Results from Craniocaudal Carotid Body Tumor Resection: Should It be the Standard Surgical Approach?

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WHAT THIS PAPER ADDS

This study shows that intra and post-operative results, achieved with this craniocaudal surgical technique, compare favorably with those achieved with the conventional technique, as reported in the literature. As carotid body tumors are rare and the surgical treatment has not been standardized, results can be disappointing. This study, along with previous studies on the craniocaudal technique, offers the best available evidence that the craniocaudal approach should be the surgical technique of choice.

Objectives: To evaluate results after carotid body tumor (CBT) surgery using a novel dissection technique.
Methods: A retrospective analysis of all operated CBT in the last 6 years was carried out and results were compared with the current literature and our previous series, which reported another 111 cases operated on until 2005.
Results: Forty-five CBTs were removed in 41 (56% hereditary cases) patients (seven Shamblin I, 22 II, and 16 III). There were no cases of permanent cranial nerve injury or stroke.
These pre- and postoperative results compare favorably with our previous series and are superior to, generally smaller, studies reported in the contemporary literature.
Conclusions: This large series of surgically-treated CBTs supports craniocaudal dissection as the surgical technique of choice as it limits blood loss and facilitates safe CBT resection.

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INTRODUCTION

Carotid body tumors (CBT), also known as carotid paragangliomas, are neoplasms localized in the bifurcation of the common carotid artery. Like other paragangliomas, these tumors are highly vascularized. Although considered benign and slow-growing, growth of CBT is related to neuropraxia of cranial nerves.[1] Surgery is widely accepted as the preferred treatment for CBT, with the goal of treating or preventing local advancement of the tumor. In the early stages of the CBT the aim of the surgical management is the complete removal of CBT to prevent further growth and incorporation of neurovascular structures, the latter leading to increased intra-operative blood loss and postoperative morbidity. In the more advanced stages surgery may be indicated to relieve patient's discomfort. Owing to the properties of this tumor and its localization adjacent to multiple neurovascular structures, the resection may be extremely challenging.

Historically, the surgical procedure started by devascularization of the CBT with ligation of the caudal feeding branches from the external carotid artery. Subsequently, resection of the CBT was started at the carotid bifurcation, dissecting towards the cranial side.[1] With this technique there was still considerable intra-operative blood loss and a significant percentage of postoperative cranial nerve damage (15–20%).[2] In 2008, a modified operative technique was described whereby the dissection is performed in a craniocaudal fashion.[2] This technique is based upon the course of the ascending pharyngeal artery, which is suggested to be the tumor's main proximal blood supply and usually enters the CBT from its cranial side.[3] The craniocaudal approach carries the advantage of identifying the adjacent nerves on the tumor's cranial side at an early stage to prevent accidental damage in case of hemorrhage later during the operation. Compared with other studies on conventional surgical techniques, this novel craniocaudal approach resulted in more favorable outcomes considering blood loss and postoperative cranial nerve damage.[2]

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Since 2005 the craniocaudal approach became standard operative practice at the Leiden University Medical Centre. The aim of this study was to evaluate intra-operative blood loss and postoperative outcomes of all surgically treated CBT patients since 2005. In addition, the influence of tumor and patient characteristics on postoperative outcome were investigated and results were compared with the current literature.

MATERIALS AND METHODS

A retrospective analysis was performed including all 45 consecutively operated CBTs in 41 patients at Leiden University Medical Center between 2006 and 2011. This retrospective study did not require ethical review from our institutional review board. All patients received low-molecular heparin immediately pre-operatively and underwent CBT surgery according to the craniocaudal method. In short, the craniocaudal dissection technique is based upon early identification of the vagal, hypoglossal, and accessorial nerves, control of the internal carotid artery, and ligation of the ascending pharyngeal artery, all at the CBT's cranial side. Thereafter, dissection is carried out in a cranial-to-caudal fashion.[2] Data were studied and reported according to pre, intra-, or postoperative periods.

