Results of surgical resection of carotid body tumors: A twenty-year experience

January F Moore[1] ⓘD, John D Casler[2], Warner Andrew Oldenburg[1], Ronald Reimer[2], Robert E Wharen Jr[2], H Gordon Deen[2], Houssam Farres[1] and Albert G Hakaim[1]

Abstract

This study examines whether surgical resection of carotid body tumors (CBTs) is acceptable in light of potential significant neurologic complications. This IRB-approved retrospective study analyzed data from 24 patients undergoing surgical treatment for CBTs between April 1998 and April 2017 at Mayo Clinic (Florida campus only). For patients who underwent multiple CBT resections, only data from the first surgery was used in this analysis. CBT resection occurred in 24 patients with the following demographics: fourteen patients (58.3%) were female, median age was 56.5 years, median BMI was 29. A prior history of neoplasm was found in ten patients (41.7%). A known family history of paraganglioma was present in five patients (20.8%). Two patients were positive for succinate dehydrogenase mutation (8.3%). Multiple paragangliomas were present in seven patients (29.2%). There was nerve sacrifice in three patients (12.5%) during resection. Carotid artery reconstruction and patch angioplasty occurred in one patient (4.2%). Complete resection occurred in 24 patients (100.0%). Postoperatively, one patient (4.2%) suffered stroke. No mortalities occurred within or beyond 30 days of surgery. Persistent cranial nerve injury occurred in two patients (8.3%) with vocal cord paralysis. There was no recurrence of CBT through last follow-up. Five patients (20.8%) were diagnosed with other neoplasms after resection, including basal cell carcinoma, contralateral carotid body tumor, glomus vagale, and glomus jugulare. There was 100% survival at 1 year in patients followed for that time (*n* = 17). Surgical treatment remains the first-line curative treatment to relieve symptoms and ensure non-recurrence. While acceptable, neurologic complications are significant and therefore detailed preoperative informed consent is mandatory.

Paragangliomas (PGL) are rare tumors, with an estimated incidence of 1:30,000 cases annually[1] and representing less than 1% of all head and neck tumors.[2] Head and neck paraganglioma, also known as glomus tumors, arise from the parasympathetic paraganglia of the skull base and neck.[3] Tumors of the carotid body occur most frequently, constituting approximately 60% of head and neck paragangliomas, with a lesser incidence of tumors of the tympanic, jugular, and vagal paraganglia.[4] Sympathetic paraganglioma and pheochromocytoma are known for excess production of catecholamines while head and neck paraganglioma tend to be nonsecreting.[5] Additionally, parasympathetic paraganglioma are highly vascularized and slow-growing, and often present as painless masses

[1]Division of Vascular Surgery, Mayo Clinic, Jacksonville, FL, USA
[2]Department of Neurologic Surgery, Mayo Clinic, Jacksonville, FL, USA

Corresponding author:
Albert G Hakaim, Division of Vascular Surgery, Department of Surgery, Mayo Clinic Florida, 4500 San Pablo Rd S., Jacksonville, FL 32224, USA.
Email: Hakaim.albert@mayo.edu

and/or with symptoms due to the pressure of the enlarging tumor on other structures.[1]

Clinical presentation varies by location and type- carotid body tumors and glomus vagale often present as a painless neck mass perhaps with hoarseness.[6] Genetic predisposition and markers for these tumors have recently been the subject of several studies, and hereditary syndromes are often seen in younger patients with multiple tumors.[1] However, incomplete penetrance of mutations can result in the masking of hereditary syndromes.[2,5–7]

Treatment is usually determined on a case-by-case basis, and through factors such as symptomaticity, malignancy (though often benign), size, location, and degree of involvement with important blood vessels and nerves. Surgical resection is the mainstay of treatment for symptomatic, multiple, and larger tumors, with radiotherapy and surveillance used in cases where the risk of this treatment outweighs the benefits.[8,9]

In this study, we present the characteristics and outcomes of patients undergoing surgical resection of carotid body tumors at our institution in the past 20 years.

