulić§, Jelena Stevanović*, Nemanja Rančić†‖

Military Medical Academy, *Institute of Radiology, ‡Clinic for Maxillofacial Surgery, ‖Center for Clinical Pharmacology, Belgrade, Serbia; †University of Defence, Faculty of Medicine of the Military Medical Academy, Belgrade, Serbia; §Clinical Center Kragujevac, Center for Urgent Medicine, Kragujevac, Serbia

[1]both authors contributed equally to this manuscript and share the first authorship

Abstract

Background/Aim. Paragongliomas are rare hypervascular neoplasms. The aim of this study was to present the experience in the treatment of paragangliomas using preoperative embolization. **Methods.** This retrospective cross-sectional study included 10 patients (7 women and 3 men; median age 55 years) with paragangliomas that were embolized before surgery. **Results.** Three patients had tympanicum paragangliomas, two carotid bodies, three jugular and two jugulare-tympanicum paragangliomas. During the operation, only one out of 10 patients had bleeding which required blood transfusion. This patient received 1,130 mL of blood transfusion due to surgical complication. **Conclusion.** Adequate preoperative selective embolization of paragangliomas is essential in the preoperative preparation of these patients, because this strategy is feasible with low complication rates.

Key words:
blood transfusion; embolization, therapeutic; head and neck, neoplasms; paraganglioma; preoperative period; treatment, outcome.

Apstrakt

Uvod/Cilj. Paragangliomi su retke hipervaskularne neoplazme. Cilj rada je bio da se prikaže iskustvo u lečenju paraganglioma preoperativnom embolizacijom. **Metode.** U retrospektivnu studiju preseka bilo je uključeno10 bolesnika (7 žena i 3 muškaraca; medijana godina starosti iznosila je 55) sa paragangliomima koji su bili embolisani pre operacije. **Rezultati.** Tri bolesnika su imala timpanične paragangliome, dva karotidne, tri jugularne i dva jugularno-timpanične paragangliome. Tokom operacije, samo jedan od 10 bolesnika imao je krvarenje koje je zahtevalo nadoknadu krvi. Ovaj bolesnik je primio 1 130 mL krvi zbog hirurške kompilikacije. **Zaključak.** Adekvatna preoperativna selektivna embolizacija paraganglioma je osnovna tehnika u preoperativnoj pripremi ovih bolesnika, budući da se radi o izvodljivoj proceduri sa niskom stopom komplikacija.

Ključne reči:
transfuzija krvi; embolizacija, terapijska; glava i vrat, neoplazme; paragangliom; preoperativni period; lečenje, ishod.

Introduction

Paragangliomas (glomus tumors or chemodectoma) are rare hypervascular neoplasms. They arise from paraganglionic cells located in the walls of blood vessels or in specific nerves [1]. They can be located in the carotid body (*glomus caroticum*) as the most common site [1], tympanic plexus (*glomus tympanicum)*, located within the adventitia layer of the jugular bulb wall (*glomus jugulare*) and vagal nerve typically near the jugular foramen. The rare locations are trachea, larynx and nose cavity [2]. In most cases these tumors are benign, slow-growing and locally destructive neoplasms, and a small percentage of tumors produce catecholamines [1, 3]. The incidence of the paragangliomas is one per million people [3],

Correspondence to: Dejan Kostić, Military Medical Academy, Institute of Radiology, Crnotravska 17, 11 000 Belgrade, Serbia.
E-mail: drdkostic@gmail.com

where head and neck paragangliomas comprise 3% of all paragangliomas [1]. The majority of these tumors manifest in the fifth and sixth decade of life, predominantly in women [1, 3, 4].

Symptoms depend on the localization and type of paraganglioma. *Glomus tympanicum* causes conductive hearing loss, pulsatile tinnitus which is synchronized with the heart beat, and, on rare occasions, otorrhea hemorrhage. *Glomus jugulare* tumors can cause jugular foramen syndrome (paresis of cranial nerve IX and X), which is pathognomonic for this type of tumor. Paragangliomas may also present as hypertension and tachycardia if they are functional catecholamine–producing tumors (dopamine, norepinephrine, somatostatin), and rarely producing vasoactive intestinal polypeptide, calcitonin [2, 4].

