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New predictors of complications in carotid body tumor resection

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ABSTRACT

Objective: This study examined the relationship between two new variables, tumor distance to base of skull (DTBOS) and tumor volume, with complications of carotid body tumor (CBT) resection, including bleeding and cranial nerve injury.

Methods: Patients who underwent CBT resection between 2004 and 2014 were studied using a standardized, multi-institutional database. Demographic, perioperative, and outcomes data were collected. CBT measurements were determined from computed tomography, magnetic resonance imaging, and ultrasound examination.

Results: There were 356 CBTs resected in 332 patients (mean age, 51 years; 72% female); 32% were classified as Shamblin I, 43% as Shamblin II, and 23% as Shamblin III. The mean DTBOS was 3.3 cm (standard deviation [SD], 2.1; range, 0-10), and the mean tumor volume was 209.7 cm^3 (SD, 266.7; range, 1.1-1642.0 cm^3). The mean estimated blood loss (EBL) was 257 mL (SD, 426; range, 0-3500 mL). Twenty-four percent of patients had cranial nerve injuries. The most common cranial nerves injured were the hypoglossal (10%), vagus (11%), and superior laryngeal (5%) nerves. Both Shamblin grade and DTBOS were statistically significantly correlated with EBL of surgery and cranial nerve injuries, whereas tumor volume was statistically significantly correlated with EBL. The logistic model for predicting blood loss and cranial nerve injury with all three variables—Shamblin, DTBOS, and volume ($R^2 = 0.171$, 0.221, respectively)—was superior to a model with Shamblin alone ($R^2 = 0.043$, 0.091, respectively). After adjusting for Shamblin grade and volume, every 1-cm decrease in DTBOS was associated with 1.8 times increase in risk of >250 mL of blood loss (95% confidence interval, 1.25-2.55) and 1.5 times increased risk of cranial nerve injury (95% confidence interval, 1.19-1.92).

Conclusions: This large study of CBTs demonstrates the value of preoperatively determining tumor dimensions and how far the tumor is located from the base of the skull. DTBOS and tumor volume, when used in combination with the Shamblin grade, better predict bleeding and cranial nerve injury risk. Furthermore, surgical resection before expansion toward the base of the skull reduces complications as every 1-cm decrease in the distance to the skull base results in 1.8 times increase in >250 mL of blood loss and 1.5 times increased risk of cranial nerve injury. (J Vasc Surg 2017;65:1673-9.)

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Carotid body tumors (CBTs) are rare and usually benign neuroendocrine neoplasms that have a predictable but slow growth rate and the potential for malignant transformation. Surgical resection has been the primary treatment of CBTs, before they become painful and involve cranial nerves, as previous studies have found little utility in primary radiotherapy, chemotherapy, or embolization for definitive therapy.[1] Although surgical resection is the recommended treatment modality, it is associated with significant risk, with up to 30% to 40% morbidity and mortality.[2] Currently, the Shamblin classification system, which is based on the degree of encasement of the adjacent carotid arteries, is used to assess a patient's risk of intraoperative bleeding, cranial nerve injury, and potential need for carotid artery resection and revascularization.[3]

A pilot study of 80 CBTs during a 20-year period at the University of California, Los Angeles (UCLA) revealed that specific tumor characteristics, such as tumor volume and the distance of the tumor from the base of skull, were correlated with increased intraoperative bleeding and cranial nerve injuries. We conducted this multi-institutional study to determine if the addition of these two new variables, distance to base of skull (DTBOS) and total tumor volume, could be used independently or in conjunction with Shamblin grade to better predict risk of bleeding and cranial nerve injury.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective multicenter analysis of the Vascular Low-Frequency Disease Consortium database
- **Take Home Message:** Decreased tumor distance from skull base as well as increased tumor volume and Shamblin grade were associated with cranial nerve injury and blood loss in 356 patients undergoing carotid body tumor resection.
- **Recommendation:** The authors suggest considering tumor volume and distance from skull base along with Shamblin grade to determine risk of complications after carotid body tumor resection.

