# Multidisciplinary care improves outcomes for patients with carotid body paragangliomas—The UCLA experience

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# Abstract

Objective: To evaluate the effects and outcomes of multidisciplinary surgical approaches in the management of carotid body tumors (CBT).

Methods: A single-center retrospective study at the University of California-Los Angeles Medical Center was conducted on patients who presented with CBTs and underwent surgical resections from 1998 to 2020. Statistical analysis was performed using IBM SPSS v27 and Excel.

Results: A total of 75 patients with 79 CBT resections were included. Operating surgical subspecialties included: 41.8% vascular surgery, 24.1% otolaryngology head and neck surgeons (OHNS), and 31.6% combined OHNS and vascular. 68.4% of tumors underwent preoperative embolization. EBL was directly correlated with tumor size. CBT size was similar for OHNS (30 mm) and vascular (31 mm) but was significantly larger for combined OHNS and vascular cases (38 mm). EBL was higher in combined cases (301 mL) compared to OHNS (124 mL) or vascular (203 mL) alone. Incidence of postoperative cranial nerve deficits was 7.8%, with combined OHNS and vascular cases having an incidence of 4.0% when compared to OHNS (5.3%) versus vascular surgery alone (12.1%).

Conclusion: CBTs can be managed effectively by single surgical specialties with similar outcomes between vascular surgery and OHNS. In larger, higher grade tumors, however, a combined vascular and OHNS approach had lower incidence of postoperative cranial nerve injuries when compared to single specialty resections, despite a larger EBL. Thus, a multidisciplinary surgical approach suggests favorable outcomes with fewer incidence of cranial nerve deficits for larger, more complex CBT resections.

Level of Evidence: 2b-Individual retrospective cohort study.

#### KEYWORDS

carotid body tumors, estimated blood loss, paragangliomas

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# 1 | INTRODUCTION

Carotid body tumors (CBT) are highly vascular, glomus tumors arising from paraganglion cells of the carotid body. They represent only 0.6% of head and neck tumors and are usually benign with a metastasis rate of 2%–9%.<sup>1,2</sup> While they are usually benign, the location and growth of these tumors can lead to symptoms of enlarging neck mass, dysphagia, voice changes, headache, syncope, Horner syndrome, and compressive symptoms of cranial nerves IX, X, XII and the sympathetic chain.<sup>1</sup> Most CBT's are nonfunctional, but catecholamineproducing tumors are possible leading to symptoms of paroxysmal hypertension.<sup>2</sup> CBT's are classified by Shamblin class. Class I tumors have minimal attachment to carotid vessels, Class 2 tumors are larger in size with moderate arterial attachments, and Class 3 tumors largely encase the carotid arteries.<sup>3</sup>

Due to the risk of compressing neurovascular structures, surgery is recommended over observation or radiation of the tumor.<sup>2</sup> Surgical treatment, however, can be challenging particularly in larger tumors and higher Shamblin classes. Higher grade tumors can have multiple feeding arteries and adhere to the carotid artery wall, contributing to a greater risk of blood loss and cranial nerve deficits.<sup>4</sup> Reported neurovascular complications following CBT resection include injuries to the vagus, hypoglossal, cervical sympathetic, and superior laryngeal nerves leading to issues with swallowing and voicing.<sup>5</sup> Rate of temporary postoperative defects was reported at up to 68%, with 17%–38% having permanent defects after 18 months.<sup>5,6</sup>

Reducing intraoperative blood loss and incidence of cranial nerve deficits is crucial in large tumors. Pre-embolization of CBTs can be helpful in decreasing blood loss and reducing risk for cranial nerve deficits by reducing the number of feeding arteries to the vessel.<sup>1,2</sup> However, embolization presents with risks, including local inflammation, neural damage, and a 3% risk of downstream emboli.<sup>7,8</sup> Timing of pre-embolization before surgical resection is also important to consider due to the risk of tumor revascularization prior to resection.<sup>9</sup> Other studies found no significant differences in EBL from pre-embolization.<sup>10-12</sup> Overall, selective pre-embolization is more commonly performed in Shamblin II/III CBTs that are generally more complex with longer estimated operation times, but ultimately depends on surgeon preference and are recommended to be performed by qualified interventional physicians.<sup>13</sup>