Otoscopic examination shows characteristic reddish-blue pulsatile mass, localized behind the tympanic membrane [2]. Classical radiography (X-ray) of the skull base can show widening of the foramen jugulare. Clinical diagnosis is confirmed by imaging methods – ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI). Images with bone window are used for better visualization of the bone resorption caused by the *glomus tympanicum*. MRI is important for assessing the soft tissue involvement. T1 and T2 sequences after gadolinium enhancement are mainly used, and sometimes fat-suppression sequences [1]. Combination of CT and MRI is a gold standard for the diagnoses of these tumors [2]. Digital subtraction angiography (DSA) is very important and is used for the identification of tumor feeding arteries during embolization planning [1, 3, 4].

Therapy for the paragangliomas is total surgical resection, but because of its rich vascularization and high risk of hemorrhage, preoperative embolization is beneficial for reducing blood loss in the surgical field [4–8].

The aim of this study was to present the experience in the treatment of paragangliomas with preoperative embolization.

Methods

This was a retrospective cross-sectional study of 10 patients with paragangliomas that were embolized before surgery. We included all patients who were embolized before the surgery of paragangliomas during the seven-year period, from 2012–2018. Patients with paragangliomas were treated with preoperative embolization using a sclerosing agent (smaller particles from 100-300 μ) in the Institute of Radiology, Military Medical Academy, Belgrade, Serbia, and a total surgical resection with a function preserving intent in Surgical Clinics Group at the Military Medical Academy. We retrospectively analyzed the patients' medical and imaging records.

After clinical examination as a part of the diagnostics, a multislice CT (MSCT) examination was performed (64- and 128-slices MSCT, Aquilion system, Toshiba®; field of view 20 cm, section thickness 1 mm, contrast material volume 80 mL (iohexol), contrast material injection rate 3 mL/s). The MSCT examination was used to assess tumor size, relationship to surrounding anatomical structures and tumor vascularization.

After clinical diagnosis, patients underwent imaging diagnosis with US (Figures 1A and 1B) and CT (Figures 2A,

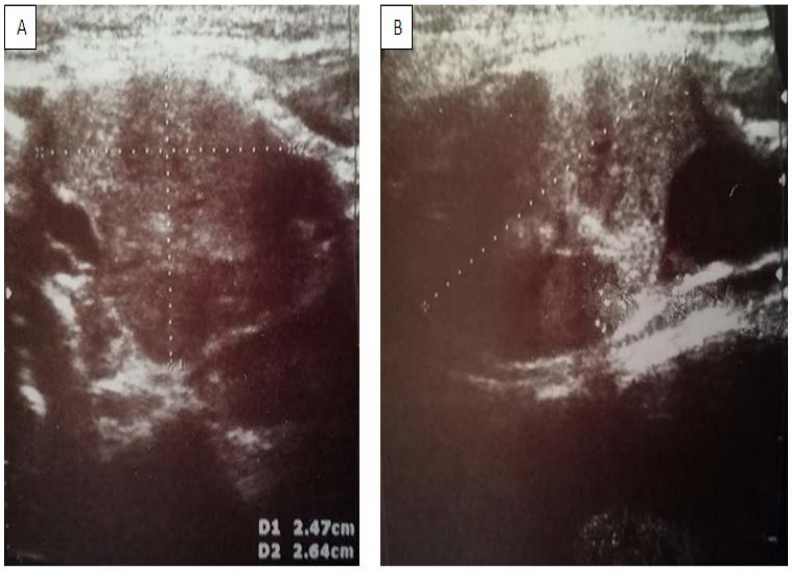

Fig. 1 – Ultrasonic finding: heteroechoic, dominant hyperechoic change, relatively clearly limited.
A) anteroposterior x craniocaudal diameter about 25 × 27 mm;
B) lateral-lateral diameter about 19 mm.

2B and 2C) and preoperative endovascular embolization. Preoperative embolization started with a diagnostic DSA *via* a transfemoral Seldinger approach. Right transfemoral access was obtained using a 6 Fr sheath-guiding catheter (Merit Medical). A guide wire (length 150 mm and 0.035 In) and 5 Fr diagnostic angiographic catheter (SIM II or JB Terumo® or Optitorque®) was then advanced into the common carotid artery on the side the tumor resided. After that, the injection of radiocontrast iohexol (Omnipaque®, GE Healthcare Ireland limited, Ireland) by Avanti avast® pump (rate flow 6 mL/s) was used to visualize vascularization of tumor DSA (Figure 3A). Angiography was performed *via* the diagnostic catheter, placed into common carotid artery and other blood vessels, to determine the arterial feeders of the tumor.