METHODS

All patients who underwent CBT resection in the years between 2004 and 2014 at 16 institutions were included in the study. Patients were identified using pre-existing investigator databases as well as the following procedural and diagnosis codes: *Current Procedural Terminology* (American Medical Association, Chicago, Ill) codes 60600 and 60605 (excision of CBT) and 21552, 21554, 21555, and 21556 (excision of soft tissue of neck or anterior thorax); and *International Classification of Diseases, Ninth Revision* codes C75.4 (malignant neoplasm of carotid body), C75.5 (malignant neoplasm of aortic body and other paraganglia), D18.09 (hemangioma of other sites), D44.6 (neoplasm of carotid body), D44.7 (neoplasm of aortic body and other paraganglia), Q85.03 (schwannomatosis), and 194.5 (CBT). All cases identified by these search methods at each institution but did not have CBT diagnosis on the anatomic pathology report were subsequently excluded.

Each patient's medical records were reviewed for demographic, preoperative, operative, and postoperative information and complications. Primary study end points included estimated blood loss (EBL) and cranial nerve injury during surgical treatment of CBTs, reported by the surgeon or found on follow-up clinical notes within 30 days of surgery. Numerical "0" was used to represent EBL for patients with "minimal" blood loss documented in their operative reports. CBT dimensions were measured from preoperative computed tomography (CT) scan, magnetic resonance imaging (MRI), or ultrasound imaging. Tumor volume was calculated with ellipsoid volume estimation: $V = 4/3\,\pi\,abc$, where a, b, and c represent the three axis diameters (Fig). For this study, we assumed that b equals c because many of the patient charts contained only two-dimensional measurements of the tumor. DTBOS (the distance from the most superior aspect of the CBT to the bone prominence at the base of the skull) was measured using CT or MRI. Patients who had only ultrasound imaging could not have DTBOS measured.

Vascular Low-Frequency Disease Consortium database management. The Vascular Low-Frequency Disease Consortium is a multi-institutional collaboration that aims to improve clinical care of patients with rare or less frequent vascular diseases. Each participating institution had a principal investigator who was responsible for obtaining Investigational Review Board approval at their respective institutions. The protocol was approved by each participating institution's Institutional Review Board, and informed consent of the patient was waived because of the retrospective nature of the study.

Information identifying the patients was maintained and managed for data verification purposes at each institution, and then deidentified data were transferred to a central database. The Vascular Low-Frequency Disease Consortium server was located in the Vascular and Endovascular Surgery Division at UCLA. All patient data in the server were coded with randomly generated patient numbers.

The lead investigators at UCLA examined the data submitted from each institution for completeness and accuracy, and all incomplete or inconsistent data were verified with the principal investigator at the identified institution. The principal investigator from each institution was responsible for the validity and completeness of the data submitted to the study database. All study investigators collaboratively determined data points, collected data, interpreted data, and wrote and edited abstracts and manuscripts.

Statistics. Data were collected using Microsoft Excel (Microsoft, Redmond, Wash) and analyzed with SAS 9.4

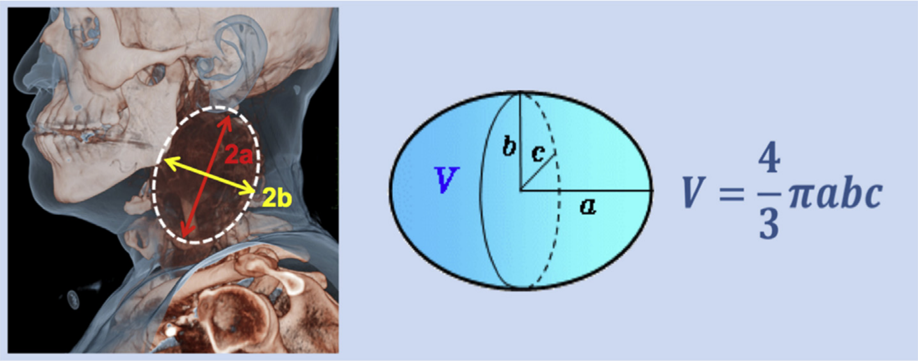

Fig. Ellipsoid approximation for volume calculation.

software (SAS Institute, Cary, NC). Continuous variables were represented as mean ± standard deviation (SD) with range values unless noted otherwise. Correlation statistics were calculated using Pearson correlation and logistic regression for continuous and binary dependent variables, respectively. Statistical significance was defined by $P < .05$. Comparison of models was done using the area under the curve statistic, McFadden R^2 values, with values closer to 1 representing the superior model. Odds ratios were calculated to quantify the risks for each 1-cm decrease in the DTBOS. Statistical significance was defined by 95% confidence intervals that do not include 1. Missing data were managed with multiple imputations and correlation with analysis of the subset of the data set with no missing data.