Due to the often distorted anatomy and higher risk surgeries in Shamblin II/III resections, a multidisciplinary surgical approach has been adopted by many institutions. A common multidisciplinary approach is vascular surgery with otolaryngology head and neck surgeons (OHNS), which benefits from vascular surgeon expertise of dissecting carotid artery branches and vessel reconstruction and OHNS expertise of mobilizing nervous structures in the neck.<sup>14–17</sup> Neurosurgeons and oral maxillofacial surgeons can also be involved. Interventional neuroradiologists are important for tumor staging and pre-embolization.<sup>14,15,18</sup> In familial cases and genetic syndromes like multiple endocrine neoplasia type 2, neurofibromatosis type 1, or von Hippel Lindau, endocrinologists and geneticists play vital roles on the multidisciplinary team.<sup>19</sup> A retrospective study performed by Massachusetts General Hospital and Harvard Medical School found that multispecialty surgical management of CBT had favorable results with unparalleled complication rates and shorter operative times.<sup>15</sup>

While there is literature describing the benefits of multidisciplinary management of CBT resection, studies comparing this multidisciplinary approach to single subspecialty operations have not been performed. In this paper, we compare the outcomes of CBT resections for OHNS and vascular surgery alone with combined OHNS and vascular cases.

# 2 | METHODS

Institutional review board approval was obtained for the retrospective chart review of 75 patients who had 79 CBT resections between 1998 and 2020 at Ronald Reagan UCLA Medical Center. Medical records were reviewed for information regarding the operating surgical subspecialty, tumor size, tumor pathology, embolized arteries, resected lymph nodes, EBL, cranial nerve deficits, and other adverse events. Single surgical specialty groups were compared against each other and against the combined OHNS and vascular surgery group. Outcome variables included mean EBL and tumor size. Statistical analysis including independent samples *t*-tests, Pearson's correlation, ANOVA, and Fischer Exact tests were performed using IBM SPSS Version 27 and Excel. A *p*-value <.05 was considered statistically significant.

# 3 | RESULTS

A total of 79 CBT resections were performed between 1998 and 2020 at the UCLA Medical Center. There were 75 total patients ranging from 16 to 82 years old, with an average age of 50. The group was composed of 44% males and 56% females, with 11.4% having undergone a previous resection for a contralateral CBT. 12.7% of patients had a family history of CBTs. There were 46.8% of the resected CBT's on the left side, 53.2% on the right, and 29.1% bilateral (Table 1). Patients with concurrent paragangliomas included four left glomus

 TABLE 1
 Clinical and demographic characteristics of cohort.

	Mean	Standard deviation	
Age	49.6	15.5	
	Number	Percentage	
Male	35	44.3%	
Female	44	55.7%	
Left	37	46.8%	
Right	42	53.2%	
Bilateral	23	29.1%	
Other paragangliomas	9	11.4%	
Family history	10	12.7%	
Previous resection	9	11.4%	

vagale, three right glomus vagale, one glomus tympanicum, one right pheochromocytoma, and one bilateral pheochromocytoma. The primary presenting symptom was a neck mass (Table 2). Four patients had initial neurologic deficits including hoarseness and ipsilateral hearing loss, which resolved after surgical resection. Operating surgical subspecialties were primarily composed of 41.8% vascular surgery, 31.6% combined OHNS and vascular, and 24.1% OHNS (Table 3). Two patients were operated by combined OHNS and neurosurgery and combined neurosurgery and plastic surgery respectively.

68.4% of CBT resections underwent preoperative embolization, with an average decrease in blush of 71%. The most commonly embolized vessels were the ascending pharyngeal, occipital, and superior thyroid arteries. Embolized tumors tended to have larger diameters than non-embolized tumors (34 vs. 30 mm) and larger EBL (226 vs. 197 mL) (Figure 1A,B). In general, for every 10 mm increase in CBT, there was a corresponding 98.8 mL increase in EBL ( $R^2 = 0.94$ , p = .06) (Figure 2). Of note, as the 3-dimensional tumor measurements were not available for a number of patients and not all imaging studies were available for review, tumor diameter was used as a measure of size as opposed to volume.