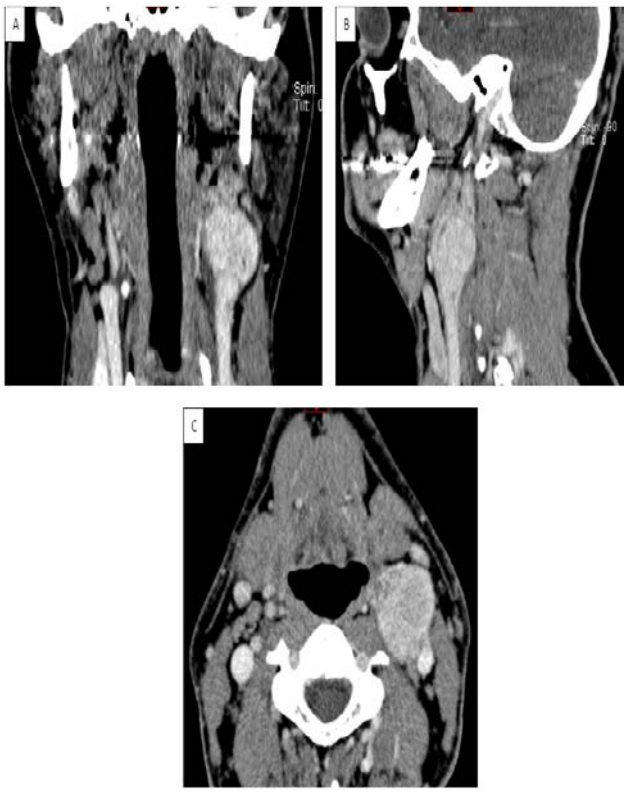

Fig. 2 – Multislice computed tomography findings of the neck: hypervascular expansive lesions at the level of bifurcation of common carotid artery which move the external and internal carotid arteries – carotid glomus. A) coronal; B) sagittal; C) axial slices.

After completion of the diagnostic angiogram, a 2.7 Fr microcatheter (Progreat®, Terumo interventional systems) was placed through the diagnostic catheter and advanced into selective branches of arteries where selective arteriograms could be performed for improved tumor visualization (Figure 3B). Smaller particles (100–300 μ, Bead Block™, BTG International Ltd, UK) were used for embolization. Beads were placed in one mL syringes which were attached to the microcatheter and injected in pulses that were synchronized with systolic heartbeat monitored by radioscopy (Figure 3C). If the flow to the tumor was not diminished, larger bead sizes were incrementally selected until there was the cessation of flow or reflux of the contrast along the microcatheter. This technique was repeated for all branches that were large enough to accommodate the microcatheter. A final angiogram from the common carotid artery was performed to evaluate the degree of embolization and ensure patency of the internal carotid artery circulation (Figure 3D).