All the tumors were classified by the Shamblin classification. Shamblin I tumors are small, localized tumors. Shamblin II tumors approach surrounding vessels or partly enclose them. Shamblin III tumors are large and fully enclose adjacent vessels.[4]

The follow up consisted of a clinical check-up by both an ear, nose, and throat specialist and a vascular surgeon. Fig. 1 shows how follow up is being performed at our institution. Long-term follow up from our previous study[2] was also done to investigate what the recurrence rate of the CBT was in craniocaudally approached CBTs. Data were reported as mean $\pm$ SD. To explore the correlation between two numeric variables a scatterplot was used. To investigate whether Shamblin classification was of significant influence on the total intra-operative blood loss (as estimated by the amount of used gauzes and suctioned blood in the container), a post hoc one-way analysis of variance (ANOVA) was performed. In order to explore the relationship between Shamblin

Table 1. Pre-operative characteristics of patients, tumors, and diagnostics.

	n	%	Mean
Total patients	41		
Men	18	44	
Women	23	56	
Age (y)			38
Existence of complaints (mo)			31
Body mass index			24
Right-sided CBT	9	22	
Left-sided CBT	8	20	
Bilateral CBT	24	58	
Family history of CBT	23	56	
Computed tomography	1		
Angiography	0		
Magnetic resonance imaging	45		
Pre-operative cranial nerve injury	13	29	

Note. CBT = carotid body tumor.

classification and the occurrence of postoperative cranial nerve damage, a linear-by-linear chi-square test for trends was used. A Mann—Whitney test was used to compare numeric with categorical variables. *p*-values were considered significant if $<.05$.

Finally, the results of this study were compared with other recent studies involving the surgical resection and management of CBT, in which at least 10 patients were included. A literature search was performed in PubMed. The query consisted of the combination of two subjects: carotid body tumor and surgery/resection. Results were limited to articles published in English from 2005 onwards. The final search was performed on 14 June 2013. The search yielded 201 results (Supplementary Fig. S1).

RESULTS

Between 2006 and 2011, 41 consecutive patients were operated on. All patients were included in this study. Table 1 shows the pre-operative characteristics of the studied group. There were 18 men and 23 women, with a mean age of 38 years (range, 16—61 years). Two patients presented after testing positive for a *SDHD* mutation, and proved to have CBT on imaging workup (n = 2, 4.3%). The

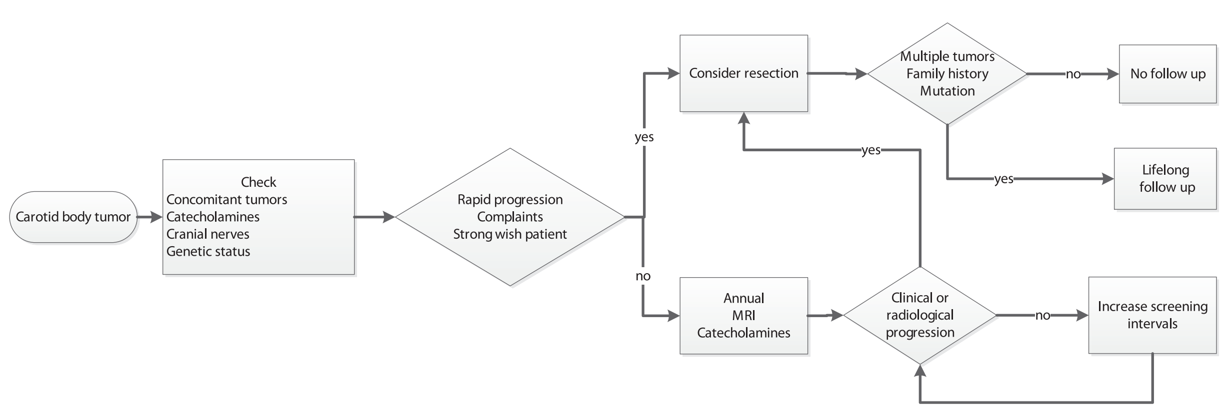

Figure 1. Follow-up algorithm. *Note*. MRI = magnetic resonance imaging; CBT = carotid body tumor. [a]*SDHD* and *SDHB* mutations both result in a greater chance of developing chromaffine-positive pheochromocytoma, but SDHB more often than SDHD.

