



Original Article

Microsurgical treatment of carotid body tumors using periadventitial dissection: Analysis of outcomes and prognostic factors in a neurological referral center

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ABSTRACT

Background: Surgical resection for carotid body tumors (CBTs) is the gold standard of treatment and continues to be a challenging procedure, commonly associated with high vascular injury rates and neurological complications.

Methods: It is a retrospective case series study between January 2002 and November 2020, with a mean follow-up of 29 months in a single nationwide referral center. Thirty-one patients diagnosed with a carotid body tumor and treated with microsurgical periadventitial resection were included in the study. Patients' demographics, comorbidities, clinical, radiological factors, and tumor grade, evaluated by the Shamblin scale, were obtained. Statistical analysis was performed on all collected data.

Results: In this study, we included 31 patients (32 tumors), 80% of the patients were female, and 20% were male, with a mean age of 53 years. One patient presented with bilateral lesions, while 17 tumors were located on the left side. The most frequent symptom was a painless, slow-growing neck mass in 74% of patients. Using the Shamblin classification, 13% of tumors were Grade I, 53% Grade II, and 34% Grade III. In the postoperative period, 3% of patients presented with permanent cranial nerve deficit, while none had vascular injuries or postoperative stroke. A tumor >5 cm increased the risk for nerve lesion by 11 times (OR 12.6, CI 95% 7.4-11.4, $P < 0.001$).

Conclusion: Preoperative embolization followed by periadventitial resection by means of a microsurgical technique is a safe and effective approach to remove CBT, with 3% cranial nerve injury rate and no need for vascular sacrifice or reconstruction.

Keywords: Carotid body tumor, Microsurgical treatment, Paraganglioma, Periadventitial dissection, Shamblin grade

INTRODUCTION

Carotid body tumors (CBTs) are included in the classification of paragangliomas. These tumors are rare, with an estimated incidence of 1:30,000–100,000 and only 3% appearing in the head and neck.^[8,11,15,42,44,50] Between 6% and 10% meet malignancy criteria, presenting with

regional lymph node spread or distant metastasis.^[10,16,42,50] Three types have been described: familial, sporadic, and hyperplastic, with the familial type accounting for 10% and presenting a higher likelihood of malignancy.^[9,18,35,38,44,48,51] Surgical resection is the treatment of choice for CBTs, with safe total resection being the overall goal. The highly vascularized nature of the tumor makes its treatment challenging and accounts for significant morbidity and mortality.^[13,34,41] Prompt surgical excision has been advocated to minimize the risk of complications and malignant transformation.^[13,27,37] Severe vascular and neurological complications are associated with surgery for CBTs,^[1] while preoperative embolization has been reported to reduce blood loss, surgical time, and perioperative complications.^[1,3,23,29,33,40,43,49] The optimal approach for lesions with high grades of invasion remains controversial, with most of the reported series showing a high rate of vascular injury, carotid sacrifice, and cranial nerve lesions.^[5,7,24,26,31,46,47,53]

The aim of this study is to review a single-institution experience in the surgical management of CBTs and evaluate the outcomes and complications using a periadventitial microsurgical technique preceded by preoperative embolization.

MATERIALS AND METHODS

Study design

A single-center and retrospective case series of patients with CBTs treated with the periadventitial microsurgical technique by the senior surgeon (EN) between January 2002 and November 2020 was performed. Preoperative, intraoperative, and postoperative data were collected from charts and analyzed for each patient. Tumors were classified according to the criteria established by Shamblin *et al.*^[47] Class I: small tumors and easily dissected away from the vessels; Class II: tumor partially surrounds the vessels; and Class III: tumors are large and encase the carotid vessels.^[47]

Before the surgery, in all case, a detailed digital subtraction angiography (DSA) was performed through the femoral artery. Then, a computed tomography (CT) angiogram, magnetic resonance imaging (MRI), or magnetic resonance angiography were obtained. Tumor volume was estimated on the preoperative MRI by the following formula: $\frac{4}{3} \pi \cdot (abc)$ with a, b, and c being the tumor diameters in each of the three dimensions. According to postoperative imaging studies (CT scan and MRI), the resection degree was classified as complete or incomplete. Surgical bleeding was estimated by the anesthesiologist based on the count of gauze pads and containers and reported in each of the patient's charts. Finally, recurrence was defined as tumor growth in any of

its dimensions during follow-up and until the patient's last recorded visit.