**TABLE 2**Initial cohort presenting symptoms of CBT.

Number		Percentage
Neck mass	55	69.6%
Neck mass-pulsatile	6	7.6%
Dysphonia	4	5.1%
Dysphagia	4	5.1%
Ipsilateral hearing loss	1	1.0%
Anisocoria	1	1.0%
Syncope	6	7.6%
HTN	3	3.8%
Palpitations	4	5.1%
None	12	15.2%

#### TABLE 3 Operative factors.

Operating surgical subspecialty	Number	Percentage
Vascular	33	41.8%
OHNS + vascular	25	31.6%
OHNS	19	24.1%
OHNS + neurosurgery	1	1.3%
Neurosurgery $+$ plastic surgery	1	1.3%
Preoperative embolization	54	68.4%
Ascending pharyngeal	51	94.4%
Occipital	21	38.9%
Superior thyroid	22	40.7%
Lingual	4	7.4%
Facial	2	3.7%
Unnamed ECA branches	6	11.1%

No statistically significant difference in EBL was noted for surgeries with and without embolization when controlled for tumor size (p = .34). Of note, seven outliers were determined from interquartile range calculations in SPSS based on EBL and tumor size. Six of the outliers included surgeries for large Shamblin grade III tumors that required surgical repair of vessels including shunts. EBL for these cases were above 600 mL, with the largest EBL of 2000 mL. Operative reports noted excessive blood loss due to large tumors markedly adherent to major vessels. The final outlier was based on a larger tumor size of 65 mm. Outliers were included in the analysis.

Four surgical cases required use of a shunt or reconstruction of vessels. In the case with the most significant blood loss of 2000 mL, the ICA was resected and reconstructed. The second case had 300 mL of blood loss during which the resected internal and external carotid artery was anastomosed to the common carotid. Two other cases had shunts performed, and the ICA or distal common carotid was resected and anastomosed.

CBT diameter was similar for OHNS (30 mm) and vascular surgery (31 mm) but was significantly larger for combined OHNS and vascular cases (38 mm) (Figure 1A). EBL was higher in combined cases (301 mL) compared to OHNS (124 mL) or vascular surgery alone (203 mL) (Figure 1B). ANOVA was performed to compare the three groups-OHNS, vascular surgery, and combined OHNS and vascular surgery, with mean EBL and mean tumor size as the outcome measures. There were significant differences between the three groups for mean tumor size (p = .01), but not for EBL (p = .14). Two-tailed t-scores for mean EBL and mean tumor size were also calculated. comparing single surgical specialties against each other as well as against the combined OHNS and vascular surgery group. Mean tumor size was significantly different between the OHNS and combined group (p = .01) as well as between vascular surgery and the combined group (p = .02). No significant differences were seen for mean EBL or between OHNS and vascular surgery alone.

There was one lymph node metastasis composed of nests of large epithelioid cells with eosinophilic cytoplasm, cytologic atypia, and infiltration, with no penetration of the node capsule. Length of post-operative stay in the hospital ranged from 1 to 9 days with a mean of 3 days. Of the 79 surgical resections, 7.8% of cases had cranial nerve deficits following CBT resection, with CN X (2.6%), XII (6.5%), and Horner's syndrome (1.3%) being the most common. Of note, many of these patients did not have long term follow-up, and it is unclear whether these deficits are due to temporary causes like neuropraxia and edema and otherwise would have resolved.