Methods

This was a retrospective analysis of characteristics of 24 patients presenting with carotid body tumors (CBTs) and who underwent surgical treatment at Mayo Clinic Florida between April 1998 and April 2017. Thirty-three patients with carotid body tumors were initially identified; of these, 24 patients (72.7%) underwent surgical intervention as primary treatment. Two of these patients presented with synchronous contralateral paragangliomas which were separately resected in subsequent surgeries at the same institution. However, only the first surgery was included in this analysis.

After IRB approval, the demographics, comorbidities, disease presentation, intraoperative characteristics, and post-operative outcomes of patients undergoing surgical intervention as primary treatment were collected from the medical records and analyzed. Due to values describing several tumor characteristics being asymmetrically distributed around the mean, data for continuous variables is reported as both a mean and standard deviation (SD), as well as median and interquartile range (IQR).

Results

At our institution, surgery was primary treatment for the majority of patients identified with carotid body tumor (72.7%). Surveillance was not medically recommended but elected by three patients (9.1%). These patients did not return for follow-up despite efforts by the institution to reestablish care. Five additional patients (15.2%) were lost to follow-up after diagnosis and prior to treatment election.

Radiotherapy was chosen as primary treatment for one patient (3.0%) as surgical resection was likely to result in severe morbidity that outweighed the benefits of excision.[10,11] After treatment, the patient had a fairly stable tumor with minimal growth for several years, however, later the patient developed moderate dysphonia, dysphagia, xerostomia, and persistent oral mucositis.

Patient demographics and comorbidities

The median age of the surgical population was 56.5 years, with an age range of 20–83 years. Fifteen patients (62.5%) suffered from multiple comorbidities prior to surgery, and hypertension and dyslipidemia were the most frequently diagnosed comorbidities. Full demographics and comorbidities are presented in Table 1.

A total of 10 patients (41.7%) had a prior history of neoplasm, including colon cancer, skin cancer, tubular adenoma, prior paraganglioma, breast cancer, and renal tumors (data not shown). One 47-year-old female presented with a familial history of CBT and had previously undergone surgical resection of CBT and radiotherapy for recurrent glomus jugulare.

Five patients (20.8%) had a known family history of paraganglioma; these patients had a median age at surgery of 33 years with a range of 21–59 years (data not shown). Three patients underwent genetic testing, with two positive for SDH mutation (SDH-B/C and SDH-D). The SDH-positive patients presented at ages 33 and 49; the first with a family history of carotid body tumor, and the second with no known family history of paraganglioma, prior treatment for GIST and presenting with multiple tumors (both carotid body and glomus vagale tumors).

Disease presentation and preliminary workup

Twelve patients (50.0%) were symptomatic at presentation. The most frequent initial complaint was neck mass in 45.8% of patients (Table 2). Cranial nerve dysfunction was present in seven patients (29.2%).

Computed tomography was the most frequently used imaging (Table 2, Figure 1(a)). Seven patients (29.2%) were found to have multiple paraganglioma, three patients with both carotid body tumor and glomus vagale, two patients with bilateral carotid body tumors, and two patients with glomus jugulare and carotid body tumors (only carotid body tumors were resected in these patients).

In a third of patients, carotid body tumors were incidental findings usually via radiology. However, two patients were discovered to have carotid body tumors during unrelated workup, including carotid endarterectomy and oropharyngeal carcinoma resection.

Median tumor size for all patients was 2.0 cm with a range from 1.0 to 5.2 cm (Table 2). All resected tumors

Table 1. Patient demographics and comorbidities.