Statistical analysis

Descriptive analysis of data was made using mean, median, percentages, and maximum and minimum values. Continuous variables were represented by mean and standard deviation with range values, except in cases otherwise specified. Correlation analysis between variables was obtained employing calculating the Spearman coefficient for non-Gaussian distributed variables. Linear regression and a penalized likelihood method were used to calculate a multivariable logistic regression model to assess for predictors of surgical outcome, nerve injury, and severe blood loss. Data were analyzed and processed with SPSS version 21 from IBM, Stata 2021 (Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC), and Microsoft Excel. Statistical significance was taken as $P < 0.05$. In linear and logistic regression models, significance was taken with $P < 0.05$ and when confidence intervals did not include 1.

Microsurgical technique

Patients are positioned in dorsal decubitus with a rolled sheet underneath the shoulders, with the head resting on a horseshoe head holder with the neck hyperextended and the head rotated 20° toward the contralateral side of the lesion. Asepsis of the chin, mastoid, and cervical region is performed on the lesion side, and the placement of sterile dressing is performed as usual. An incision is made on the anterior edge



Video 1: Microsurgical RESECTION OF CAROTID BODY TUMORS Video explanation: This video shows the microsurgical technique described in the article, including three representative cases according to the Shamblin classification (Shamblin I, II, and III), each with pre- and post-operative images.

of the sternocleidomastoid muscle, from the mandibular angle to the upper edge of the thyroid cartilage; the superficial fascia and the first layer of the deep fascia are opened to continue mobilizing the sternocleidomastoid muscle laterally approaching the carotid triangle (digastric muscle at the base of the triangle, the sternocleidomastoid laterally, and the omohyoid muscle medially). The sheath is incised to dissect the common carotid from the internal jugular, the vagus, hypoglossal, and superficial laryngeal nerve (when visible), up to the level of the carotid bifurcation, where the tumor is identified in its whole extension. Vessel loops are placed on the common carotid to achieve proximal control if necessary. Under magnification with a surgical microscope (*OPMI PENTERO 900 Carl Zeiss AG, Oberkochen, Germany*), the tumor is dissected from the adventitia by recognizing a white line between them. This is the most important step when treating tumors Shamblin II or III because the carotid is not easily visible and can be damaged. To get this initial dissection, we use a combination of blunt dissection, low-power bipolar coagulation, and micro-scissor cut, preserving the nerves until the lesion is progressively isolated from the external and internal carotid sides. In all Shamblin III tumors, we use intraoperative Doppler assistance in this step to identify the carotid wall. Once the carotid arteries are separated from the tumor, vascular loops are used to mobilize them when the tumor is being dissected. Next, the base of the tumor at the carotid bifurcation is approached in the same way, using the bipolar forceps in a mid-power energy range (12–15 units), avoiding heat damage to the artery wall. In this sense, the preoperative embolization and the surgical microscope are extremely helpful in maintaining the blood loss at a very low level. Finally, in most cases, a fibrous band present at the apical part of the tumor is cut to liberate the lesion completely. Following this, adequate hemostasis of the field is granted, and closure is performed in a multilayered fashion, facing the superficial fascia and subcutaneous tissue with 3–0 Vicryl with a continuous suture and the skin with 3–0 nylon subdermal stitch. Images of three representative cases are shown in Figures 1–3. It is relevant to mention that we mainly use lower cranial nerve monitoring in Shamblin III cases [Video 1].

RESULTS

A total of 31 patients involving 32 tumors (80% of women and 20% of men) with a confirmed diagnosis of CBT were included in the study. The mean age was 53 years (SD \pm 12 years, range 29–75). All patients were submitted to periadventitial microsurgical resection, as previously described in the surgical technique. Preexisting conditions were present in 42% of patients, including hypertension in 33%, diabetes mellitus type 2 in 9%, and previous vascular disease (stroke and aneurysm) in 9% of patients [Table 1].

