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Role of neck dissections in the management of carotid body tumors

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Abstract

Objective: Carotid body tumors (CBTs) are rare neoplasms of the paraganglia at the carotid bifurcation. While typically benign, CBTs occasionally exhibit malignancy, metastasizing to nearby lymph nodes. Histopathologic analysis alone is insufficient to confirm malignancy, requiring metastases to non-neuroendocrine tissue for a definitive diagnosis. The role of selective neck dissections (SNDs) in detecting malignancy and guiding subsequent management remains uncertain.

Method: A retrospective case series through electronic chart review was performed on 21 patients undergoing CBT surgeries between 2002 and 2022 at a Canadian institution. SNDs were performed on all 21 patients. Data collection included patient demographics, genetic and laboratory testing results, preoperative imaging, intraoperative and postoperative complications, histologic analysis of neck SND and tumor specimen, and follow-up results.

Results: Of the 21 surgical resections, there were three cases (14.3%) of carotid artery injuries and six cases (28.6%) of nerve injuries. One patient (4.8%) experienced three intraoperative strokes. Three patients (14.3%) were found to have lymph node involvement, confirming malignancy, and underwent further treatment with radiotherapy. Interestingly, two patients with carotid injuries had malignant tumors, demonstrating a statistical significance between carotid injury and malignancy (OR 34.00, 95% CI: 1.48, 781.83, $p = .041$).

Conclusion: SNDs are a useful adjunct in detecting malignancy during CBT surgeries. The incidence of malignancy in CBT is low but not negligible, and SND should be considered in patients to prevent inadvertent underdetection of metastatic disease. This study's 14.3% incidence of malignancy suggests that there may be a rationale for considering the universal implementation of SND during CBT resections.

Level of Evidence: 4.

KEYWORDS

carotid artery injury, carotid body tumors, histopathology, neck dissection, paragangliomas

1 | INTRODUCTION

Carotid body tumors (CBTs) are a type of paraganglioma of the head and neck characterized by the abnormal growth of neural crest cells.[1,2] Although CBTs are rare overall, accounting for 0.6% of all tumors of the head and neck,[3] they account for over 50% of head and neck paragangliomas.[4–6] These slow-growing neoplasms are known for their highly vascular nature, typically with multiple feeding arteries and adhesions to the carotid artery.[7,8] CBTs frequently develop at the bifurcation of the carotid artery, posing challenges to their management.[8] Approximately 90% of CBTs are considered sporadic, and the remaining 10% are classified as familial cases, suggesting a genetic predisposition within affected families.[4,5,9] Of the familial cases, the most common mutations are in genes associated with the mitochondrial succinate dehydrogenase (SDH) complex subunits SDHD, SDHB, SDHC, or SDHAF2.[6,9,10]

Surgical resection is widely regarded as the gold standard treatment method for CBT due to the potential for metastatic disease.[9,11–13] Given the delicate positioning of these tumors among crucial nerves and vessels in the head and neck, as well as their highly vascular nature, it is important to carefully assess the potential for complications following resection.[7,8] Key considerations include the risk of damage to the internal and external carotid arteries and the vagal and hypoglossal nerves, along with the potential for cerebrovascular events.[4–6] To aid in surgical planning, the Shamblin Classification System is used to predict the difficulty of surgical resection and risk of postoperative complications.[1,4,6,8,12] This system classifies CBT into three classes based on their size and involvement of the carotid artery. Due to the pronounced vascularity of CBT, preoperative embolization is commonly employed as a measure to mitigate excessive blood loss. However, it is worth noting that the utility of this technique has been debated, and many surgeons opt not to perform preoperative embolization.[2,5,14,15]