Variable	Total, $N = 24$
Male	10 (41.7%)
Age at surgery, years	
Mean ± SD	53.2 ± 18.4
Median (Q1, Q3)	56.5 (40.5, 67.5)
Range	20–83
BMI, kg/m^2	
Mean ± SD	29.4 ± 5.2
Median (Q1, Q3)	29.0 (25.7, 31.4)
Range	21.1–41.8
Comorbidities	
Multiple comorbidities	15 (62.5%)
Hypertension	12 (50.0%)
Dyslipidemia	10 (41.7%)
Coronary artery disease	2 (8.3%)
Diabetes	2 (8.3%)
Stroke	2 (8.3%)
Thrombocytopenia	1 (4.2%)
Other vascular disease	1 (4.2%)
Neoplasm history	10 (41.7%)
Neoplasm treatment history	10 (41.7%)
Known family history of paraganglioma	5 (20.8%)
Genetic testing	3 (12.5%)
SDH + mutation	2 (8.3%)

Table 2. Disease presentation and preliminary workup.

Variable	Total, $N = 24$
Initial complaints	
Neck mass	11 (45.8%)
Lymphadenopathy	4 (16.7%)
Hoarseness/laryngitis	2 (8.3%)
Stroke	1 (4.2%)
Vocal cord paralysis	0 (0%)
Other (nausea, weight loss, and sore throat)	1 (4.2%)
Symptomatic	12 (50.0%)
Cranial nerve dysfunction	7 (29.2%)
Radiology	
CT	19 (79.2%)
MRI	13 (54.2%)
US	6 (25.0%)
PET	3 (12.5%)
Octreoscan	2 (8.3%)
Multiple tumors	7 (29.2%)
Bilateral tumors	4 (16.7%)
Incidental finding	8 (33.3%)
Tumor size by pathology, cm	
Mean ± SD	2.4 ± 1.1
Median (Q1, Q3)	2.0 (1.5, 2.6)
Range	1.0–5.2
Benign	24 (100%)
Shamblin class	
I	7 (29.2%)
II	15 (62.5%)
III	2 (8.3%)

were considered benign by pathology. Most patients (62.5%) had Shamblin Class II tumors. One patient with bilateral carotid body tumors had Shamblin class I and II tumors. Of the two patients undergoing resection of both carotid body tumor and glomus vagale ($n = 2$), one patient had a Shamblin class I carotid body tumor and the second patient had a Shamblin class II carotid body tumor.

Procedural characteristics

Two patients underwent more than one surgery at this institution as a result of tumors presented within the study time period (Table 3), however, only the characteristics of the first surgeries are reported here. The majority of patients underwent preoperative angiography (70.8%) (Figure 1(b)). Preoperative embolization and balloon occlusion testing were conducted in five patients (20.8%). Our protocol for preoperative embolization applied to larger tumors, usually greater than 3 cm in size. The mean tumor size in patients with embolization was 3.6 and 2.1 cm in patients without embolization. There was no difference in blood loss in patients receiving embolization versus patients who did not receive embolization. However, median operative time was 147 min in patients who underwent embolization versus 118 min in the remaining patients (Median operative time in all patients was 124 min). One patient with bilateral carotid body tumors suffered stroke after balloon occlusion testing but was able to undergo resection and had no functional limitations at last follow-up visit.

In our series, either subadventitial or periadventitial approaches to resection were employed by surgeon preference. Sacrifice of cranial nerves occurred only when necessary for full resection of the tumors. Intraoperatively, nerve sacrifice occurred in three patients (12.5%)—the hypoglossal nerve in two patients, and the pharyngeal plexus branches in one patient. Carotid artery reconstruction and patch angioplasty was required in one 20-year-old male with a 4.2 cm carotid body tumor that was densely adherent to the internal carotid artery and required the transposition of the internal carotid artery to the external carotid artery.

Complete resection was achieved in 100% of patients. Procedural data is fully detailed in Table 3.