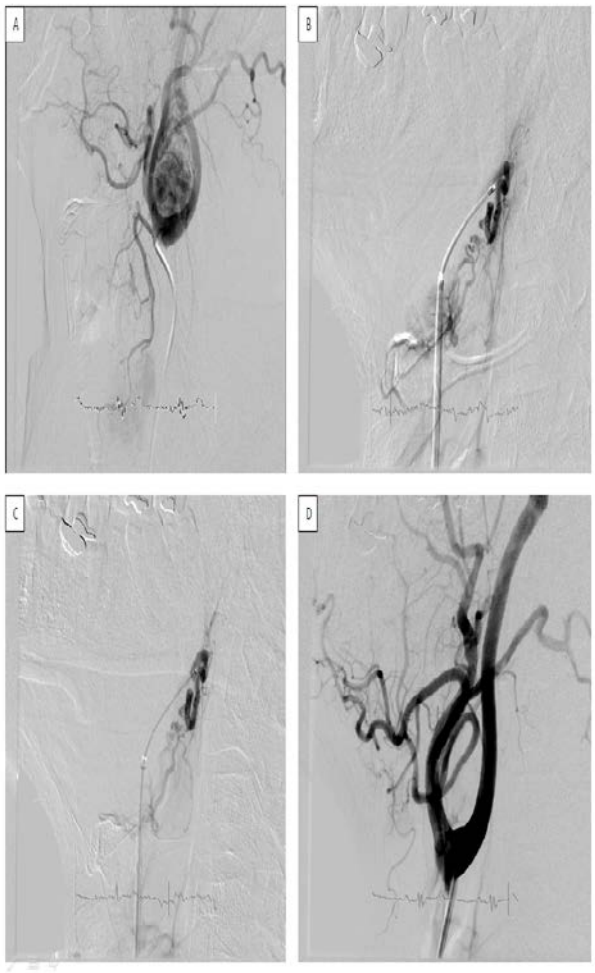

Fig. 3 – A) angiography at the level of bifurcation of common carotid artery by 5 Fr diagnostic angiographic catheter (Terumo®) showed hypervascular tumor change, which moves the external and internal carotid arteries: carotid glomus; the tumor is dominantly vascularized from the pronounced, tortuous ascending pharyngeal artery; B) selective catheterization of external carotid arteries through the diagnostic catheter and supraselective catheterization of ascending pharyngeal artery by Progreat (Terumo®) microcatheter; C) control angiography through microcatheter after the application of embolization agent (Bead Block™) size 100–300 μm; D) control angiography through the diagnostic catheter in the common carotid artery after embolization with complete tumor devascularization.

After embolization, paragangliomas were resected [6]. A retroauricular tympanic access route with canaloplasty was used for paragangliomas in the middle ear. Depending on the location and size of the paragangliomas, an endaural ap-

proach to the middle ear with additional mastoidectomy and myringoplasty was performed. Ossicular reconstruction was performed if required.

The surgical technique for carotid body paragangliomas included precise anatomic dissection and vascular control prior to the attempted tumor excision [6]. The dissection to remove the carotid body paraganglioma was carried out along the arterial subadventitial plane to allow for complete local tumor excision, as well as the preservation of critical vascular structures (Figure 4). Postoperative care included close pharmacologic control of systolic blood pressure and postoperative clinical neurologic evaluation.

Complete statistical analysis of data was performed using the statistical software package, PASW Statistics 18® [SPSS (Hong Kong) Ltd., Hong Kong]. All variables were presented as frequency of certain categories. χ^2 test was used for analyzing the significance of differences of categorical variables. Continuous variables were presented as median and interquartile range (IQR) and were compared using non-parametric Mann-Whitney *U* test. Distribution normality was tested using the Shapiro-Wilk Normality test (number of subjects was < 50). All analyses were estimated at $p < 0.05$ level of statistical significance.

All procedures performed in our study with human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Declaration of Helsinki or comparable ethical standards.

Results

We analyzed the data from 10 patients with paragangliomas (7 women and 3 men), median age 55.0 years, and with IQR from 49.75 to 61.25 years, who were treated with embolization before surgery (Table 1). Female patients were statistically significantly older in comparison to males (Mann-Whitney test; $p = 0.017$) (median age of males and females was 49.0 and 59.0 years, respectively).

Three patients had *glomus tympanicum*, two with carotid body, three with *jugulare* and two with *jugulare-tympanicum glomus* tumor (Table 1). Seven patients had