Although current literature suggests approximately 95% of these tumors are benign in nature,[5,6,9] potential for malignancy remains a crucial consideration in formulating a management plan. Assessing the preoperative malignancy risk of these tumors remains a formidable challenge due to the lack of distinct clinical features differentiating benign and malignant CBT.[2,5,16] Although imaging modalities such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) can aid in determining the size, location, and degree of vascular involvement, they lack the ability to classify these tumors as benign versus malignant.[3] Histopathological analysis, including detection of central necrosis, vascular invasion, and nuclear atypia, plays an important role in confirming a diagnosis of CBT.[3] However, both benign and malignant tumors involve the same two major cell types of paraganglia tissue, epithelioid chief cells, and sustentacular supporting cells, clustering in a “Zellbalen” pattern.[3] As a result, histopathologic analysis alone is considered insufficient to confirm malignancy.[3,5,10] Therefore, metastasis to non-neuroendocrine tissue, such as cervical lymph nodes or distant sites, is required to definitively diagnose a CBT as malignant.[3,5,16] One approach to this diagnosis is the use of intraoperative selective neck dissections (SNDs) at the time of tumor resection.[3,5,16] SND offers valuable prognostic information by allowing the resected lymph nodes to undergo histopathologic analysis to determine whether the CBT is malignant or benign. Additionally, SNDs facilitate optimal exposure of the tumor and surrounding structures by dissecting the region surrounding the carotid body, enabling precise, and effective resection. Moreover, in cases where the CBT is found to be malignant, SND plays a critical role in preventing the spread to distant sites thus improving overall survival. By employing this approach, a prompt diagnosis can be achieved shortly after surgical resection, enabling the timely formulation of an appropriate management strategy. The significance of SND in detecting malignancy of CBT remains uncertain. This study aims to assess the utility of SND in the management of CBT and determine its potential role in improving diagnostic accuracy and patient outcomes.

2 | METHODS

This study employed a comprehensive approach to data collection and analysis for assessing the necessity of intraoperative SND in detecting malignancy of carotid body tumors. A thorough review of existing literature on carotid body tumors was conducted to identify relevant variables and outcomes of interest for analysis. The variables were categorized into three stages: preoperative, intraoperative, and postoperative. A standardized data abstraction template, encompassing all pertinent variables of interest, was utilized for data extraction. The preoperative variables encompassed patient demographics, medical history, tumor location within the neck (right, left, or bilateral), imaging modality, tumor dimensions, genetic testing results, Shamblin Classification, and the administration of preoperative embolization. For patients with bilateral CBT, only the first tumor was considered in this analysis. Shamblin classification was determined by operative dictations and retrospective analysis of imaging. Intraoperative variables included procedure duration, incidence of intraoperative vessel or nerve injuries, completion of SND, and total blood loss. Postoperative variables consisted of postoperative nerve injuries, cerebrovascular events, the occurrence of First Bite Syndrome, histopathologic analysis, laryngoscopy findings, postoperative radiotherapy, and disease recurrence.

A retrospective case series was conducted through an electronic chart review, involving 21 patients who underwent carotid body tumor surgeries between 2002 and 2022 at a Canadian institution. Due to the retrospective nature of the study and the absence of identifiable patient information, this project was deemed exempt from Research Ethics Board review by the Nova Scotia Health REB (File No. 1028926). Convenience sampling was employed given the rarity of carotid body tumors and the limited sample size.[17] Data were collected from various sources including diagnostic imaging results, genetic testing outcomes, operative notes, pathology reports, and follow-up visits. The primary outcome of the study was the presence of metastatic disease identified during neck dissection. The analysis focused on factors associated with this outcome, including intraoperative carotid injury. Additional descriptive analyses were performed to characterize surgical outcomes. Disease recurrence was defined as any new local or distant occurrence of disease as confirmed by imaging results or pathology results if surgical re-resection was performed. Morbidity was defined as postoperative complications requiring reintervention or resulting in long-term disability. After completing the chart review and data abstraction process, a comprehensive analysis of the collected data was conducted to identify and examine any notable trends. Statistical significance was assessed through the utilization of a two-sided Fisher's exact test to compare the proportions of patients with and without metastatic disease to those with and without carotid injury. Confidence intervals were calculated to quantify the strength of this association.