Postoperative outcomes

Sensory changes were the most frequently reported complaint post-operatively (41.7%) (Table 4). Permanent cranial nerve injury and vocal cord paralysis were seen in two patients (8.3%), one of whom underwent subsequent thyroplasty. One patient was noted to have hypoglossal nerve sacrifice, however, there was no noted nerve sacrifice in the second patient. In total, four patients (16.7%) experienced hypoglossal nerve palsy. In three of these patients, nerve sacrifice was reported. The palsy resolved in three of the
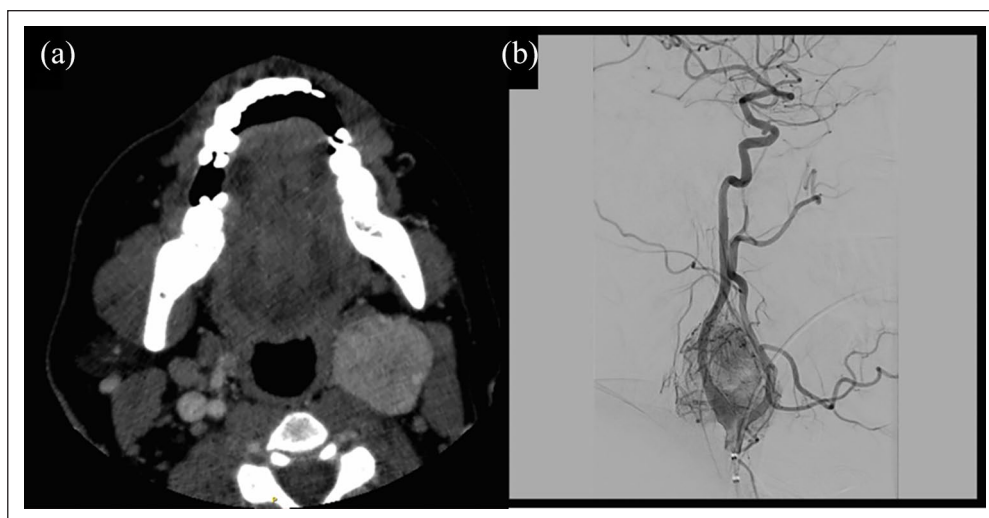
Figure 1. (a) Computed tomography showing a large carotid body tumor splaying the internal and external carotid arteries. (b) Preoperative angiography of a patient with a large carotid body tumor splaying the internal and external carotid arteries.

Table 3. Procedural characteristics.

Variable	Total, N = 24
Multiple surgeries	2 (8.3%)
Preoperative angiography	17 (70.8%)
Preoperative embolization	5 (20.8%)
Balloon occlusion test	7 (29.2%)
Nerve sacrifice	3 (12.5%)
Carotid artery reconstruction	1 (4.2%)
Patch angioplasty	1 (4.2%)
Complete resection	24 (100%)
Blood loss (mL)	
Mean ± SD	65.7 ± 80.5
Median (Q1, Q3)	50.0 (25.0, 75.0)
Range	10–400
Operative time, minutes	
Mean ± SD	140.4 ± 56.0
Median (Q1, Q3)	123.5 (99.0, 154.5)
Range	75–275

Table 4. Postoperative outcomes.

Variable	Total, N = 24
30-day complications	
Sensory changes (neck/face pain, numbness, pulsatile tinnitus, and tingling)	10 (41.7%)
Hypoglossal nerve palsy	4 (16.7%)
Vocal cord paralysis	2 (8.3%)
Cranial nerve injury (permanent)	2 (8.3%)
Hypertension	2 (8.3%)
Dysphagia	2 (8.3%)
Stroke	1 (4.2%)
Death	0 (0%)
Other[a]	5 (20.8%)
None	5 (20.8%)
Paraganglioma recurrence	0 (0%)
Other neoplasm diagnosis	5 (20.8%)
Basal cell carcinoma	2 (8.3%)
CBT contralateral	2 (8.3%)
Glomus vagale and glomus jugulare	1 (4.2%)
Multiple surgeries for paraganglioma	5 (20.8%)
Post-operative imaging	12 (50.0%)
Follow-up duration, days	
Mean ± SD	627.4 ± 1201.1
Median (Q1, Q3)	248.0 (20.5, 747.5)
Range	7–5845
1-year survival (n = 17)	17 (100%)
2-year survival (n = 12)	12 (100%)
5-year survival (n = 5)	5 (100%)