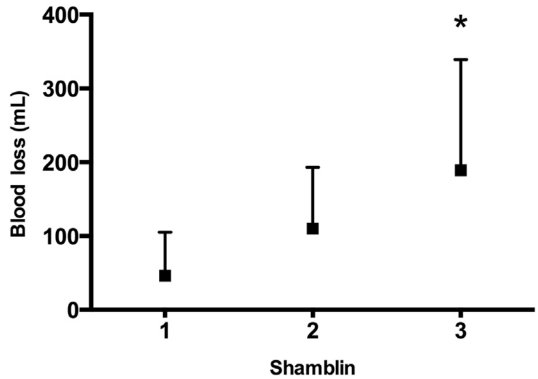

Figure 2. Mean operative blood loss of 45 carotid body tumor resections. *Note*. *$p < .05$ (post hoc one-way analysis of variance).

primary symptom at presentation was a growing neck mass leading to either mechanical or cosmetic complaints ($n = 29$, 61.7%). Another frequent complaint was problems with swallowing ($n = 3$, 6.4%), while tinnitus, dizziness, and throat pain were less frequently, secondarily reported. In total, 10 patients presented pre-operatively with neuropraxia, concerning the hypoglossal nerve ($n = 5$) and the marginal mandibular branch of the facial nerve ($n = 5$).

In this study, 23 out of 41 (56%) patients suffered hereditary CBT. From these 23 patients 17 (74%) had bilateral CBT. In total, 24 patients suffered bilateral CBT, with the hereditary part being 17 (71%). Eight tumors were located on the left (none of them were hereditary cases) and nine tumors were located on the right, with six (66.7%) being of hereditary origin.

Seven tumors were classified as Shamblin I, 22 as Shamblin II, and 16 as Shamblin III. The mean gross size of the tumors was 3 cm^3 for the Shamblin I, 14 cm^3 for the Shamblin II, and 22 cm^3 for the Shamblin III tumors.

All the patients underwent magnetic resonance imaging (MRI) for preoperative diagnostics. One patient also underwent computed tomography. None of the patients was treated with pre-operative embolization.

The mean operation time was 210 $\pm$ 99 minutes, and overall mean blood loss was 129 $\pm$ 120 mL. The blood loss related to Shamblin classification was 46 $\pm$ 59 mL, 110 $\pm$ 83 mL, and 189 $\pm$ 150 mL for class I, II, and III, respectively (Fig. 2). The peroperative blood loss during Shamblin III CBT resection proved to be significantly increased compared with Shamblin I ($p = .008$) and Shamblin II ($p = .048$, post hoc one-way ANOVA).

In four patients with generally larger tumors (Shamblin III, $n = 3$), extensive CBT incorporation of the arteries necessitated total removal of the internal and external carotid artery followed by reconstruction of the ICA using greater saphenous venous grafts. None of them suffered from temporary postoperative cranial nerve damage. In four patients, the external carotid artery had to be removed en bloc with the CBT, of which one patient developed postoperative transient neuropraxia.

In total, 12 patients (26.7%, of which one with preoperative neuropraxia) suffered from temporary postoperative cranial nerve damage: five in the Shamblin II (29.4%) and seven in the Shamblin III (77.8%) group. Temporary paresis of the hypoglossal and facial (marginal mandibular branch) nerves (both $n = 3$) was most frequently reported, and all resolved within 1 month. The linear-by-linear association test showed that there was a significant chance of developing postoperative temporary cranial nerve damage with increasing Shamblin classification ($p = .026$).

In the present study no significant correlation was found, but there was a trend between peroperative blood loss and development of postoperative neuropraxia ($p = .064$). In this series one patient (presenting with a Shamblin III CBT) suffered from a minor non-disabling stroke concerning the area of the right middle cerebral artery 7 days postoperatively. The patient's complaints resolved within a few days and there was no persistent damage clinically and diagnostically as computed tomography angiography and MRI did not show ischemia. Including this case, there were no reports of persistent cranial nerve damage amongst the entire study group. Other postoperative complications were bleeding ($n = 1$) and superficial wound infection ($n = 1$), which both needed re-operation.

The mean follow up was 2.5 years. During this period, no deaths were reported and, to date, no recurrence or distant metastasis of CBT have presented. One tumor proved to be malignant as one regional metastatic lymph node was found. Long-term follow up (mean of 11 years) from our previous study shows a recurrence rate from 17% (7/42). From those seven patients five were hereditary cases (71%).