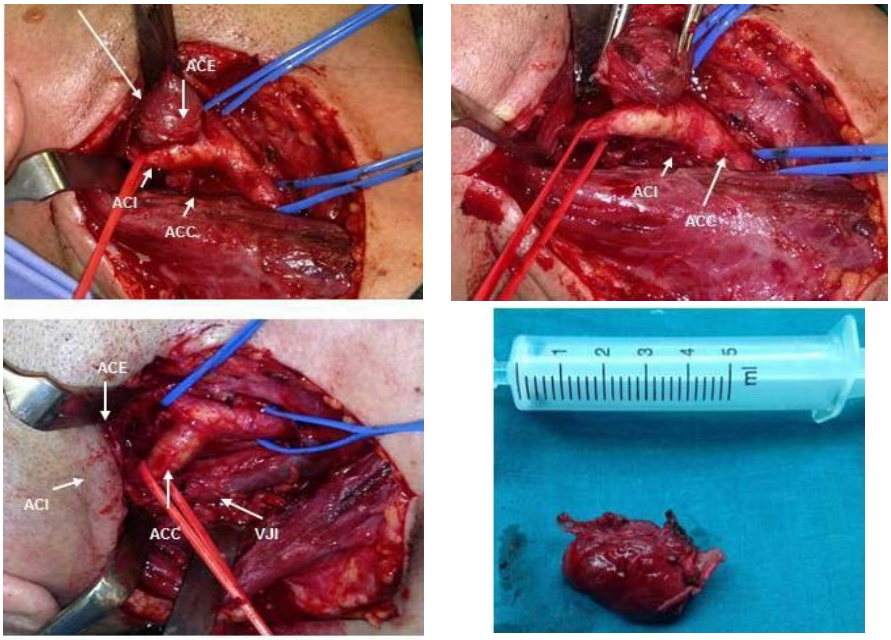

Fig. 4 – Surgical resection of carotid body tumor.
ACI – internal carotid artery; ACE – external carotid artery; ACC – common carotid artery.

Table 1

Demographic and clinical characteristics of patients with paragangliomas

Patient	Gender	Age (years)	*Glomus*	Side	Tumor diameter (mm)	Blood transfusion (mL)
1	male	50	*tympanicum*	left	26	0
2	female	61	carotid body	right	30	0
3	female	65	*jugulare*	both	39	0
4	male	46	*tympanicum*	left	32	0
5	female	59	*tympanicum*	right	12	0
6	female	52	carotid body	right	24	0
7	female	53	*jugulare*	right	24	0
8	female	62	*jugulare- tympanicum*	right	28	0
9	male	49	*jugulare*	right	30	0
10	female	57	*jugulare- tympanicum*	right	34	1,130

right side paraganglioma, while two patients had left side tumor and one patient had tumors on both sides. The largest tumor diameter median was 29.0 mm with IQR from 24.0–32.5 mm. During the operation, 9 out of 10 patients did not have bleeding which would require blood transfusion. One patient who had *jugulare-tympanicum glomus* tumor received 1,130 mL of blood transfusion because of the hemorrhage from carotid sinus during the surgical intervention.

Table 2 shows the clinical characteristics of patients treated in this study. Most patients with paragangliomas had arterial hypertension (six patients) and hearing impairment (also six patients). Five patients had tinnitus, and six patients had pulsations in the ears. Only three patients had ear pain. On MSCT examination, five patients had osteolysis.

Median number of tumor feeder branches was 1.5 from 1 to 3 (Table 2). Five tumors had one feeder branch, and five tumors had two or three feeder branches. In our patients we showed that the embolization had the extent of 100% devascularization of the paragangliomas in all patients.

Discussion

Paragangliomas are rare hypervascular neoplasms, whose surgical resection is at great risk for intraoperative bleeding. Therefore, preoperative reduction of perfusion of these tumors with embolization is very important for reducing the risk of bleeding, both for the patient and for the operation performed by a surgeon [9].

Our results show that preoperative embolization using small sized beads (100–300 μ) with superselective access to arterial feeders, results in almost complete tumor devascularization by 100% patients.

The results of our study in 10 patients showed that devascularization eliminated the need for intraoperative blood transfusion. An exception was one patient who required significant blood transfusion during the surgery (1,130 mL) due to the hemorrhage from carotid sinus.

Surgical resection of paragangliomas can be complicated due to massive bleeding because of their high vascularity [10]. With the evolution of preoperative planning, surgical techniques, and diagnostic evaluations, the risk of artery injury is minimal [11]. The risk of injury to the carotid artery following the treatment of carotid body tumors is size specific: tumors larger than 5 cm are likely to require carotid reconstruction. Unlike jugulotympanic paragangliomas and carotid body tumors, vagal paragangliomas are not closely associated with the carotid artery, although the internal carotid artery may be involved in its petrous portion in advanced disease. Rarely an injury may occur, even with adequate surgical exposure and microsurgical tech-