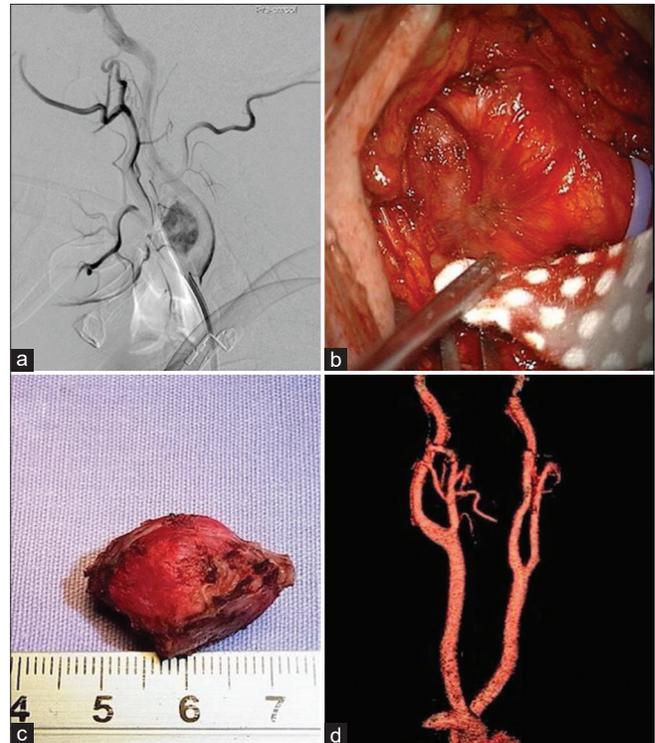


Figure 1: Case 1. Right side carotid body tumor (CBT), Shamblin I. (a) Preoperative DSA showing the vascularity of the tumor. (b) Surgical exposure of the carotid bifurcation. The tumor is visible between the external and internal carotid arteries. (c) Tumor after extraction from the surgical bed. (d) Postoperative computed tomography (CT) angio showing complete resection of the tumor.

All patients, except for one, had a primary resection of the CBT. One patient with a Shamblin Grade III tumor underwent two previous partial resections at an outside institution before undergoing total microsurgical resection in our center.

Regarding location, 17 (53%) patients were left sided and one patient presented with bilateral tumors. About 97% of the patients resided at more than 1500 m above sea level (range 1560–2760 m above sea level). The most frequent symptom was the presence of a deep, painless, and slow-growing cervical mass on 23 (74%) patients, followed by vertigo (19%), headache (13%), dysphagia (10%), and others (18%, i.e., odynophagia, tinnitus, and visual disturbances). The mass effect caused by the tumor was associated with dysphagia in three patients. Two patients were asymptomatic, and the tumor was diagnosed by routine testing for nonrelated diseases.

For the diagnostic workout, a CT scan or a CT angiogram was performed on 25 (81%) patients, MRI and DSA were obtained for all patients. Regarding Shamblin grade, the most frequent was type II in 53% of the tumors followed