[a]Hematoma, hoarseness, mouth droop, smile asymmetry, and submental lymphedema.

four patients. A smaller incidence of dysphagia (8.3%), hypertension (8.3%) and stroke (4.2%) occurred postoperatively. Stroke occurred in an 83-year-old female with incidentally discovered CBT during workup for carotid artery stenosis (78% stenosis of the right internal carotid artery) and hemispheric stroke. Carotid endarterectomy was then performed concurrently with carotid body tumor resection. Postoperatively the patient had cerebrovascular accident that resulted in left-sided weakness. The patient was discharged to an inpatient rehabilitation facility and eventually returned home. There were no 30-day mortalities, and all patients were alive at last follow-up. No tumor recurrence was noted in any patients.

Five patients (20.8%) underwent subsequent surgeries for paraganglioma identified prior to the first surgery or diagnosed at a later date. Five patients (20.8%) were diagnosed with additional neoplasms after initial surgery: basal cell carcinoma (two patients), contralateral carotid body tumors (two patients), glomus vagale, and glomus jugulare (one patient).

Median follow-up duration was 248 days. There was 100% survival in patients still followed at 1-, 2-, 5-year periods.

Discussion

Surgery has been the gold standard for curative treatment of carotid body and tumors, with high reported rates of local control (94%–100%),[12] although there is significant risk of injury to the carotid arteries and cranial nerves due to tumor location.[13,14] Our study showed that these adverse outcomes occurred at acceptably low rates.

Gordon-Taylor (1940) described a subadventitial approach that is used for Shamblin classes I and II where the tumor is more easily dissected.[14,15] In our series, both subadventitial or periadventitial approaches to resection were employed, and no complications with the vasculature were evident on available post-operative imaging and follow-up. However, surgical techniques that remove or weaken the carotid adventitia during resection of head and neck cancers have been critiqued as increasing the likelihood of carotid artery rupture, especially if the patient receives radiation.[16–18] Pseudoaneurysm may also be a complication of the weakening of the carotid artery wall.[19] Subadventitial dissection would potentially have a higher likelihood of leading to pseudoaneurysm and rupture. Given a history of or the potential use of anti-cancer therapies, a periadventitial surgical approach is recommended to avoid weakening the vasculature.

Two patients in our study had a history of radiotherapy to the neck area for treatment of other neoplasms (glomus jugulare, oropharyngeal cancer) and two patients received chemotherapy in the past for colon cancers. Chemotherapy may contribute to vascular toxicity by causing endothelial damage and dysfunction.[20,21] Radiation has been shown to induce aneurysm and carotid artery rupture.[17,22,23] Radiation has also been linked to adverse effects including mucositis, xerostomia, dysphagia, dysphonia, nerve paralysis, coronary artery disease, carotid artery stenosis, cerebrovascular accident, and radiation-induced cancer.[24–30] However, radiotherapy is used for head and neck paraganglioma when the risk of morbidity from resection is high, particularly in non-CBT paraganglioma.[11,31] Valero et al.[31] recently reported treatment outcomes of 103 patients with head and neck paraganglioma (68 with CBTs, 35 with non-CBTs). Stable disease or partial regression was reported in all patients treated with radiotherapy (10/103); dermatitis and mucositis occurred in 40% of these patients. Twenty patients elected surveillance; 30% of these patients later required active treatment due to tumor progression. This result was noted within the 21%–58% range of reported tumor progression during surveillance in similar studies. Vagus nerve dysfunction was the most common long-term functional outcome in both surgical and radiotherapy groups (28.2% in 103 patients; 5.9% in CBT group vs 71.4% in the

non-CBT group), and cranial nerve deficits were mostly seen in the non-CBT group. The study concluded that surgical resection was effective treatment for CBT, and non-surgical treatments should be considered for non-CBT head and neck paragangliomas. Mendenhall et al.[32] also recently reported high rates of long-term local control after fractionated radiotherapy for head and neck paragangliomas (44 CBTs of 176 benign head and neck paragangliomas). There were no radiation-induced malignancies or severe complications resulting in surgery or death. Six patients developed progression of tumor and/or metastasis at a median 6.8 years, resulting in death in three patients. Ninety patients initially presented with cranial nerve deficits, which resolved in six patients. An acknowledged limitation of the study was a lack of post-treatment assessment of the carotid arteries for possible impacts.