Table 2

Clinical symptoms and signs of patients with paragangliomas

Clinical symptom/sign	Patients									
	1	2	3	4	5	6	7	8	9	10
Arterial hypertension	yes	yes	yes	no	no	yes	yes	yes	no	no
Heart arrhythmia	no	no	yes	no	no	yes	no	no	no	no
Hearing impaired	yes	no	no	yes	yes	no	yes	yes	no	yes
Types of hearing loss	conductive	-	-	conductive	mixed	-	sensorineural	sensorineural	-	mixed
Tinnitus	yes	no	no	yes	yes	no	no	yes	no	yes
Pulsation in the ears	yes	no	no	yes	yes	no	yes	yes	no	yes
Bleeding from ear	yes	no	no	no	yes	no	no	yes	no	no
Ear pain	no	no	no	no	no	no	no	yes	yes	yes
Visualization of tympanic membrane	no	no	no	no	yes	no	yes	no	no	no
Color of tympanic membrane	-	-	-	bluish	-	-	-	bluish	-	-
Dizziness	no	no	no	no	no	no	no	no	no	yes
Vomiting	no	no	no	no	no	no	no	no	no	yes
Nistagmus	no	no	no	no	no	no	no	no	no	no
Osteolysis	no	no	no	yes	yes	no	yes	yes	no	yes
Number of feeder branches	1	1	2	1	3	1	2	1	2	3

nique. If the patient is at high risk for a vessel injury within the petrous carotid portion and balloon occlusion testing has been safely and satisfactorily performed, then the surgeon may consider permanent preoperative occlusion of the carotid distal to the tumor.

Preoperative embolization of paragangliomas is a very safe adjuvant therapy before surgical resection [1]. Bead embolization dramatically reduced tumor vascularity. The classic angiographic appearance of a paraganglioma is that of a hypervascular mass with robust feeding arteries and intense tumor blush [12]. Successful embolization hinges upon occlusion of all feeding vessels, based upon DSA [13]. A delay of 1–2 days between embolization and total surgical resection allows time for local edema or inflammation to resolve with minimal time for revascularization or recruitment of feeding arteries [13, 14]. The effectiveness of embolization hinges upon occlusion of the feeding tumoral vessels of paragangliomas. The catheterization technique should be superselective, aiming only for feeding vessel of the paraganglioma [1].

Other studies show reduction of 60% to 68% intraoperative blood loss in patients who underwent preoperative embolization when compared with those who did not [15, 16]. In the study by White et al. [13], it was shown that post-embolization angiography revealed an average decrease in blood flow to tumor of 75%. An 80–90% reduction in tumor vascularity is often obtained [4, 13]. The intraoperative blood loss for each tumor type was 289 mL for carotid body, 243 mL for *glomus vagale*, and 1,018 mL for *glomus jugulare*. Larouere et al. [5] showed that the average blood loss for the embolized patients was 650 mL (range from 500–1,000 mL). In the non-embolized patients, the average blood loss was 1,375 mL (range from 1,200–1,725 mL).

Jackson et al. [17] suggested that preoperative embolization in the patients with paragangliomas leads to a decrease in intraoperative blood loss and operative time. The mean estimated blood loss among the patients with embolization was 0.52 standard deviations lower (0.77 to 0.28 lower) than that of patients without embolization.

Therapy for paragangliomas is total surgical resection, but because of its rich vascularization and high risk of hemorrhage, preoperative embolization is beneficial for reducing blood loss in the surgical field [4, 5]. On the other hand, for small localized *glomus tympanicum* tumors, transcanal endoscopic ear surgery is a favorable surgical method [18]. These tumors present high bleeding risk during resection [18]. Embolization can be curative with surgical resection, palliative or supportive, but the main reason for this procedure is to detect and obliterate the abnormal vascular structures of the tumor. This way it is possible to decrease the vascularity and volume of the tumor, and make it safer for the surgery [4].

Limitations of the study

Unlike other reported studies, there is no control group of non-embolized tumors to compare embolization efficacy as manifested by operative blood loss. We also had a small number of these patients.

Conclusion

Adequate preoperative selective embolization of paragangliomas is essential in the preoperative preparation of these patients, because this strategy is feasible with low complication rates.