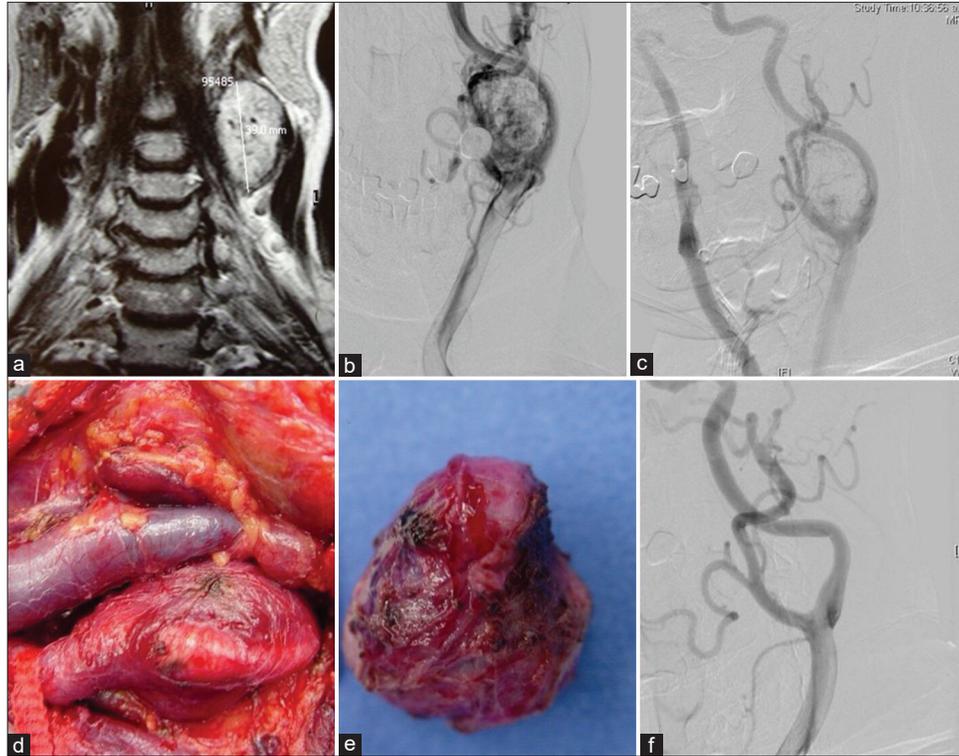


Figure 2: Case 2, Left side CBT, Shamblin II. (a) MRI coronal T2-weighted view. (b) Preoperative DSA showing the rich vascularity of the tumor. (c) After embolization with polyvinyl alcohol particles, there is an excellent reduction in vascularity. (d) Surgical exposure. The internal jugular vein is seen medial to the carotid artery. The tumor is adherent to the bifurcation and the initial portion of the external carotid artery. The internal carotid artery is not visible here. (e) Tumor after extraction from the surgical bed. A reddish color reveals its vascular nature. (f) Postoperative DSA showing no tumor.

by type III in 34% and type I in 13%. The mean maximal diameter of the tumor was 4 cm (SD \pm 1.52 cm, range 2–10 cm) with a mean volume of 25 ml (SD \pm 40 ml, range 1.26–232.48 ml). In 94% of the patients, preoperative embolization was performed, achieving an average of 80% of decrease in tumoral blood flow. All the patients had complete resection of the tumor, regardless of the Shamblin grade. Transient cranial nerve deficit was observed in 3 (10%) patients in the immediate postoperative period; two patients presented with glossopharyngeal and vagus nerve deficit as well as Horner's syndrome as a transitory lesion, and one patient presented hypoglossal nerve deficit. None of the patients required carotid sacrifice or vascular reconstruction, regardless of the extent of carotid invasion (Shamblin grade). No patient presented postoperative stroke or death. The average follow-up was 2.4 years (SD \pm 2.3 years, range 0.5–10 years), and at the end of follow-up, only 1 (3%) patient remained with a hypoglossal nerve deficit.

The correlation between Shamblin grade, the diameter of the tumor, tumoral volume, and surgical bleeding was analyzed. We found in the univariate linear regression model that the maximal diameter of the tumor was significantly correlated

with the Shamblin grade ($r = 0.61$, $P < 0.001$) and the amount of surgical bleeding ($r = 0.48$, $P = 0.005$). In contrast, surgical bleeding was not significantly correlated with Shamblin grade ($r = 0.29$, $P = 0.09$). Moreover, the univariable linear regression models showed a significant association between the maximal tumoral diameter and the amount of surgical bleeding ($r^2 = 0.56$, $P < 0.001$), and between tumoral volume and surgical bleeding ($r^2 = 0.76$, $P < 0.001$).

In addition, we found that every 1 ml of tumoral volume was associated with a 1% increase in risk for a cranial nerve injury (OR 1.02, 95% CI 1.001–1.03, $P = 0.046$). Notably, we found that tumors with a maximal diameter >5 cm increased the risk for cranial nerve injury by more than 13 times (OR 12.61, 95% CI 1.25–127.2, $P = 0.03$). We did not find significant associations between the risk for cranial nerve injury and the Shamblin grade of the tumor (OR 2.9, 95% CI 0.3–33, $P = 0.2$).