RESULTS

Demographics of the patients and tumor characteristics. A total of 16 institutions participated in this study, with 9 located in the United States and 7 internationally located in Brazil, Colombia, Germany, Greece, Hong Kong, Italy, and Mexico. During the 10-year study period, 356 patients (72.2% female) had resection of a CBT. The mean age of the patients was 51.2 years, ranging from 20 to 84 years. The majority of the population was identified as being of white/Caucasian ethnicity (38.8%), with the smallest ethnic group being black/African American (2.5%). (Table I)

The most common presenting symptom was asymptomatic neck mass (n = 267 [75%]); the next most common presentation was painful or pulsatile neck mass (n = 38 [7%]). A family history of CBTs was found in 23 patients (6.5%); approximately 7% (n = 24) of patients had bilateral resection of their CBTs at the same institution during the 10-year study period. Tumors were classified as Shamblin I (31.7%; n = 113), Shamblin II (43.3%; n = 154), and Shamblin III (23.0%; n = 82). All had at least one preoperative imaging method (CT, MRI, or ultrasound), and 70% had CT or MRI imaging, which was used to measure the tumor diameters and DTBOS; 52.5% (n = 187) had CT or computed tomography angiography, 16.3% (n = 58) had MRI or magnetic resonance angiography, and 24.4% (n = 86) had ultrasound imaging. The average tumor volume was 209.7 ± 266.7 cm^3 and ranged from 1.05 cm^3 to 1642.0 cm^3. The mean DTBOS was 3.3 cm (SD, 2.05; range, 0-10 cm). Analysis of the tumor characteristics by Shamblin grade revealed that tumor volume for each grade was significantly different ($P < .001$) but that the DTBOS was not ($P = .588$; Table II).

Twenty-two (6%) of the CBTs were confirmed by pathologic examination to be malignant; of these, seven were metastatic (2%). Some of these patients were tested for mutation of the gene encoding succinate dehydrogenase (SDH), usually when there was a family history of CBTs, the SDH mutation, or bilateral CBTs. Twenty-one (7%) patients had an SDH mutation.

The majority of CBT resections did not have any intraoperative cerebral or nerve monitoring (n = 225 [63%]), whereas 15 (14%) cases used nerve stimulation to assess for intraoperative cranial nerve injuries. Other intraoperative monitoring included cerebral perfusion (eg, brain mapping, transcranial Doppler ultrasound, and electroencephalography; n = 104 [29%]).

Outcomes. Twenty-one percent (n = 72) of the patients had preoperative embolization. There was no consistent indication identified for the embolization; the decision to perform preoperative embolization was usually based on the individual surgeon's preference. The average EBL for CBT excision was 257 mL (range, 0-3500 mL). Twenty-one patients (6%) received transfusions either intraoperatively or in the first 24 hours after the operation. These patients received an average of 2.2 units of packed red blood cells (SD, 1.3; range, 1-6). For the patients who required a transfusion, their mean EBL was 1310 ± 971 mL (range, 0-3500 mL). After surgery, 24% (n = 87) of patients were noted to have cranial nerve injury, and 1.5% (n = 5) were reported to have had a stroke.

Thirty-five (10%) of the patients had one or more cranial nerve injuries as a result of the CBT excision (Table III). Thirty-two (38%) had permanent injury, whereas 53 (62%) had temporary injuries. Analysis of these patients revealed that the vagus nerve (cranial nerve X) and the hypoglossal nerve (cranial nerve XII) were the most commonly injured, at 11% and 10%, respectively. One

Table I. Patient and tumor characteristics (N = 356)

Patient characteristics	Mean ± SD (range) or No. (%)
Age, years	51.2 ± 14.5 (range, 20-84)
Female	257 (72.2)
Ethnicity	
White/Caucasian	138 (38.8)
Black/African American	9 (2.53)
Asian/Pacific Islander	16 (4.49)
Hispanic/Latino	149 (41.9)
Unknown	44 (12.4)
Family history of CBTs	23 (6.46)
Tumor characteristics	
Preoperative imaging (n = 330)	
Ultrasound	86 (24.4)
CT or CTA	187 (52.5)
MRI or MRA	58 (16.3)
Shamblin grade (n = 349)	
I	113 (31.7)
II	154 (43.3)
III	82 (23.0)
DTBOS, cm (n = 162)	3.30 ± 2.05 (range, 0-10)
Maximal diameter, cm (n = 335)	3.68 ± 1.50 (range, 1-11.3)
Volume, cm^3 (n = 319)	209.7 ± 266.7 (range, 1.05-1642.0)
Operative details	
Preoperative embolization (n = 350)	72 (20.6)
Bilateral resection	24 (6.74)
EBL, mL (n = 343)	256.8 ± 426.2 (range, 0-3500)
Transfusion, pRBC units (n = 21)	2.24 ± 1.30 (range, 1-6)
Outcomes	
Cranial nerve injury	87 (24.4)
Stroke	5 (1.40)
Death	1 (0.281)

