



Surgical outcomes for carotid body tumour resection without preoperative embolization: a 10-year experience

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Background: Carotid body tumours (CBTs) are neoplasms originating from the paraganglionic cells of the carotid body. Excision is the main route of treatment. This study sought to assess the surgical outcomes of post-carotid body tumour resection without preoperative embolization and discern any underlying relationships between modified Shamblin classes (MSC) and related complications.

Methods: A retrospective medical record review of prospectively collected data is performed at Sulaymaniyah Teaching Hospital between 2008 and 2019, for 54 patients. Presurgical and postsurgical variables such as comorbidities and complications were noted, respectively.

Results: Patient ages ranged between 26 and 60 years ($\bar{x} = 40.06$) with a minimal female predominance (57.4%). Complications included one minor stroke. MSC and postoperative complications were significantly related ($P \leq 0.001$). Our analyses also suggested a significant relationship between intraoperative blood loss and the incidence of postoperative complications ($P = 0.001$, $\chi^2 = 25$). The MSC III subtype was significantly associated with intraoperative blood loss ($P = 0.000$), length of stay ($P = 0.000$), and operating time ($P = 0.001$).

Conclusions: Our study purports a strong relationship between greater MSC and complications of all types. As such, surgeons may benefit from preoperative strategies to minimize complications.

Keywords: carotid body tumours, complications, cranial nerve injury, modified shamblin class, preoperative embolization, stroke

Introduction

Epidemiology

Carotid body tumours (CBTs) are neoplasms originating from the paraganglionic cells of the carotid body. The carotid body is a chemoreceptor organ, localized to the bifurcation of the common

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HIGHLIGHTS

- Carotid body tumours are rare head and neck tumours
- Preoperative optimization is mandatory for minimal post-operative outcomes.
- Shamblin classification is helpful for predicting postoperative complications.
- Preoperative embolization is not mandatory for the prevention of mortality.
- Surgical resection yields optimal treatment outcomes.

carotid artery^[1]. Though rare, with an incidence of 1–3/100 000, these tumours are primarily slow-growing, benign masses^[1]. Albeit unlikely, these tumours can present aggressively, with literature citing a mortality rate of 8% of untreated cases, and malignancy in 5–30%^[1]. As CBTs grow, they encase the internal and external carotid arteries. Thus, CBTs are known to invade the surrounding neurovascular structures. They can grow at a rate of up to 2 cm per 5 years, with tissue invasion potentially impairing nerve function, or generating a mass effect. However, most CBTs present as a painless, pulsating neck mass, or are found incidentally on imaging^[2].

The aetiologies

The aetiology of carotid body enlargement are multifactorial. Normally, the carotid body carefully monitors blood oxygen,

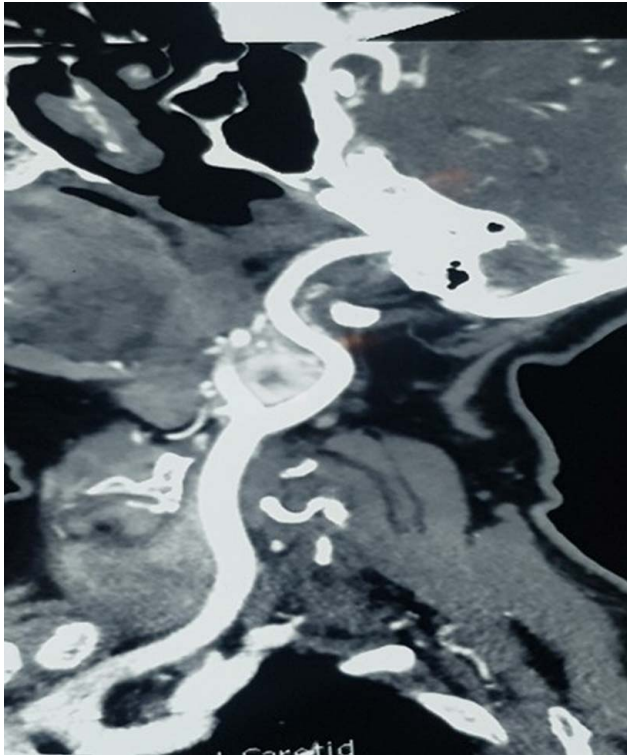


Figure 1. Computed tomographic angiography of the carotid bifurcation shows a large carotid body tumour.