R E F E R E N C E S

1. *Devuyst L, Defreyne L, Praet M, Geukens S, Dhooge I.* Treatment of glomus tympanicum tumors by preoperative embolization and total surgical resection. Am J Otolaryngol 2016; 37(6): 544–51.
2. *Blackburn W, Leung G, Morash C.* Brain Tumour Foundation Award 2007. Glomus jugulare tumours: are they really so benign? Can J Neurosci Nurs . 2007; 29(2): 21–8.
3. *Kocur D, Ślusarczyk W, Przybyłko N, Hofman M, Jamróz T, Suszyński K,* et al. Endovascular Approach to Glomus Jugulare Tumors. Pol J Radiol 2017; 82: 322–6.
4. *Tasar M, Yetiser S.* Glomus tumors: therapeutic role of selective embolization. J Craniofac Surg 2004; 15(3): 497–505.
5. *Larouere MJ, Zappia JJ, Wilner HI, Graham MD, Lundy LB.* Selective embolization of glomus jugulare tumors. Skull Base Surg 1994; 4(1): 21–5.
6. *Persky M, Tran T.* Acquired Vascular Tumors of the Head and Neck. Otolaryngol Clin North Am 2018; 51(1): 255–74.
7. *Wax MK, Briant TD.* Carotid body tumors: a review. J Otolaryngol 1992; 21(4): 277–85.
8. *Gardner P, Dalsing M, Weisberger E, Sawchuk A, Miyamoto R.* Carotid body tumors, inheritance, and a high incidence of associated cervical paragangliomas. Am J Surg 1996; 172(2): 196–9.
9. *Moscote-Salazar LR, Dolachee AA, Narvaez-Rojas A, Al-Saadi HA, Najim AA, Khudhair jassam A*, et al. Preoperative embolization of skull–base tumors: Indications, utility, and concerns. J Acute Dis 2019; 8(3): 89–94.
10. *Tokgöz SA, Saylam G, Bayır Ö, Keseroğlu K, Toptaş G, Çadallı Tatar E, et al.* Glomus tumors of the head and neck: thirteen years' institutional experience and management. Acta Otolaryngol 2019; 139(10): 930–3.
11. *Hu K, Persky MS.* Treatment of Head and Neck Paragangliomas. Cancer Control 2016; 23(3): 228–41.
12. *Wasserman PG, Savargaonkar P.* Paragangliomas: classification, pathology, and differential diagnosis. Otolaryngol Clin North Am 2001; 34(5): 845–62, v–vi.
13. *White JB, Link MJ, Cloft HJ.* Endovascular embolization of paragangliomas: A safe adjuvant to treatment. J Vasc Interv Neurol 2008; 1(2): 37–41.
14. *Persky MS, Setton A, Niimi Y, Hartman J, Frank D, Berenstein A.* Combined endovascular and surgical treatment of head and neck paragangliomas - a team approach. Head Neck 2002; 24(5): 423–31.
15. *Antonelli AR, Cappiello J, Di Lorenzo D, Donajo CA, Nicolai P, Orlandini A.* Diagnosis, staging, and treatment of juvenile nasopharyngeal angiofibroma (JNA). Laryngoscope. 1987; 97(11):1319-25.
16. *Pryor SG, Moore EJ, Kasperbauer JL.* Endoscopic versus traditional approaches for excision of juvenile nasopharyngeal angiofibroma. Laryngoscope 2005; 115(7): 1201–7.

17. *Jackson RS, Myhill JA, Padhya TA, McCaffrey JC, McCaffrey TV, Mhaskar RS*. The Effects of Preoperative Embolization on Carotid Body Paraganglioma Surgery: A Systematic Review and Meta-analysis. Otolaryngol Head Neck Surg 2015; 153(6): 943–50.
18. *Ohki M, Kikuchi S*. A Small Glomus Tympanicum Tumor Resected by Minimally Invasive Transcanal Endoscopic Approach. Case Rep Otolaryngol 2019; 2019: 5780161.
19. *Mourad M, Saman M, Stroman D, Brown R, Ducic Y*. Evaluating the role of embolization and carotid artery sacrifice and reconstruction in the management of carotid body tumors. Laryngoscope 2016; 126(10): 2282–7.

Received on August 9, 2019
Revised on October 11, 2019
Accepted on October 24, 2019
Online First October, 2019