In our study, permanent cranial nerve injury resulting in vocal cord paralysis occurred in 8.3% of patients (Table 4). This is lower than noted with Neskey et al.,[33] who reported that 18% of carotid body tumor patients had persistent deficits 2.5 years after surgical resection. However, Power et al. showed similar permanent nerve deficits in 6.0% of carotid body tumor patients.[13] The overall stroke rate of 4.2% was similar to that seen by Dixon et al. (5.8%),[34] and also Neskey et al. (4.0%).[33] However, Power et al.[13] reported only one stroke (1.0%) in 131 patients undergoing carotid body tumor resection.

Of the patients with other neoplasms identified before or after the study surgery, seven patients (29.2%) had diagnosed paraganglioma, pheochromocytoma, renal cell cancers or gastrointestinal stromal tumors. These neoplasms are associated with hereditary SDH-related paraganglioma syndromes.[6] Paraganglioma are classified as sporadic or familial, where familial tumors are often associated with germline mutations of succinate dehydrogenase genes SDH-B/C/D and sometimes with VHL and RET.[1,2] However, even paraganglioma clinically classified as sporadic have been found with germline SDH mutation, and are considered "occult familial."[1,2] SDH mutations are associated with higher rates of malignancy in paragangliomas, however reports are variable, from 17% to 71%.[5] In our study, five patients had a family history of paraganglioma and presented at a younger median age of 33 (vs 56 years for the total surgical population), as seen in other studies (Table 1).[1] Genetic testing was performed for only three patients, two of whom were positive for SDH mutations, and only one of whom had a known family history (Table 1). Given the difficulties of clinical diagnosis due to variable presentations, genetic testing has been proposed as a universal protocol in paraganglioma patients.[1,35,36] However, the cost of testing is high and confirming a familial condition usually only affects future surveillance. Recently, immunohistochemistry (IHC) testing has been shown as a possible inexpensive method to screen paraganglioma patients for further testing.[6,35] If genetic testing is

not conducted and hereditary paraganglioma is suspected, frequent monitoring is prudent. Close surveillance has recently been recommended for patients with a prior history of CBT or hereditary paraganglioma, due to an increased risk of secondary primary paraganglioma.[36]

Observation is not generally recommended in patients with CBT due to the potential progression of nerve deficits and the low but unpredictable potential for malignant behavior. If surveillance is elected, recent recommendations for head and neck paraganglioma include MRI imaging every 6–12 months with an additional annual assessment, although there is no consensus.[12] However, given that rates of cranial nerve deficit from resection significantly increase with tumor size, and reported rates of tumor progression are variable, it has been recommended that CBTs smaller than 5 cm be resected.[12,31]

This study was limited by its retrospective nature, small sample size, short follow-up duration, and loss of patients to follow-up.

Conclusion

In sum, surgical intervention for carotid body tumors remains the first-line curative treatment to relieve symptoms and ensure non-recurrence. In our series, there was an acceptable rate of morbidity given the benefits of resection and favorable survival outcome.

Authors' contributions

AH conceived the study, researched literature and was involved in data analysis. JM was involved in gaining ethical approval, data collection, literature review, data analysis and manuscript drafting. All authors reviewed, edited and approved the manuscript.

Declaration of conflicting interests

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Ethical approval

Ethical approval for this study was given by Mayo Clinic Institutional Review Board #16-010046.

Informed consent

Informed consent was waived by the Institutional Review Board due to the retrospective and deidentified nature of this study.

Trial registration

Not applicable due to the retrospective nature of this study.

ORCID iD

January F Moore https://orcid.org/0000-0001-7733-893X

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