CO₂, and proton concentrations. The carotid body protects from hypoxia by providing sympathetic innervation and stimulating ventilation. CBTs are thought to undergo hypertrophic/hyperplastic growth in response to chronic hypoxia^[3]. In 1976, Arias-Stella and Valcarcel observed that Peruvians living at higher altitudes had greater carotid body size^[3]. They posited this was due to their chronic exposure to elevated oxygen demands.

Worldwide, the incidence of CBTs is greater in populations residing at higher altitudes^[4]. Also, CBTs are more common in conditions that create physiological hypoxia, such as cirrhosis or COPD^[4]. While most CBTs occur sporadically, 10–30% of CBTs are familial with an autosomal dominant pattern of inheritance^[5]. CBTs also have syndromic associations with multi-tumour non-paraganglionic syndromes, such as in multiple endocrine neoplasia (MEN) type II^[6].

Diagnostic workup

Diagnostic and preoperative evaluation of CBTs requires imaging^[1]. Ultrasound may be used for screening, or as an indication for further imaging. Yet, ultrasound cannot accurately inform the extent of tumour infiltration, or tumour size^[7]. Instead, the literature suggests either computed tomographic angiography (CTA) or MRI for accurate diagnosis and evaluation of tumour morphology, location, and invasion^[7]. Particularly, CTA can provide high-fidelity images of the vasculature surrounding and feeding the tumour. MRI provides the advantage of a characteristic, “salt-and-pepper” pattern indicative of a CBT, due to visualization of high-velocity blood flow

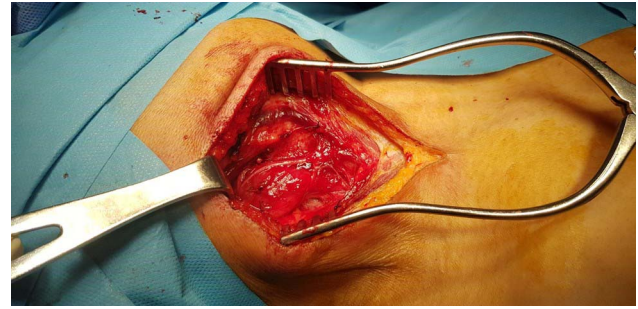


Figure 2. Longitudinal right anterior neck triangle, carotid body tumour found within carotid bifurcation.

(black dots) contrasted by haemorrhaging or slow flow (white dots)^[7].

Rarely, digital subtraction angiography (DSA) is used when CT or MRI are insufficient for diagnosis, or embolization is considered^[8]. DSA provides detailed blood flow and vessel anatomy information, such as cerebral collateral circulation, arterial narrowing, or abnormal vessel growth, otherwise not visualized by CT or MRI^[8].

Radiological classifications

Determining the Shamblin class of a CBT can be attempted after imaging to guide the surgical approach^[7]. The Modified Shamblin classification assigns a class from I to IIIb to CBTs based on its infiltrative relationship to the carotid artery and degree of vascularity^[9]. A Class I describes an easily excisable localized tumour less than 4 cm in size that does not surround the vessels. Class II entails a tumour greater than 4 cm in size that surrounds the carotid vessels^[9]. Class IIIa and IIIb are tumours greater than 4 cm (3a) or less than 4 cm (3b) with intimate involvement of the carotid vessels and may require vascular sacrifice, repair, or vessel replacement^[9]. Still, CBTs are challenging to assign a Shamblin class to preoperatively with imaging, as infiltration of the carotid wall by the tumour must be visualized during surgery^[7].

Treatment modalities

Surgery remains the gold standard in treatment for CBTs^[8]. All surgical approaches involve complete excision alongside the conservation of the delicate neurovascular structures in the



Figure 3. Right-sided carotid body tumour Shamblin IIIa post-total resection with preservation of all cranial nerves.