CBTs, Carotid body tumors; *CT,* computed tomography; *CTA,* computed tomography angiography; *DTBOS,* distance to the base of skull; *EBL,* estimated blood loss; *MRA,* magnetic resonance angiography; *MRI,* magnetic resonance imaging; *pRBC,* packed red blood cell; *SD,* standard deviation.

patient had documented injury of the marginal branch of the facial nerve. All other injuries to the branches of the facial nerve were reported as a facial nerve injury (n = 10 [3%]). The least common cranial nerve injuries occurred in the recurrent laryngeal and spinal accessory nerves, 0.8% and 1.1%, respectively. All other recurrent laryngeal nerve injuries were reported as vagus nerve injures. Table III lists the distribution of other cranial nerve injuries. Indirect laryngoscopy results were not required to provide evidence of nerve injury.

Approximately 50% of the patients (n = 167) experienced at least one complication, including aspiration, wound hematoma, wound infection, bypass occlusion, carotid artery injury, first bite syndrome, jaw claudication, dysphagia, dysphonia, EBL >250 mL, cranial nerve injury (both temporary and permanent), stroke, respiratory failure, and mortality. The mean length of hospital stay after surgery was 3.3 days (SD, 3.9; range, 0-31). One patient was discharged on the same day as surgery, whereas most (n = 226 [62%]) required a 1- or 2-day hospital stay. Three (0.8%) deaths were reported, one caused by oral cancer, another from myocardial infarction resulting in anoxic brain injury, and the third caused by a stroke. There were seven strokes, with approximately 2% occurring immediately postoperatively.

Comparing logistic models. Both Shamblin grade and DTBOS were correlated with bleeding and cranial nerve injuries; however, tumor volume correlated only with bleeding (Table IV). When these variables were analyzed with logistic models for "fit" with McFadden R^2 statistics, we found that models that included all three variables—Shamblin grade, DTBOS, and tumor volume—were more predictive of the outcomes of interest than the Shamblin grade alone. Logistic model analysis revealed that the R^2 values for the Shamblin grade alone in predicting EBL >250 mL and cranial nerve injury are 0.043 and 0.091, respectively. When the volume and DTBOS variables are added to the Shamblin grade, the R^2 values increase to 0.171 and 0.221 for bleeding risk and cranial nerve injury, respectively. The increased R^2 values demonstrate that volume and DTBOS of the CBT, when added to the Shamblin grade, improve the predictive power of bleeding and cranial nerve injury risk (Table V).

Bleeding risk. We further quantified risk by calculating odds ratios for bleeding and cranial nerve injury for each 1-cm decrease in DTBOS. When the DTBOS was 1 cm closer to the base of the skull, there was a 179% increase in risk of bleeding more than the average EBL (>250 mL). Furthermore, the risk of requiring transfusion increased by 136% for every 1-cm decrease in distance the CBT is located from the base of the skull (Table VI).

Cranial nerve injury risk. Analysis based on DTBOS revealed that risk of at least one cranial nerve injury increases by 151% for every 1-cm decrease in DTBOS. The risk for the two most common cranial nerve injuries (ie, vagus and hypoglossal nerves) more than doubles when the CBT is located 1 cm closer to the base of the skull; specifically, there is a 174% increase in risk of hypoglossal nerve injury and a 253% increase in risk of vagus nerve injury. Furthermore, the risk of injury to multiple cranial nerves increases by 266% for each 1-cm decrease in DTBOS (Table VI).