DISCUSSION

Paragangliomas are part of the neuroendocrine tumors that arise from the embryonic neural crest cells.^[29,33] They are the most common neuroendocrine tumors in the head and

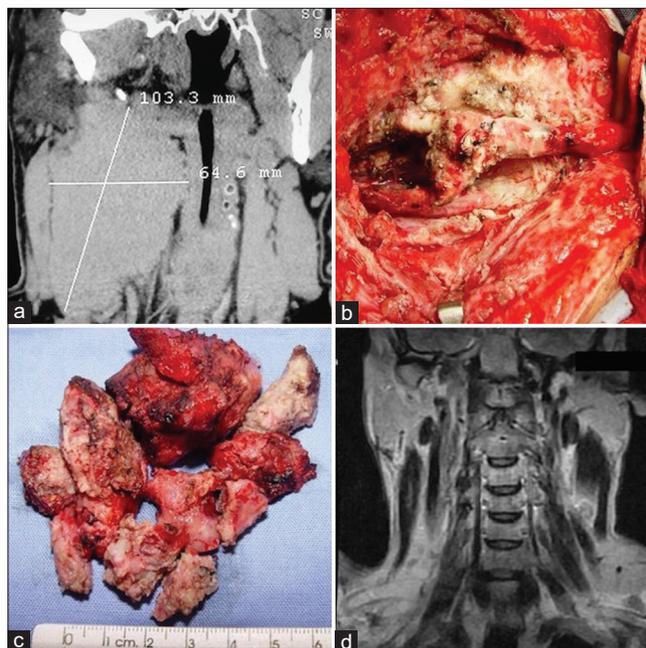


Figure 3: Case 3. Right side CBT, Shamblin III. A 32-year-old male patient had been operated on two different times. In both cases, surgery was stopped due to severe bleeding. (a) CT scan shows the maximum diameters of the lesion and the displacement of the trachea and esophagus. (b) Final view after the tumor was excised under the microscope. The carotid artery is intact after careful dissection. (c) The tumor was obtained in several pieces. No significant bleeding was present during surgery. (d) The control MRI 6 months after surgery shows no residual tumor.

neck,^[14,17,19,20,22,40,45] reported to be more frequent in women during the third to fourth decade of life.^[29,33,43] In our series, 25 of the 31 patients were women, and contrary to the cited literature, we observed that more than half of the patients presented in the fourth and fifth decade of life, with a mean of 53 years at the time of surgery. Sajid *et al.* observed that chronic hypoxia is associated with a higher incidence of hyperplastic CBTs.^[44] In alignment with this study, only four of our patients resided under 2000 m above the sea, with the remaining living over 2200 m above sea level.

As Arya *et al.* described, “incorporating volume in the classification to predict the Shamblin would have misled the attempt to predict the vascular outcome concerning the ICA.”^[3] In our study, we observed that regardless of the size of the lesion, an interval between the tumor and the ICA was present in all of our cases, showing no real invasion of the arterial wall, in accordance with the previous reports.^[34] Still, a higher Shamblin grade is indeed expected with more extensive tumors, as revealed by the significant correlation between tumor diameter and Shamblin grade in our patients.

The definitive treatment for CBTs is complete surgical removal with adequate preservation of the neurovascular

Table 1: Patient and tumor characteristics.