Table 1	
Patient demographics	
Patient characteristics	Frequency (percentage), n (%)
Sex	
Female	31 (57.4)
Male	23 (42.6)
Family history	
Absent	52 (96.3)
Present	2 (3.7)
Presentation	
Painless right-sided neck lump	26 (48.1)
Painless left-sided neck lump	25 (46.3)
Painless bilateral neck lump	2 (3.7)
Unilaterally painful left or bilateral lump	1 (1.9)
Modified Shamblin class	
Class I	9 (16.7)
Class II	24 (44.4)
Class IIIa	16 (29.6)
Class IIIb	5 (9.3)
ASA class	
Class I	42 (77.8)
Class II	10 (18.5)
Class III	2 (3.7)
Pre-existing hypertension	
Absent	49 (90.7)
Present	5 (9.3)
Pre-existing palpitations	
Absent	53 (98.1)
Present	1 (1.9)
Pre-existing T1DM	
Absent	53 (98.1)
Present	1 (1.9)
Pre-existing T2DM	
Absent	51 (94.4)
Present	3 (5.6)

ASA, American Association of Anesthesiologists; T1DM, Type one Diabetes Miletus; T2DM, Type two Diabetes Miletus.

area^[8]. Resection is indicated in the following: (1) Malignant CBT at presentation; (2) lack of reliable long-term screening to follow the cytologic progression of the tumour; (3) there is no evidence in the literature that correction of physiological causes of CBT, such as CBTs borne by chronic hypoxaemia, will result in regression of the tumour; (4) resection of Shamblin group I tumours poses a minimal risk; and (5) all CBTs are likely to become symptomatic^[8].

Shamblin class informs surgical difficulty and risk, as a higher Shamblin class is prognosticating of nerve injury, blood loss,

Table 2			
Descriptive statistics			
	Minimum	Maximum	Mean (std. deviation)
Age (year)	26	60	40.06 (9.510)
Duration of mass growth (year)	0.167	6.00	1.964 (1.307)
CT surface area (cm ²)	2.86	60.00	14.105 (12.397)
Duration of operation (min)	90	200	120.37 (29.006)
ICA or CCA clamping performed	Not performed	51	94.4 (not performed)
	Performed	3	5.6 (performed)
Blood loss (ml)	200	1400	569.44 (238.79)

CCA, common carotid artery; CT, computed tomographic; ICA, Internal carotid artery.

Table 3	
Complications	
Postoperative complications	Frequency (percentage), n (%)
Stroke	
Absent	53 (98.1)
Present	1 (1.9)
Haematoma	
Absent	51 (94.4)
Present	3 (5.6)
Nerve damage	
No nerve damage	44 (81.5)
Hypoglossal nerve damage	5 (9.3)
Vagal nerve damage	4 (7.5)
Superior laryngeal nerve damage	1 (1.9)

surgical time, and other complications^[7]. Shamblin Class I CBT, and some Class IIs, can be resected by sub-adventitial excision^[8]. Group II tumours are more likely to require shunts. Whereas, a Shamblin III may require resection of the entire ECA, ICA, or merit a graft^[8].

CBTs are highly vascularized tumours that reside within a highly vascular territory. The risk of extensive and emergent blood loss with surgical intervention is high^[10]. To reduce the risk of bleeding, selective angiography with embolization (EMB) is used for CBTs of high vascularity^[10]. EMB is indicated in Shamblin Class IIIA or B tumours but can be considered in patients with a Shamblin Class II CBT^[10]. EMB provides further surgical benefits by enhancing safety in resection and reducing the capacity for adverse events^[10].

Considerable evidence exists to support radiotherapy as an effective treatment for CBTs. Studies suggest that radiation as primary therapy may yield similar curative outcomes to surgery while avoiding surgery-induced neurovascular complications^[2]. Treatment of 1000 patients with 45 Gy demonstrated equivalent survival and tumour control rates to surgical management, with minimized neurovascular morbidity^[2].