DISCUSSION

Cranial nerve injury is the most common complication of CBT excision.[4,5] Trends in morbidity associated with CBT resection have improved over the years with

Table II. Tumor characteristics by Shamblin grade

Tumor characteristics	Shamblin I, mean ± SD (range)	Shamblin II, mean ± SD (range)	Shamblin III, mean ± SD (range)	*P* value
DTBOS, cm	3.43 ± 1.75 (0-10)	3.60 ± 2.10 (0-10)	2.78 ± 2.16 (0-9)	.588
Maximal diameter, cm	2.67 ± 1.00 (1-8)	3.85 ± 1.40 (1.25-11.3)	4.71 ± 1.41 (1.4-8)	<.001
Volume, cm^3	63.7 ± 110.3 (1.05-874.6)	207.9 ± 244.2 (13.3-1437.3)	326.7 ± 346.3 (8.44-1642.0)	<.001

DTBOS, Distance to the base of skull; *SD,* standard deviation.

Table III. Cranial nerve (*CN*) injuries

Injured CNs (N = 85)	No. (%)	Temporary, No. (%)	Permanent, No. (%)
CN VII (facial nerve)	10 (2.80)	10 (100)	0 (0)
CN IX (glossopharyngeal nerve)	12 (3.37)	10 (83.3)	2 (16.7)
CN X (vagus nerve)	39 (11.0)	17 (43.6)	21 (53.8)
Superior laryngeal nerve	19 (5.34)	11 (5.26)	8 (42.1)
Recurrent laryngeal nerve	3 (0.842)	1 (33.3)	2 (66.7)
CN XI (accessory nerve)	4 (1.12)	4 (100)	0 (0)
CN XII (hypoglossal nerve)	35 (9.83)	24 (68.6)	11 (31.4)
Sympathetic ganglion	10 (2.80)	6 (60.0)	3 (30.0)
Any CN injury (at least 1 injury)	87 (24.4)	—	—
Multiple CN injuries (>1 injury)	35 (9.83)	—	—

Table IV. Correlation between tumor characteristics and outcomes variables

Outcomes	Shamblin grade	DTBOS	Volume
	Pearson (P)	*Pearson (P)*	*Pearson (P)*
EBL, mL	0.243 (<.001)	−0.292 (<.001)	0.262 (<.001)
	Regression P	*Regression P*	*Regression P*
Cranial nerve injury	<.001	.004	.120

DTBOS, Distance to the base of skull; *EBL,* estimated blood loss; *P, P* value; *Pearson,* Pearson correlation coefficient; *regression,* logistic regression.

advances in techniques; however, there have been no reported improvements in cranial nerve injuries.[6] Many studies report that patients often experience changes in their voice, difficulty with tongue movement and speech articulation, and difficulty in swallowing; these deficits are associated with injuries to the superior laryngeal, hypoglossal, and vagus nerves, respectively. Intraoperative bleeding is another important complication associated with CBT resection because inadequate control of bleeding can have serious consequences, including adjacent nerve injury and carotid artery injury as well as stroke.[2] Although previous studies have documented some of these complications,[3,7,8] there is a lack of preoperative information that can help quantify an individual's risk for cranial nerve injury and bleeding.

Our series of CBTs, the largest to date, demonstrates that we can help quantify the risks of bleeding and cranial nerve injury by considering two parameters of the tumor: overall tumor volume and DTBOS. Knowing the true risks of these two important complications can greatly benefit preoperative education of the patient. Armed with the risk quantification derived from a contemporary population of patients, surgeons can better inform their patients about the risks as well as making the appropriate preparations for surgery. Furthermore, higher risk CBTs, because of size and location, may lead to surgeons' collaborating with other specialties, such as neurosurgery and otolaryngology. When patients have tumor characteristics that are more likely to be associated with cranial nerve injuries, the surgeon may also choose to use nerve stimulation to prevent and to detect injuries to cranial nerves. Alternatively, if a CBT is likely to have increased bleeding, more units of blood may be ordered before surgery or a cell-saving technique may be used. Anticipating risks based on tumor characteristics will encourage surgeons to prepare better for all possible outcomes.

The Shamblin classification[1] has been widely used by surgeons to predict the need for arterial reconstruction, and many studies have demonstrated that higher Shamblin grades are associated with higher incidence of complications[9]; however, additional tumor characteristics

Table V. Comparison of logistic models

Outcome 1: Bleeding	McFadden R^2
Model 1a: EBL >250 mL = Shamblin	0.043
Model 1b: EBL >250 mL = Shamblin, DTBOS	0.151
Model 1c: EBL >250 mL = Shamblin, DTBOS, volume	0.171
Outcome 2: CN injury	McFadden R^2
Model 2a: CN injury = Shamblin	0.091
Model 2b: CN injury = Shamblin, DTBOS	0.217
Model 2c: CN injury = Shamblin, DTBOS, volume	0.221

CN, Cranial nerve; *DTBOS,* distance to the base of skull; *EBL,* estimated blood loss.