3 | RESULTS

3.1 | Patient demographics

Chart reviews were conducted for 21 patients who underwent carotid body tumor resections. Among the included patients, 11 (52%) were female and 10 (47%) were male. Patient ages ranged from 28 to 69 years with a mean age of 43.3. The average tumor size was 5.6 cm (range, 2.2–10.0 cm). Six tumors (29%) were bilateral, but seven tumors (33%) were right-sided, and eight tumors (38%) were left-sided. Nineteen patients were assigned Shamblin Classifications: two class one, eleven class two, and six class three. One case (4.7%) presented with a family history of paragangliomas.

3.2 | Preoperative assessment

Preoperatively, five patients underwent genetic testing, with two testing positive for the SDHD gene mutation and one for the SDHC gene mutation. Positive genetic testing was associated with a younger mean age (32.7) at presentation. Three patients (14%) had secretory tumors and underwent alpha blockade prior to surgery. Twelve patients (57%) underwent preoperative embolization. There was no observable difference in the rate of intraoperative vessel injuries, blood loss, duration of operation, or overall outcomes in those patients, as compared to the patients who underwent this procedure.

3.3 | Surgical procedures

All surgical resections were performed in collaboration between otolaryngology–head and neck surgery and neurosurgery. Of the 21 surgical resections, there were three cases of (14.3%) carotid artery injuries and six cases (28.6%) of nerve injuries. Among these cases, two were repaired by vascular surgery with saphenous vein interposition grafts which were end-to-end for both CCA and ICA, and the remaining injury was repaired by neurosurgery with a Xeno-Sure Biological Patch graft. Notably, two of these three patients had a malignant CBT, demonstrating a statistically significant relationship between carotid injury and malignancy (OR 34.00, 95% CI: 1.48, 781.83, $p = .041$). Of the nerve injuries, five were to the vagal nerve and one was to the hypoglossal nerve. In two of the five patients with vagal nerve injuries, the tumor was found intraoperatively to be a glomus vagale tumor, requiring a sacrifice of the nerve. In addition to their elective tumor resection, five patients underwent additional procedures at the time of resection, including one thyroid lobectomy, one mandibulotomy, two saphenous vein grafts to reconstruct the carotid artery, and one sural nerve graft to reinnervate the spinal accessory nerve. All patients underwent intraoperative SND of levels IIA and III. Level IIB, the submuscular recess, was excluded due to the risk of devascularization of the spinal accessory nerve. The mean number of nodes resected was seven (range, one to 17). All neck dissection contents were sent for histopathological analysis along with the primary specimen. The mean duration of surgery was 304 min (range, 191–698 min) with a mean blood loss of 340 mL (range, 100–1100 mL).

3.4 | Postoperative outcomes

Postoperative complications ranged from severe to mild and self-limiting. Although only five patients were known to have injuries to the vagal nerve, eight patients (38.1%) demonstrated vocal cord paresis during follow-up laryngoscopy. Four patients (19.0%) experienced First Bite Syndrome, three of which were self-limiting, but one patient required botox injections. One patient (4.8%) experienced contralateral hand weakness and ipsilateral facial droop, later revealed by MRI of the brain to be due to three peri-operative embolic strokes. This patient had tumor embolization immediately prior to resection under the same general anesthetic.

Histopathological analysis was conducted for all resected tumors and neck dissection contents. Overall, three patients (14.3%) were found to have lymph node involvement, indicating the presence of malignancy. These three patients underwent further treatment with adjuvant radiotherapy. Of these three patients, two showed no disease recurrence, but one patient (4.8%) later developed terminal metastatic disease. This patient was younger than all other patients in the study, at 28 years, but did not receive genetic testing. Patient demographics and tumor characteristics are summarized in Table 1.

4 | DISCUSSION

4.1 | Literature review

The management of CBT lacks universal clinical guidelines, and the existing literature on the use of SND during CBT tumor resection presents mixed findings. Some authors advocate for mandatory SND, citing the need to rule out malignancy by examining regional lymph nodes.[3,16] Conversely, others argue that neck dissections do not significantly impact overall patient outcomes and should not be obligatory, though they acknowledge the value of neck

TABLE 1 Summary of patient demographics and tumor details.