Yet, complete tumour resolution using radiotherapy is rare, and instead, a positive treatment outcome is defined as regression of the tumour or maintenance of the current tumour size. Hinerman *et al.*^[11] suggest radiotherapy as the primary treatment in the management of Class III tumours, as evidence suggests a high complication risk when treated with surgical excision.

Patients and methods

Preoperative optimization

This manuscript has been prepared following the Standards for the Reporting of Diagnostic Accuracy Studies (STARD)

Table 4	
Logistic regression analysis	
Comparison Groups	Sig.
Modified Shamblin Class and complications	0.001
Blood loss (ml) and complications	0.008
CT surface area (cm ²) and operating time (min)	< 0.001
CT surface area (cm ²) and blood loss (ml)	0.029
CT surface area (cm ²) and operating time (min)	< 0.001

Significance set at $P < 0.05$.

CT, computed tomographic; Sig., significance.

Table 5
Chi-square analysis

	χ^2	df	Sig.
MSC and complication	24.994	1	<0.001

Significance set at $P < 0.05$.
MSC, modified Shamblyn classe; Sig., significance.

guidelines. The Ethics Committee of our institution approved this study. Written informed consent was obtained from all patients after a detailed explanation of the study. A retrospective medical record review of prospectively collected data completed on all consecutive referrals for surgical CBT management seen by the senior author in our hospital between 2008 and 2019. Our work has been reported in line with the PROCESS criteria for case series^[12]. This study was registered on ResearchRegistry.com (registration number: researchregistry9646).

All patients diagnosed with CBT after clinical and radiological assessment during the data collection period were consecutively included. No patients were excluded even those who have signs of preoperative cranial nerve involvement. A detailed medical history and physical examination were performed, with a focus on the neck and chest regions. Preoperative cranial nerve involvement was recorded when present.

All patients underwent Doppler ultrasound of the neck vessels and computed tomography angiography of the carotid arteries (CTA) to locate the position of the tumour, assess adherence to the carotid arteries, and determine the Shamblyn grade of the CBT (Fig. 1).

Operative technique

All operations were performed under general anaesthesia with endotracheal intubation. Patients were positioned supine with the neck rotated to the opposite side. Prophylactic intravenous antibiotic was administered 60 min prior to anaesthesia induction.

The carotid arteries were exposed through a standard longitudinal cervical incision along the anterior border of the sternocleidomastoid muscle (Fig. 2). Control of the common, internal, and external carotid arteries was obtained, and the hypoglossal and vagus nerves were identified. Whenever a carotid artery clamp was required, a bolus dose of 5000 international units of unfractionated heparin was administered. Using bipolar diathermy, a capsular-adventitial or sub-adventitial (the white line) dissection plane was established at the inferior margin of the tumour at the carotid bifurcation and extended cephalad onto the internal and external carotid arteries (Fig. 3). Some branches of the external carotid artery were ligated as needed to facilitate dissection. All the surgeries are performed by the same consultant vascular surgeon. Most of the patients were admitted to the intensive care unit for the first postoperative day, and the conventional ward after that.

Statistical analysis

The Statistical Package for Social Sciences (IBM SPSS Statistics 26) was used for all statistical analyses. Logistic regression was utilized to identify independent risk factors and derive associations dependent on Shamblyn Class. Descriptive and inferential statistical analyses were performed for the study. Mean \pm SD (Min–Max) was used to report continuous measurements, while number (%) was