Table VI. Risks associated with 1-cm decrease in distance to base of skull (DTBOS)

Bleeding	Odds ratio (95% CI)
EBL >250 mL	1.79 (1.25-2.55)
Transfusion	1.36 (0.94-1.97)
CN injury	Odds ratio (95% CI)
Glossopharyngeal (CN IX)	2.08 (1.10-3.93)
Vagus (CN X)	2.53 (1.54-4.15)
Superior laryngeal	1.39 (0.97-1.97)
Hypoglossal (CN XII)	1.74 (1.24-2.45)
Any CN injury	1.51 (1.19-1.92)
Multiple CN injuries	2.66 (1.67-4.21)

CI, Confidence interval; *CN,* cranial nerve; *EBL,* estimated blood loss.

that may help preoperatively predict the true risks of excision have not been reported.[10] We have found that a better approach for predicting complications of CBT resection is to measure additional tumor parameters and to add them to the Shamblin classification. The results of our study show that the addition of DTBOS and tumor volume better predicts bleeding and cranial nerve injury risk, and the addition of these two variables supplements the Shamblin grade in better predicting complications than the Shamblin grade alone. Furthermore, we have used specific measurements of the tumor and applied them to this improved model to quantify the actual risk of specific cranial nerve injuries and the risk of blood loss. For every 1 cm the CBT is located closer to the base of the skull, there is 1.8 times the risk of greater than average intraoperative blood loss, 1.4 times increased risk of transfusion, 1.5 times increased risk of cranial nerve injury, and 2.7 times increased risk of multiple cranial nerve injuries.

SDH mutations have been found among families with a high incidence of CBTs.[9,11-13] Power et al recently demonstrated that this mutation is highly correlated with a family history of CBTs and bilateral CBTs. Furthermore, it is recommended that patients be tested for the SDH mutation as this mutation is thought to reflect a subgroup of patients with CBTs who require additional tests and preoperative planning.[14] Since only a few of our participating institutions tested patients for this mutation, it is difficult to draw meaningful conclusions about the role of this mutation related to tumor size, location, malignant change, or complications.

Preoperative embolization is often used to improve the success of surgical resection for CBTs. It has been shown to reduce blood loss[9] and is thought to be helpful for also decreasing cranial nerve injuries. However, there are no guidelines for which CBT patients should receive embolization before resection. We were unable to determine the appropriate role of embolization in our study because there were varying practices among the surgeons at the 16 institutions that participated in our study. Some surgeons embolized none, whereas others embolized all CBTs, and there were many practices between these two extremes. We did find that many of the tumors that had preoperative embolization were located closer to the base of the skull. Future studies that prospectively investigate preoperative embolization will lead to a better understanding of the benefits of preoperative embolization.

The limitations of this study are inherent in the retrospective nature of the study. A randomized trial to compare preoperative diagnostic methods and to determine the actual contribution of each diagnostic study to prevention of complications was not possible because CBTs do not occur in high frequency and because surgeons currently have different protocols for preoperative workup, surgical technique, and postoperative care. In addition, we were able to obtain precise DTBOS measurements only in patients who had MRI or CT imaging preoperatively.

CONCLUSIONS

This study highlights the importance of determining the DTBOS as well as the volume of a CBT preoperatively to assist in preoperative counseling about the risk of nerve injury and bleeding. It also supports the continued use of the Shamblin classification, which provides additional information and, when combined with DTBOS and tumor volume, gives a more complete picture of operative risk. In addition, this study demonstrates that the DTBOS is a predictor of bleeding and cranial nerve complications and therefore suggests that CBTs located close to the base of the skull may benefit from preoperative collaboration with a head and neck surgeon or neurosurgeon.