Of the patients who experienced postoperative cranial nerve deficits, there was one patient in the OHNS group, four patients in the vascular group, and one patient in the combined OHNS and vascular group. When comparing the incidence of cranial nerve deficits within each surgical specialty, OHNS had an incidence of 5.3%, vascular surgery 12.1%, and combined OHNS and vascular surgery had an incidence of 4.0% (Table 4). There was no significant difference in incidence of postoperative cranial nerve deficits between surgical specialties (p = .559). Of note, due to the small sample size, the Fisher exact test was performed. There was only one case in each of the

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**FIGURE 2** Relationship between EBL and CBT tumor diameter. Graphical representation of the relationship between EBL and CBT tumor diameter shows a positive correlation ( $R^2 = 0.9364$ , p = 0.06). For every 10 mm increase in CBT diameter, there is a corresponding 99 mL increase in EBL. Trendline was calculated using the average EBL for each grouped size category.

combined neurosurgery and plastic surgery group or combined OHNS and neurosurgery groups, and neither experienced postoperative cranial nerve deficits. Patients were also followed for postoperative adverse events which included new-onset arrythmias and hypertension (Table 4). Combined OHNS and vascular surgery cases had the highest incidence of adverse events at 5.1%. However, all four patients with new-onset atrial fibrillation resolved prior to discharge. One patient had new-onset hypertension postoperatively which also resolved by postoperative day 3. The differences between the combined vs. single surgical specialty cases were significant for postoperative arrythmias (p = .01), but not significant for postoperative hypertension. There were four recurrences and one case of metastatic disease extending into one out of 8 lymph nodes.

# 4 | DISCUSSION

Surgical treatment of carotid body tumors is complex particularly in Shamblin II/III grade tumors due to the larger size, distorted anatomy, and proximity to major blood vessels. Shamblin grade III tumors, number of lymph nodes removed, and tumor distance to the base of skull have been independently associated with increased risk for cranial nerve deficits.<sup>6,20</sup> Thus, a multidisciplinary surgical approach has

**FIGURE 1** Average EBL and tumor diameter for embolized versus non-embolized CBT's and by surgical specialty. (A) Bar chart representation of mean tumor size by operating surgical specialty and embolization. Through t-score analysis, mean tumor size was significantly larger for the combined OHNS and vascular surgery group when compared against the individual surgical specialties OHNS and vascular surgery. (B) Bar chart representation of mean EBL by operating surgical specialty and embolization.

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Operative complications	OHNS	Vascular	OHNS + vascular	Total	Incidence
CN deficit	1	4	1	6	7.8%
X (Dysphonia)	0	2	0	2	2.6%
XII (Tongue deviation)	1	3	1	5	6.5%
Horner's syndrome	1	0	0	1	1.3%
Percentage of patients within each specialty	5.3%	12.1%	4.0%		
Other adverse events	0	1	4	5	6.3%
Arrythmias	0	0	4	4	5.1%
HTN	0	1	0	1	1.3%
Percentage of patients within each specialty	0.0%	1.3%	5.1%		

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Operative complications following CBT resection. TABIF 4

been adopted by many institutions particularly for larger tumors. A common multidisciplinary approach is vascular surgery with OHNS, with the vascular surgeon focus on dissecting carotid artery branches and vessel reconstruction and the OHNS focus on mobilizing nervous structures in the neck.<sup>14–17,19,21</sup> Neurosurgeons and oral maxillofacial surgeons can also be involved, along with interventional neuroradiologists who assist in tumor staging and preembolization.14,15,18

A multidisciplinary surgical approach may be beneficial in reducing the incidence of cranial nerve deficits after CBT resection. A retrospective study of 74 resections performed by Mohebali et al. found that multispecialty surgical management of CBT had unparalleled complication rates and shorter operative times, with no permanent postoperative cranial nerve injuries reported.<sup>15</sup> Reported incidence of cranial nerve deficits following CBT resections in the literature varies from 17% to -38%, with the incidence of temporary defects reported as high as 68%.<sup>2,5,6,16</sup> Of the 79 surgeries performed in our cohort, 7.8% had post-resection neurological deficits including hoarseness (CN X), tongue deviation (CN XII), and Horner's syndrome. The six patients who experienced cranial nerve defects in our study comprised of four resections by vascular surgery, one by OHNS, and one by combined OHNS and vascular surgery. Incidence of cranial nerve deficits by specialty were 12.1%, 5.3%, and 4.0% respectively, with no significant difference between the three groups (p = .559). Of note, our study was likely underpowered and patients in our cohort were not followed long term. Thus, it is not known if some of these deficits were secondary to neuropraxia and may have eventually resolved with time.