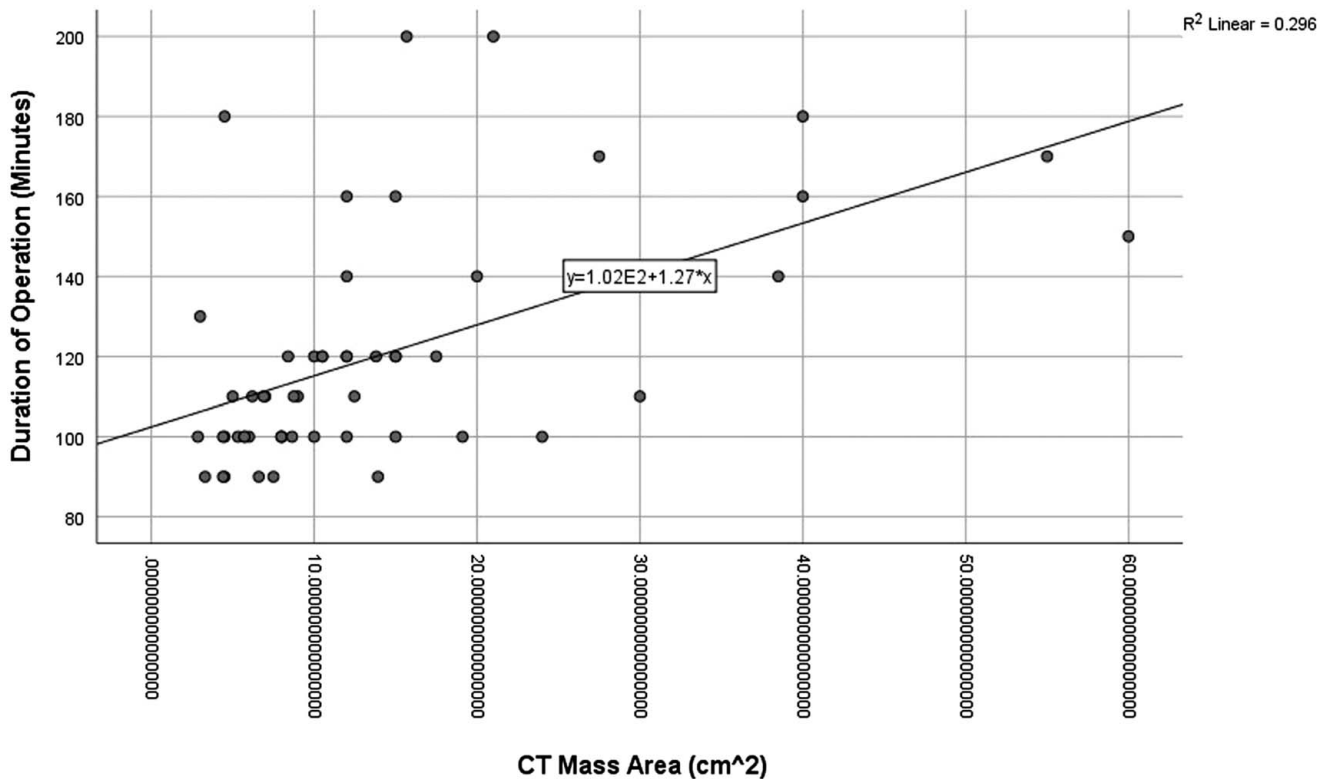


Figure 4. Scatterplot comparing computed tomographic (CT) surface area (cm²), operating time (min).