Variables	Patients (n=31)
Total tumors	32
Age, mean (SD), years	53 (12)
Sex, no. (%)	
Male	6 (20)
Female	25 (80)
Side, no. (%)	
Right	14 (43)
Left	17 (53)
Bilateral	1 (3)
Height of residence, mean (SD), meters above sea level	2285 (348)
Preoperative imaging, no. (%)	
Computed tomography	25 (76)
Magnetic resonance imaging	31 (100)
Digital subtraction angiography	31 (100)
Shamblin grade, no. (%)	
I	4 (13)
II	17 (53)
III	11 (34)
Diameter, mean (SD), cm	4 (1.5)
Tumor volume, mean (SD), ml	25.1 (41)
Preoperative embolization, no. (%)	31 (96)
Percentage of embolization, mean (SD)	80 (18)
Blood loss, mean (SD), ml	288 (437)
Surgical time, mean (SD), min	235 (76)
Complete resection, no. (%)	32 (100)
Transient cranial nerve injury, no. (%)	2 (6)
Permanent cranial nerve injury, no. (%)	1 (3)
IX, X cranial nerve injury, Horner syndrome, no. (%)	2 (6)
XII cranial nerve injury, no. (%)	1 (3)
Vascular sacrifice or reconstruction, no. (%)	0
Stroke or death, no. (%)	0
Follow-up, mean years (SD)	2.4 (2.2)

structures.^[26] Despite the advances in surgical techniques, perioperative complications, in the form of cranial nerve injury, vascular injury, or morbid intraoperative hemorrhage, remain considerable.^[53] The advocated surgical technique in this study is the sub-adventitial resection, dissecting through the avascular space between the tumor and the carotid vessels, described as a white line by Gordon-Taylor.^[7,18] It also includes a complete exposure of the carotid bifurcation, proximal and distal control of the carotid vessels, and preservation of the internal carotid artery.^[2,7] Having this knowledge as a foundation, the senior author developed the aforementioned microsurgical technique using a sub-adventitial plane for achieving complete resection, aiding in plane localization under microscopic magnification and meticulous microsurgical dissection (operating microscope, bipolar forceps, and micro-instruments), and opposing to several observations regarding the lack of a dissection plane.

Table 2: Reported series in the literature.

Series	Patient No.	Surgery, No.	Age, years	Embolized patients (%)	ECA ligation (%)	ICA ligation (%)	ICA reconstruction (%)	CN deficit (%)	Transient CN deficit (%)	Permanent CN injury (%)	Stroke (%)	Deaths (%)
Shamblin <i>et al.</i> , 1971 ^[47]	90	70	NS	NS	33	21	NS	55	NS	NS	22	6
Liapis <i>et al.</i> , 2000 ^[30]	18	16	19	NS	0	0	0	25	25	0	0	0
Aygerinos <i>et al.</i> , 2011 ^[4]	27	27	46	15	0	0	0	29	22	NS	NS	4
Künzel <i>et al.</i> , 2014 ^[28]	24	20	51	0	0	0	0	35	5	30	NS	NS
Hinojosa <i>et al.</i> , 2015 ^[21]	68	68	54	0	0	19	NS	25	25	NS	4	NS
Nora <i>et al.</i> , 1988 ^[37]	139	139	52	1	33	NS	25	40	21	19	14	3
Davila <i>et al.</i> , 2016 ^[15]	183	183	49	NS	8	0	11	9	3	6	2	0
Kim <i>et al.</i> , 2017 ^[25]	356	356	51	21	NS	NS	NS	24	9	15	2	0
Mourad <i>et al.</i> , 2016 ^[36]	96	96	49	52	9	0	14	12	6	6	0	0
Cobb <i>et al.</i> , 2017 ^[12]	547	547	55	14	NS	NS	NS	0	NS	NS	2	1
This series	31	32	53	94	0	0	0	9	6	3	0	0

ECA: External carotid artery, ICA: Internal carotid artery, CN: Cranial nerve, NS: Not specified