DISCUSSION

Considerable blood loss, persistent cranial nerve damage, and stroke are complications encountered during and after CBT surgery. While stroke has become a rare complication, cranial nerve damage appears the most important adverse outcome nowadays. The recent evaluation of surgically-treated CBT cases after the introduction of a new craniocaudal approach[2] suggested a considerable decrease of these main complications. While in the previous series all operations were performed or supervised by one surgeon, the craniocaudal approach is now reproducible and performed by all vascular surgeons at our institution.[2] Today—several years later with increased surgical experience on this subject and raised awareness of possible complications—improved results considering postoperative morbidity can be expected. The present follow-up study is one of the largest studies concerning the management of CBT. The primary outcomes of the study were peroperative blood loss and temporary or persistent cranial nerve damage.

First, the mean estimated blood loss of 129 mL in the present study compares favorably with other recently published studies concerning the surgical management of CBT (outlined in Table 2),[2,5–16] as well as our previous series (mean estimated blood loss 281 mL).[2] This difference may be explained by the experience our institution has in treating CBT as a result of the tertiary reference role. The

Table 2. Summary of larger (>10 carotid body tumors [CBT]) contemporary studies evaluating CBT management.

Study	Years	Patients (n)	Men/women	Mean age (y)	CBT (n)	Shamblin (I,II,III)	PFH (%)	PBL (mL)	CND (%)	Postoperative stroke
Avgerinos et al.[5]	35	27	48/52	46	27	8,11,10	7	420/780/1366[c]	—	—
Desmond and Christopher[12]	9	10	40/60	31	11	3,6,2	20	—	10	—
Ma et al.[11]	12	18	56/44	52	18	10,5,3	—	—	0	—
Lim et al.[6]	?	13	46/54	44[b]	15	1,4,8	0	280/700[d]	23	2
Kruger et al.[10]	25	39	44/56	49	49	?,?,5	28	—	18.3	—
Ma et al.[14]	12	53	30/70	43[b]	57	16,30,11	6	—	6	2
Qin et al.[7]	25	33	47/53	36	33	3,2,9	0	860	—	—
Makeieff et al.[9]	17	52	67/33	43	57	15,28,14	7	145/263[d]	14.03	1
Dalainas et al.[13]	20	17	12/88	48	18	3,6,8	0	—	5.8	0
Ozay et al.[8]	7	14	36/64	43	14	5,4,5	7	397	0	0
Fruhmann et al.[16]	25	50	17/33	55	63	13,28,22	2	—	0	1
Li-Shan et al.[15,a]	62	111	—	—	117	—	—	—	25.6	3
Van der Bogt et al.[2]	42	94	44/50	41	111	51,35,25	—	901/281[e]	21/5[e]	0

Note. PFH = positive family history; PBL = peroperative blood loss; CND = persistent cranial nerve damage.
[a] Only the abstract was available.
[b] Median instead of the mean.
[c] Shamblin I/II/III respectively.
[d] The first value stands for the mean of the Shamblin group I and II, the second value is the mean for the Shamblin III group.
[e] The first value refers to surgery following the standard procedure, while the second value represents results of the cranial-caudal approach.

results of a recent study by Makeieff et al.[9] are comparable with this study, with a mean blood loss of 145 mL in Shamblin I and II tumors, and a mean of 263 mL in Shamblin III tumors. However, despite this low blood loss, a considerably higher rate of postoperative complications, reported as persistent cranial nerve damage, was encountered in 14% of their patients.

Second, in the present study, patients suffering from postoperative temporary neuropraxia all recovered spontaneously. This absence of persistent cranial nerve damage after any of the CBT operations is remarkable, as other studies report significant occurrence of this disabling complication. Lim et al.[6] have reviewed 15 tumors and experienced 23% persistent cranial nerve damage, although it must be stated that this study included a relatively large amount of complex Shamblin III tumors ($n = 8$, 61%). Kruger et al.[10] described an incidence of 18.3% in a study of 49 CBTs in 39 patients, without providing exact information regarding Shamblin classification. Smaller studies performed by Ma et al.[11] and Ozay et al.[8] showed comparable rates of persistent cranial nerve damage to the present study, although our study included considerably more Shamblin III CBTs.