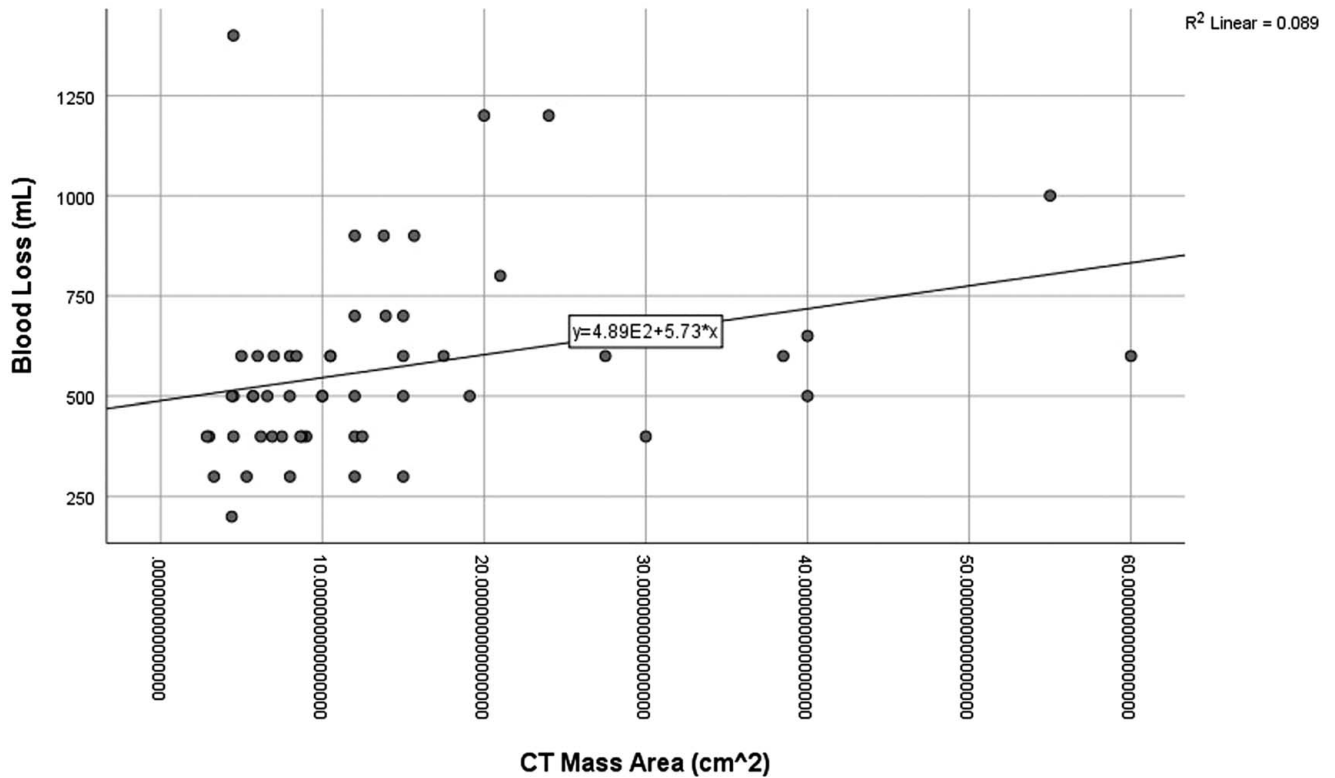


Figure 5. Scatterplot comparing computed tomographic (CT) surface area (cm²) and blood loss (ml).

used for categorical measurements. ANOVA testing applied to compare clinical outcomes. Statistical significance was set at a *P* value of less than 0.05.

Results

During the period of data collection, 54 patient files were included and reviewed. No exclusion criteria were applied. Among them, 57.4% were female. The CBTs were 48.1% right-sided, 46.4% left-sided, and 5.5% bilateral. When classified by modified Shamblin class (MSC), there were 9 class I(16.7%), 24 class II (44.4%), 16 class IIIa (29.6%), and 5 class IIIb (9.3%). Five patients had pre-existing hypertension, one patient had palpitations and four patients had type 2 Diabetes Mellitus (Table 1).

All patients underwent surgery through the same protocol of preoperative workup, intraoperative approach, and post-operative follow-up. Patient ages ranged between 26 and -60 years (\bar{x} =40.06). The mean CT mass surface area was 14.105 cm². The mean blood loss was 569.44 ml, while the mean operating time was 120.37 min (Table 2). Internal carotid artery

clamping or CCA clamping was performed only in three patients (Table 2).

As for postoperative complications, one patient suffered a minor stroke as the patient developed only grade 2 contralateral upper limb weakness, 3 patients suffered operative site haematomas, and 11 patients suffered nerve injuries. Of these, 5 patients had hypoglossal nerve injuries, 4 patients had vagus nerve injuries and 1 patient had superior laryngeal nerve injury. Forty-four patients had no nerve damage after resection (Table 3). Half of all nerve injuries resolved within a year. All other injuries stayed permanently. All tests were performed with 95% CI and *P* values less than 0.05 were regarded as significant.

A χ^2 test performed for MSC and postoperative complications showed a statistically significant association between the two ($P \leq 0.001$) (Table 4).