AUTHOR CONTRIBUTIONS

Conception and design: GK, PL, RM, KZ

Analysis and interpretation: GK, PL, RM, KZ, AM, KLO, GO, JD, JO, SH, LD, TB, SF, HG, MK, EH, GD, FS, MS, CD, JK, AP, ED, CB, EK, JH, FM, SC, MM, KR, MB, JB, AL, CA, AF

Data collection: GK, PL, RM, KZ, AM, KLO, GO, JD, JO, SH, LD, TB, SF, HG, MK, EH, GD, FS, MS, CD, JK, AP, ED, CB, EK, JH, FM, SC, MM, KR, MB, JB, AL, CA, AF
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Critical revision of the article: GK, PL, RM, KZ, AM, KLO, GO, JD, JO, SH, LD, TB, SF, HG, MK, EH, GD, FS, MS, CD, JK, AP, ED, CB, EK, JH, FM, SC, MM, KR, MB, JB, AL, CA, AF
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REFERENCES

1. 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.
2. Kruger AJ, Walker PJ, Foster WJ, Jenkins JS, Boyne NS, Jenkins J. Important observations made managing carotid body tumors during a 25-year experience. J Vasc Surg 2010;52:1518-23.
3. Dardik A, Eisele DW, Williams GM, Perler BA. A contemporary assessment of carotid body tumor surgery. Vasc Endovascular Surg 2002;36:277-83.
4. Lim JY, Kim J, Kim SH, Lee S, Lim YC, Kim JW, et al. Surgical treatment of carotid body paragangliomas: outcomes and complications according to the Shamblin classification. Clin Exp Otorhinolaryngol 2010;3:91-5.
5. Westerband A, Hunter GC, Cintora I, Coulthard SW, Hinni ML, Gentile AT, et al. Current trends in the detection and management of carotid body tumors. J Vasc Surg 1998;28:84-92.
6. Hallet JW Jr, Nora JD, Hollier LH, Cherry KJ Jr, Pairolero PC. Trends in neurovascular complications of surgical management for carotid body and cervical paragangliomas: a fifty-year experience with 153 tumors. J Vasc Surg 1988;7:284-91.
7. Luna-Ortiz K, Rascon-Ortiz M, Villavicencio-Valencia V, Granados-Garcia M, Herrera-Gomez A. Carotid body tumors: review of a 20-year experience. Oral Oncol 2005;41:56-61.
8. Amato B, Bianco T, Compagna R, Siano M, Esposito G, Buffone G, et al. Surgical resection of carotid body paragangliomas: 10 years of experience. Am J Surg 2014;207:293-8.
9. Power AH, Bower TC, Kasperbauer J, Link MJ, Oderich G, Cloft H, et al. Impact of preoperative embolization on outcomes of carotid body tumor resections. J Vasc Surg 2012;56:979-89.
10. Luna-Ortiz K, Rascon-Ortiz M, Villavicencio-Valencia V, Herrera-Gomez A. Does Shamblin's classification predict postoperative morbidity in carotid body tumors? A proposal to modify Shamblin's classification. [erratum in Eur Arch Otorhinolaryngol 2006;273:1161]. Eur Arch Otorhinolaryngol 2006;263:171-5.
11. Dahan A, Taschner PE, Jansen JC, van der Mey A, Teppema LJ, Cornelisse CJ. Carotid body tumors in humans caused by a mutation in the gene for succinate dehydrogenase D (SDHD). Adv Exp Med Biol 2004;551:71-6.
12. Lima J, Feijão T, Ferreira da Silva A, Pereira-Castro I, Fernandez-Ballester G, Máximo V, et al. High frequency of germline succinate dehydrogenase mutations in sporadic cervical paragangliomas in northern Spain: mitochondrial succinate dehydrogenase structure-function relationships and clinical-pathological correlations. J Clin Endocrinol Metab 2007;92:4853-64.
13. Fakhry N, Niccoli-Sire P, Barlier-Seti A, Giorgi R, Giovanni A, Zanaret M. Cervical paragangliomas: is SDH genetic analysis systematically required? Eur Arch Otorhinolaryngol 2008;265:557-63.
14. Davila VJ, Chang JM, Stone WM, Fowl RJ, Bower TC, Hinni ML, et al. Current surgical management of carotid body tumors. J Vasc Surg 2016;64:1703-9.

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APPENDIX.

Institutions and cases

Universidad Nacional de Colombia – 84
Instituto Nacional de Cancerologia – 60
Mayo Clinic, Rochester – 54
UCLA – 34
Stanford – 24
University of Messina – 24
University of Arkansas for Medical Sciences – 19
University of Athens – 11
University Clinics Hamburg-Eppendorf – 9
NYU – 8
Queen Mary Hospital – 8
St. Vincent Healthcare – 6
University of Rochester – 6
Houston Methodist Hospital – 5
Johns Hopkins – 2