	Sex	Age[a]	Tumor size (cm)	Side of neck	Shamblin classification	Secretory tumor	Carotid injury	Positive lymph nodes
Case 1	F	<43	5.5	R[b]	II	✓	X	0
Case 2	F	>43	4.2	L[b]	III	X	X	0
Case 3	M	>43	3.8	R	II	X	X	0
Case 4	F	>43	2.3	L	II	X	✓	2
Case 5	M	<43	10.0	R	III	X	X	0
Case 6	F	>43	5.6	L	II	X	X	0
Case 7	M	<43	5.5	L	III	X	✓	4
Case 8	M	<43	2.7	L	II	X	X	0
Case 9	M	>43	3.5	R[b]	III	X	X	0
Case 10	M	>43	8.0	L	II	✓	X	0
Case 11	F	<43	2.9	R	II	X	X	0
Case 12	F	>43	NR	L	I	X	X	0
Case 13	M	<43	5.1	R[b]	II	X	X	0
Case 14	F	<43	7.1	L	III	X	X	0
Case 15	M	<43	7.0	R	III	X	X	2
Case 16	F	>43	6.0	R	II	X	X	0
Case 17	F	<43	3.0	R	NR	X	X	0
Case 18	F	<43	5.7	R[b]	II	X	X	0
Case 19	M	>43	5.2	L	II	X	X	0
Case 20	M	<43	2.9	R	NR	X	✓	0
Case 21	F	<43	2.2	L	I	✓	X	0

Abbreviation: NR, not recorded.
[a]Patient age was categorized using a threshold of mean age to avoid inadvertent reidentification.
[b]These patients had bilateral tumors, with only one included in this study.

TABLE 2 Summary of literature review findings.

		Sample Size, *n*			Malignancy Rate, *n* (%)			CA injury Rate, *n* (%)		
Authors	Year	ND	No ND	Total[a]	ND	No ND[b]	Total	ND	No ND	Total
Ma et al.	2022	68	58	126	7 (10.3)	2 (3.5)	9 (7.1)	NR	NR	NR
Yang et al.	2022	133	0	133	10 (7.5)	0	10 (7.5)	NR	NR	3 (2.3)[c]
Davila et al.	2016	99	84	183	0	1 (0.5)	1 (0.5)[d]	NR	NR	20 (10.9)
Illuminati et al.	2021	23	65	88	1 (4.3)	1 (4.3)	2 (2.3)	1 (4.3)	6 (9.2)	7 (8.0)
Javidiparsijani et al.	2023	20	10	30	2 (10)	1 (10)	3 (10)	NR	NR	NR
Patetsios et al.	2002	34	0	34	3 (8.8)	0	3 (8.8)	8 (23.5)	0	8 (23.5)

Abbreviation: NR, not recorded.
[a]Total refers to number of CBT, not number of patients.
[b]Malignancy in patients in the "No ND" group was discovered by recurrent disease and subsequent ND.
[c]The rate of vessel injury in this study was only reported for malignant cases.
[d]This patient was in the ND group and had negative nodes at the time of primary resection.

dissections in disease staging and planning adjuvant treatment.[5] Certain studies have demonstrated that SND, particularly targeting level IIA, can indeed enhance patient outcomes without causing additional cranial nerve injury.[16]

Due to the rarity of CBTs, there are a limited number of studies assessing malignancy rates over the period of our data. Among the existing studies, reported malignancy rates range from 0.5% to 10.0% (Table 2).[5,16,18–21] Davila et al. (2016) investigated a cohort of 183 patients, with 99 undergoing neck dissections, and reported a malignancy rate of 0.5%, representing a single patient with negative nodes at the time of resection. This rate is significantly lower than our observed rate of 14.3%, which may be partially attributable to the lower rate of neck dissections performed in their study (54.1%). In contrast, Yang et al. (2022) examined 133 CBT patients, all of whom underwent