Logistic regression analysis between MSC and postoperative complications was highly significant ($P = 0.001$, $\chi^2 = 25$). Other logistic regression analyses suggested a significant relationship between intraoperative blood loss and the incidence of post-operative complications ($P = 0.008$). These findings are summarised in (Table 5). Furthermore, we compared other preoperative variables such as age, sex, presentation, duration of mass growth, pre-existing comorbidities, and ASA class to the surgical outcome. We found that only MSC was associated with complications ($P = 0.004$).

Tumour surface area on CT was also used to determine linear relationships between size and various outcomes. Linear regression analysis showed a significant relationship between CT area and operation time ($P = 0.000$) as shown in (Fig. 4). Furthermore, linear regression showed a significant correlation between blood

Table 6
Linear regression analysis

Comparison groups	Sig.
CT surface area (cm ²) and operating time (min)	< 0.001
CT surface area (cm ²) and blood loss (ml)	0.029
CT surface area (cm ²) and operating time (min)	< 0.001

Significance set at $P < 0.05$.
CT, computed tomographic; Sig., significance.

Table 7
ANOVA analysis

Between groups	Sum of squares	df	Mean square	F	Sig.
Shamblin class and blood loss (ml)	956350.694	3	318783.565	7.716	< 0.001
Shamblin class and operating time (min)	12100.787	3	4033.596	6.207	0.001
Shamblin class and hospital stay	57.677	3	19.226	17.959	< 0.001
CT surface area (cm ²) and type of nerve injury	5484.337	4	1371.084	25.239	< 0.001

CT, computed tomographic; Sig., significance.

loss and CT area ($P=0.029$, $R^2=0.3$) (Fig. 5). Finally, the CT area was strongly correlated with postoperative hospital stay ($P=0.009$) (Table 6).

Table 7 shows that ANOVA testing was significantly associated with the following analyses: MSC and intraoperative blood loss ($P=0.000$), MSC and length of stay ($P=0.000$), and MSC and operating time ($P=0.001$). ANOVA testing suggested a significant association between CT area and Type of nerve injury ($P=0.000$).

Discussion

Our research sought to explore which clinical and surgical relationships most explained the outcome after CBT resection. We observed a significant relationship between MSC and the incidence of postoperative complications. Particularly, the risk of complications increases with a higher CBT class. MSC was also strongly associated with increased operating time, hospital stay, and blood loss. Blood loss was found to be correlated with the rate of complications. Using tumour surface area on CT yielded similar statistical relationships as those of MSC.

Our findings mirror those of the existing literature. In the largest systematic review of CBT outcomes, Robertson and colleagues reported findings related to postoperative complications. Regarding the incidence of postoperative stroke, Robertson observed a significant association between stroke and the gradation of MSC^[4]. Particularly, higher class CBTs were associated with a higher risk of stroke at a rate of 60%, 25%, and 15%, respectively, for classes 1, 2, and 3^[4].

We perceive, that the increased rate of stroke, may be associated with a potential increase in blood loss after class 3 resections. Increased blood loss may potentiate greater embolic risk. Furthermore, Robertson and colleagues reported a relationship between CBT class and cranial nerve injury. Although the risk of CN injury after class 1 resection is only 4%, this rises dramatically to 14%, and 17% in class 2 and 3 tumours, respectively^[4].

An issue posed by our analysis is that of blood loss and its relationship with complications. EMB is considered in contexts of increased blood loss and to improve surgical ease. the choice to pursue EMB remains controversial. A meta-analysis by Abu-Ghanem *et al.*^[13] advises that EMB offers no preoperative or postoperative utility to patients. Other literature suggests an increased risk of stroke postoperatively.

However, A meta-analysis by Texakalidis *et al.*^[14] showed that patients who underwent EMB had statistically significant reductions in blood loss, and operating time. Other literature suggests that increased blood loss in class III tumours may be reduced by up to 200 ml with preoperative embolization^[4,13,15]. Given our data suggest important clinical outcomes are associated with blood loss, it may be meaningful for physicians to consider EMB in patients who require resection of MSC III CBTs.