In addition to greater risk of neurological complications, a positive correlation between Shamblin grade or tumor size and intraoperative blood loss has previously been reported.<sup>22</sup> This trend is in accordance with what we observed in our cohort, in which there was a corresponding 99 mL increase in EBL for every 10 mm increase in CBT diameter ( $R^2 = 0.94$ ). In a systematic review of 465 patients who underwent CBT surgery and embolization by Economopoulos et al., the average EBL was 368 mL with an average tumor size of 49 mm.<sup>13</sup> Tumors in our cohort were generally smaller and had lower EBL. In general, the

choice of preoperative embolization varies based on the patient and surgeon preference. Criteria like tumor size above 4 cm or location above the second cervical vertebrae have previously been used to determine which tumors to embolize. The most commonly embolized artery reported in the literature is the ascending pharyngeal artery, which is consistent with our results.<sup>14</sup> In our cohort, embolized tumors had larger tumor diameters (34 vs. 30 mm) and higher EBL of 226 mL compared to 197 mL in non-embolized CBTs (p = .08, p = .34). Although our results comparing embolized and non-embolized tumors were not significant, the general trend of greater blood loss in the embolized group has been documented previously with an average EBL of up to 437 mL reported by Mohebali et al.<sup>15</sup> Furthermore, the impact of preoperative embolization on the outcomes of CBT resections are controversial, with many studies reporting no significant difference in EBL.<sup>12</sup>

Among the surgical specialties, CBT diameter was similar for OHNS (30 mm) and vascular surgery (31 mm) but significantly larger for combined OHNS and vascular cases (38 mm) with a pvalue of .01 and .02 respectively. EBL was higher in combined cases (304 mL) compared to OHNS (124 mL) or vascular (203 mL) alone, with p-values of .05 and .29 respectively. This higher EBL in combined cases is likely due to the added complexity and larger sizes of CBT.<sup>2</sup> Of the 79 surgeries performed, 5 patients experienced adverse events of new-onset arrythmias and hypertension. Combined OHNS and vascular cases had the highest percentage of new-onset arrythmias at 5.1% (p = .01), but of these patients, all new-onset arrhythmias and hypertension resolved by discharge. There were four recurrences and one case of metastatic disease. Our recurrence rate of 5% is comparable to previously reported rates.<sup>15</sup> Based on previous literature, overall survival rate is primarily influenced by remote metastasis and local recurrence.<sup>22,23</sup> Given that adverse events were not drastically different between surgical specialties, we maintain that multidisciplinary surgeries have similar or better outcomes in CBT resections when compared to OHNS or vascular surgery alone.

One of the limitations to this single-institution study is the relatively subjective estimation of EBL in surgeries, which has been documented previously in regards to endoscopic sinus surgeries and likely holds true for carotid body tumor resections.<sup>24</sup> Furthermore, there was an expected selection bias in that larger and more complex tumors with higher Shamblin grades were more likely to be resected under a combined surgical team due to the expected surgical difficulties and more complex anatomy. A larger sample size across different institutions will be necessary to quantify the extent of benefits in regards to cranial nerve deficits and adverse events specifically. Despite these limitations, the fact that combined cases still had a lower incidence of cranial nerve deficits despite larger tumor size and higher EBL presents a strong case for a multidisciplinary approach to CBT resection. These findings can be extrapolated to other head and neck surgeries, especially those that may risk vascular compromise.

# 5 | CONCLUSION

CBTs can be managed safely and effectively by both vascular and OHNS with minimal differences in EBL or adverse events. Combined OHNS and vascular cases had similar outcomes and lower rates of postoperative cranial nerve injury when compared to single surgical specialty cases despite involving significantly larger tumors and larger EBL. Complex CBT resections benefit from a multidisciplinary surgical approach particularly for larger tumors and more difficult resections. This approach may present more favorable outcomes and minimize the incidence of postoperative cranial nerve deficits.

#### AUTHOR CONTRIBUTIONS

Kirsten Wong: Presentation, analysis, writing. Kenric Tam: Design, writing. Eric Tran: Design, analysis. Dipti Sajed: Data acquisition. Maie St. John: Design, writing.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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