SND during primary resection and reported a malignancy rate of 7.5%. Although this rate aligns more closely with our findings, it remains substantially lower. Additionally, Ma et al. (2022) found a significantly higher rate of disease recurrence in patients who did not undergo SND at the time of primary tumor resection. In their study, SND was found to be an independent risk factor for relapse-free survival (RFS) with the SND group having a significantly higher and longer RFS than the non-SND group.[16] The higher malignancy rate observed in our study is likely due to our institution's practice of performing SNDs on all patients, which inevitably results in a higher detection rate of malignancy compared to other studies where the frequency of SNDs varies, potentially leading to missed cases of malignancy.

Our study found a 14.3% rate of carotid artery injury, representing a statistically significant relationship between carotid artery injury and malignancy. Carotid injury was not specifically addressed in many studies, and among those that did, not all differentiated whether the injuries occurred in cases of malignant CBTs. Of the studies that mentioned this complication, several reported higher rates of carotid artery injury compared to rates of malignancy.[5,18,21] Davila et al. (2016) reported a 10.9% rate of carotid artery injury despite a 0% malignancy rate at the time of resection. In contrast, Yang et al. (2022) observed that among 10 cases of malignant CBTs (7.5%), three cases (30%) were associated with carotid artery injuries.

Our cohort consisted of 52.4% female participants, which is slightly lower than the proportions reported in the literature.[3,22] Additionally, two of the three malignant CBTs were in male patients. However, these differences are likely attributable to the small sample size of our study.

One of the major challenges in the management of CBT is the limited ability to diagnose malignant paragangliomas using preoperative imaging or solely by histologic analysis of the primary tumor specimen.[3,5,20,23,24] Although functional imaging, such as octreotide and Gallium-68 PET/CT scans, can identify paragangliomas and assess metastatic spread, their ability to definitively predict malignancy remains limited. Imaging findings must be correlated with histopathological examination for accurate diagnosis. Therefore, incorporating intraoperative SNDs provides an effective solution by allowing for prompt identification and staging of potential metastatic disease that may have otherwise been missed. This approach enables timely management and prevents the progression of distant disease. Importantly, performing SNDs does not considerably prolong the duration of the operation or add substantial complexity.[5] Furthermore, this approach eliminates the need for a second surgery and its associated risks in cases where metastatic disease is suspected following the primary operation. For patients with nonmetastatic disease, knowledge of the benign nature of their tumor offers relief, reassurance, and permits less stringent monitoring and surveillance imaging. These findings support the universal implementation of SND during CBT resection to enhance malignancy detection and reduce disease recurrence, thereby improving patient outcomes.

4.2 | Limitations

This study has three limitations: its small sample size, its retrospective nature, and the presence of confounding variables. The small number of cases restricts the generalizability of the conclusions drawn from this data. Additionally, with all patients in this study having undergone SND at the time of primary tumor resection, we are unable to speak to the benefit of SND on long-term outcomes. However, previous studies suggest there is no difference in long-term outcomes for either group.[5] The retrospective nature of this study introduces limitations in terms of data availability. However, due to the rarity of this condition and with this study being limited to one institution, obtaining a larger sample size or using a prospective design presents significant challenges. Lastly, the presence of unmeasured or unknown confounders may influence the observed associations.

5 | CONCLUSION

Although the incidence of malignancy in carotid body tumors is low, it is not negligible. Therefore, selective neck dissections should be considered for all patients undergoing CBT resection to avoid missing malignant cases and prevent metastatic spread. The 14.3% incidence of malignancy in this study suggests that this approach can provide several benefits, including enhancing diagnostic accuracy by allowing for the detection of malignancy, enabling staging of the disease, and allowing for the timely formulation of management plans. The opportunity for prompt management and avoidance of a second surgery offers patients both physical and psychological benefits. However, further studies with larger patient populations are warranted to corroborate these findings and establish more robust guidelines for the management of carotid body tumors.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interests.

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