Further research should contextualize the value of EMB in the short and long term. The relationship between blood loss, MSC, tumour size, and complications also requires further explanation, as it may elucidate the value of EMB. Furthermore, long-term follow-up data ranging over the decades may be valuable, as CBTs are traditionally slow-growing tumours.

Though half of our patients recovered from their nerve injury, patients with MSC III CBTs should be advised of the high risk of complications and long-term morbidity from nerve injury. Historically, CBT resection conferred a great risk of mortality^[16]. Contemporary approaches to CBT resection suggest that mortality may be completely avoidable^[15]. In these contexts, it may be important to explore the value of multidisciplinary intervention in the treatment of CBTs, including the input of vascular surgeons, head and neck (HEENT) surgeons, and radiology specialists.

Mohebbali *et al.*^[17] observed significantly better surgical outcomes with a combined approach, entailing preoperative evaluation by HEENT surgeons, followed by an operative intervention by vascular surgery, for us this concept was not applicable. CBTs disfigure standard anatomical structures as they grow. Furthermore, they may encroach on the skull base as their size increases, which anatomically exists outside the common scope of practice for vascular surgeons. These characteristics challenge vascular surgeons, by complicating proper identification of nervous structures and forcing surgical intervention near unfamiliar territory respectively. Kim *et al.*^[18] suggest these factors explain the increased incidence of cranial nerve injury. HEENT specialists may offer preoperative insight into potential anatomical distortions created by high-grade CBTs and assist vascular surgeons in generating less nerve-related morbidity.

Importantly, our participant count is greater than most other monocentric studies. Consistent workup, surgical approach, and technique were controlled for using data from a single surgical practice. Our data also reflect the findings of major papers, suggesting external validity. Bolstering this fact further is that the data reflected similar nerve injury and stroke rates to other series^[19-23]. Ultimately, this study provides stronger evidence for greater risks associated with class 3 CBTs.

Still, this study has methodological limitations. Lack of comparison groups, and randomization, serve as sources of bias. The data may be limited in applicability to other populations, as it emerges from a racially, geographically, and ethnically homogenous population. Some research suggests racialized differences in CBT presentation, which may limit the study's external validity^[14].

Furthermore, the author used CT mass surface area to assign Shamblin class. While the assignment of the Shamblin class differs between authors, as some may use tumour volume post resection, tumour volume on imaging, or perioperative assessments, the

lack of a standardized approach may challenge the transmissibility of our findings to existing literature.

Finally, this study may be subject to selection bias, in that patients were not randomly selected from the population, and instead presented based on their willingness to request surgery from this surgeon in specific. Thus, the generalization of the results and conclusion of this study need to be taken into consideration. We recommend a further multidisciplinary team approach for a larger sample case series in the field of CBT management.

Conclusions

The Shamblin III category CBTs is at high risk of perioperative complications. The present study suggests that surgical resection should be performed once CBT is confirmed without waiting for preoperative embolization. Tumour resection, without preoperative embolization, is feasible for patients with Shamblin grade III tumours. Reconstruction or ligation causes potential damage to the nervous system and is only required in patients when no plan of dissection could be found between the tumour and the ICA adventitia.

Ethics approval

This study was approved by our institution's ethics committee (approval number: 642H/on September 22nd, 2020).

Consent to participate

Obtained from all participants.

Consent for publication: verbal and written consent was obtained from all participants.

Consent to publish: Written consent was obtained from all participants that photos taken within the operation may be used for scientific publications only.

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Author contribution

B.R.: drafting, data analysis, statistical analysis, draft revision. V.A.: drafting, statistical analysis, draft revision, patient follow-up. A.B.: the surgeon in charge of study design, follow-up, data collection, manuscript. revision, and statistical analysis. S.Y.H. B.: assisted in surgeries, follow-up, study design, data collection, drafting. F.Y.: assisted in surgeries, follow-up, study design, data collection, drafting.

Conflicts of interest disclosure

Not applicable.

Research registration unique identifying number (UIN)

This study was registered on ResearchRegistry.com (registration number: researchregistry9646).

Guarantor

Aram Baram is the guarantor of this study.

Availability of data and material

All our raw data are available upon request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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