Shamblin *et al.*, in 1971, suggested a surgical classification into three groups. This classification was based on the tumor relationship with the vessel, the intraoperative findings, and postoperative specimen examination, as mentioned above. Shamblin's classification was used for preoperative risk stratification. According to this classification, the bigger the tumor, the greater the risk of vascular and cranial nerve injury. In their study, more than 5 cm tumor held mortality between 1 and 3% after surgical intervention.^[47] Our study found that tumors >5 cm increased the risk for cranial nerve injury by more than 11 times. Nevertheless, we did not find a significant association between cranial nerve injury and Shamblin grade. Lim *et al.* compared Shamblin I and II with Shamblin III tumors and found increased operative time, blood loss, and cranial nerve injury in patients with Shamblin III lesions.^[31] As opposed to this study, we did not observe a relationship between blood loss and Shamblin grade, possibly due to the fact that most patients had preoperative embolization. However, maximal tumor diameter and volume were both significantly correlated with higher operative bleeding in our cohort. Surgical morbidity has been associated with intraoperative bleeding, cranial nerve injury, and stroke.^[5,24] In our series, the mean bleeding was 287 ml, and the percentage of immediate postoperative cranial nerve deficit was 9%, with only one patient presenting permanent nerve injury. Despite the

high reported rates of stroke and death in the literature, in our cohort, no strokes or deaths were associated with CBT resection. In addition, the operative time and blood loss in this study are lower than most of the results reported in the literature.^[5,24]

Schick *et al.* first introduced the concept of preoperative embolization for CBT resection in 1980.^[46] Preoperative embolization aims to decrease the tumor volume, blood loss, and operative time.^[39,52] Abu Ghanem's meta-analysis and Litle consecutive series found no difference between surgically treated patients with preoperative embolization and nonembolized patients.^[1,32] In addition, although Bercin reported the impact of embolization on seven patients compared with five surgically treated patients, the authors found no difference in blood loss between groups, although the size of the sample hinders the statistical power of the findings.^[6] Kasper *et al.* found no difference in bleeding between embolized and nonembolized patients. Still, there were significant differences between groups accounting for a bigger size and higher Shamblin grade in the embolized group.^[24] Power *et al.* concluded that large carotid body paragangliomas could safely be resected with or without preoperative embolization, but preoperative embolization may simplify the surgical excision and reduce blood loss.^[41] In contrast, Jackson *et al.* published a systematic review and meta-analysis, which suggests

that preoperative embolization decreased intraoperative blood loss and operative time.^[23] In our series, 29 (94%) of the patients had embolization of at least 80% of the tumoral blood supply, possibly explaining our low average bleeding. Embolization was performed in Shambling II and III tumors using polyvinyl alcohol particles that provide inexpensive, transitory occlusion of tumor blood vessels. Nevertheless, it is essential to remember that embolization is not innocuous since it may be associated with the migration of the embolizing material into the intracranial circulation, bleeding, and vascular injury at the puncture site.^[4,30] Thus, it should be performed by experienced endovascular therapists.

Regarding vascular reconstruction and sacrifice, the sub-adventitial resection aided with the intraoperative Doppler in our cohort allowed us to find a clear interval between the tumor and the carotid artery, avoiding the need for ligating or sacrificing any vessel, even in tumors classified as highly invasive (Shamblin III). Up to the time of publication, we have found three reported series in which no carotid ligation or vascular sacrifice was made,^[4,28,30] although most of the reported patients involve low invasive (Shamblin I or 2) tumors [Table 2].^[12,15,21,25,36,37,47]

Special mention should be made to introducing a microsurgical technique for resection (operating microscope, bipolar forceps, and microinstruments). The present article is the first reported series using this modality consistently, and according to our results, this technique should be encouraged.

Limitations

The study's retrospective nature and the small number of patients represent a limitation. Nevertheless, the senior author's experience with an infrequent disease in a large reference center with a high number of carotid artery surgeries confers weight on the collected data.

CONCLUSION

CBTs are rare and often benign tumors presenting as a slow-growing pulsatile cervical mass. They require early diagnosis and multidisciplinary treatment. Imaging studies such as Doppler, MRI, CT, and angiography are essential for an accurate diagnosis. Despite its risks, surgery is the treatment of choice. In our concept, two essential elements introduced in this series have proven to be valuable in decreasing the morbidity and mortality related to this surgery: (1) systematic preoperative embolization confers a significant reduction in blood loss and (2) periadventitial dissection based on a microsurgical technique and delicate management of the vessels and nerves: usage of bipolar coagulation instead of monopolar electrocautery allows a complete resection with

no need to perform carotid ligation or reconstruction and reduces the risk of damage to adjacent neural structures.

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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