In the present study a trend has been noticed in the chance of developing postoperative neuropraxia with increasing peroperative blood loss. This emphasizes the importance of a dry surgical field, which facilitates the identification of the adjacent nerves, arteries, and veins. The blood supply of the CBT is extensive and its main source is the ascending pharyngeal artery.[3] Although proximal ligation of the external carotid artery could also lead to a decrease in tumor blood flow, preparation of the common carotid artery and the proximal part of the external carotid artery is a challenge in itself in case of a CBT. In this respect, a craniocaudal approach might be preferred because the main blood supply of the CBT (the ascending pharyngeal artery) is encountered at the tumor's cranial side and ligated at an early stage. This provides a dry surgical field and a decrease in tumor volume, and therefore facilitates the dissection from adjacent structures.

Another way to prevent blood loss is pre-operative embolization. However, precaution should be taken when initiating embolization as side effects (e.g. distal migration of the embolization medium) can be detrimental.[17,18] At some institutions pre-operative embolization is preferred before surgical resection because this will lower the volume and blood flow of the tumor. Consequently, the CBT could be resected more easily with minimal blood loss. Shah et al.[19] recently published a study that investigated a new medium for embolization, EVOH (ethylene vinyl alcohol copolymer). No strokes and a mean of 55 mL blood loss were reported. Kalani et al.[20] showed that pre-operative embolization, using a transfemoral transarterial onyx technique, is a successful way to embolize the CBT. Tumor devascularisation of 88% was achieved, with an average peroperative blood loss of 192 mL. Although these results are encouraging, other recently published studies have shown less favorable outcomes. Gemmete et al.[21] showed that there is a higher risk of developing stroke secondary to pre-operative embolization in selected patients. With only one minor non-disabling stroke and considering the minimal blood loss since the introduction of the craniocaudal approach in 1992, pre-operative embolization is not part of CBT management at our institution. Thus, in respect of peroperative blood loss, postoperative complications, and overall safety, the current findings show that craniocaudal CBT dissection provides a dry surgical workfield and compares favorably with the conventional approach (starting at the bifurcation), either with or without embolization.

In the current series, there is a high prevalence of hereditary CBT patients (56%, of which 74% suffered bilateral CBT). The cause of this high percentage is to be attributed to the high prevalence of patients with a *SDHD* mutation in parts of the Netherlands. At our institution, because of the high incidence of the mutation, family members of our patients all receive screening. For this reason, we diagnose relatively more CBTs at an early stage, allowing a generally longer follow up before operation. The *SDHD* mutation is known for its correlation to the development of paragangliomas, including CBT.[16,22] Remarkably, among hereditary cases with unilateral tumors (26%), all were right-sided CBTs. Moreover, a greater part of all bilateral cases started on the right side, and this was significant ($p = .033$). Further research is currently ongoing and will explore the relationship between CBT side and SDHD mutation, as well as its clinical relevance.

Our previous study[2] shows a relatively high percentage of recurrence (17% of which 71% were hereditary cases) when compared with recently published studies. This may be a result of high incidence of hereditary cases in combination with a screening-intensive longer period of follow up. However, it can not be ruled out that this is due to irradical resection, although it must be stated that, to date, no recurrence from the current study group has been diagnosed.

To date, there has not been a standard treatment for CBT. The rareness of this tumor does not facilitate a large randomized controlled trial for the best surgical approach or non-surgical treatment to be assessed. For this reason, results achieved with the craniocaudal technique can only be compared with the previously obtained results from our institution or to other contemporary studies, which is scientifically suboptimal. Specialists will persist to perform a treatment that they are familiar with if this provides the best result for their ability. This includes pre-operative embolization that, as mentioned before, can lead to acceptable results in experienced hands, but is not necessary when similar results are achieved in a single surgical session. This study shows once more that safe surgical removal of CBT can be performed using the craniocaudal technique. This adapted surgical technique combined with further centralization of CBT surgery in national tertiary referral centres will likely lead to a minimum of postoperative morbidity. Based on the findings from our current and former studies, which, taken together, are the largest single-institution experience to date, we therefore suggest that the craniocaudal approach should be the surgical technique of choice for CBT resection.

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None.

CONFLICT OF INTEREST

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tube.2013.08.003.

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