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HEAD AND NECK IMAGING

ORIGINAL ARTICLE

Imaging criteria to predict Shamblin group in carotid body tumors – revisited

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PURPOSE
This study aims to compare the imaging findings of carotid body tumors on contrast-enhanced computed tomography (CT) with the intraoperative Shamblin grade and to evolve an imaging-based scoring system that can accurately predict the Shamblin grade.

METHODS
Preoperative contrast-enhanced CT scans of 40 patients who underwent surgical excision of carotid body tumors in our institution between 2004 and 2017 were retrospectively reviewed. The angle of contact with the internal carotid artery (ICA), tumor volume, presence of peritumoral tuft of veins, loss of tumor adventitia interface and distance from the skull base were assessed and compared with the intraoperative Shamblin grades of the tumor. Ordinal logistic regression was used to determine which parameters could be predictors of the Shamblin grades. Receiver operator characteristic (ROC) curves were used to score the tumor volumes.

RESULTS
Among the 42 tumors evaluated, 6 (14.3%) were surgically classified as Shamblin I, 15 (35.7%) as Shamblin II, and 21 (50%) as Shamblin III tumors. Pairwise comparison between the three Shamblin groups showed a statistically significant difference for angle of contact with ICA, maximum tumor dimension, presence of peritumoral tuft of veins and loss of tumor adventitia interface ($p = 0.001$, $p = 0.001$, $p = 0.038$ and $p = 0.003$, respectively). However, tumor volumes and distance from skull base were not significantly different between the Shamblin groups ($p = 0.136$ and $p = 0.682$). A scoring system, including four of the above mentioned parameters (angle of contact with ICA, tumor volume, presence of peritumoral tuft of veins, and loss of tumor adventitia interface) was developed with a maximum score of 8 and a minimum of 2. A statistically significant difference was found between the final scores among the three Shamblin groups ($p < 0.001$). Using ROC curves, a final score of ≥6 was found to separate Shamblin grade III tumors from grade I and II tumors (sensitivity, 95.24%; specificity, 71.43%). All patients with documented intraoperative estimated blood loss of >1000 mL had Shamblin grade III tumors. Postoperative complications like stroke, ICA thrombosis and lower cranial nerve palsies were seen only with Shamblin grade II and III tumors.

CONCLUSION
The simple scoring system we have proposed correlates well with the Shamblin grade and helps in identifying patients who have a higher risk of developing complications.

The carotid body is derived from neural crest ectoderm and mesodermal elements of the third branchial arch (1). It works as a chemoreceptor organ and is situated at common carotid artery bifurcation (2). Carotid body tumors (CBT) are relatively rare tumors of unknown etiology, however, they account for a large proportion of all head and neck paragangliomas (3, 4). Three different types of CBTs have been described: familial, sporadic, and hyperplastic. The sporadic form is the most common of the three and represents approximately 85% of all CBTs.

The gold standard of treatment of CBTs is surgery, which can be challenging because of the hypervascularity of the tumor, and dense adherence to the carotid bifurcation (5–8). In 1889, Albert performed the first successful CBT surgery and in 1940, Gordon-Taylor described a safe subadventitial dissection (9). Shamblin et al. (1) suggested an operative classification of CBTs based on carotid vessel involvement in 1971, a classification that is still widely used to grade CBTs. In this grading, Group I tumors refer to localized tumors which

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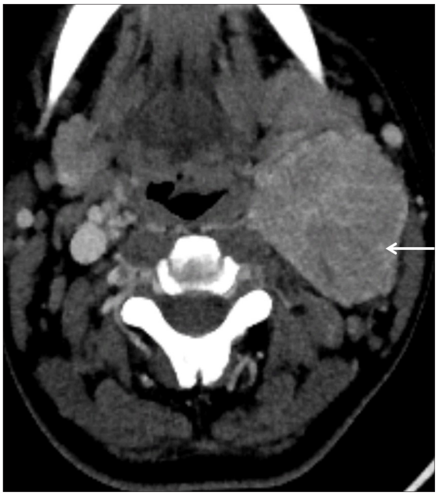

Figure 1. A 33-year-old woman with Shamblin grade III (Score 8) carotid body tumor (CBT) completely encasing the left internal carotid artery (360°) *(white arrow)* with loss of tumor adventitia interface on contrast-enhanced axial CT section of the neck.

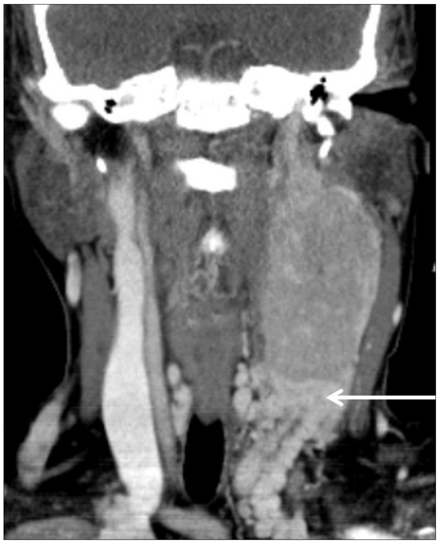

Figure 2. A 33-year-old woman with Shamblin grade III (Score 8) CBT with peritumoral tuft of veins *(white arrow)* on contrast-enhanced CT of the neck with coronal reconstruction.

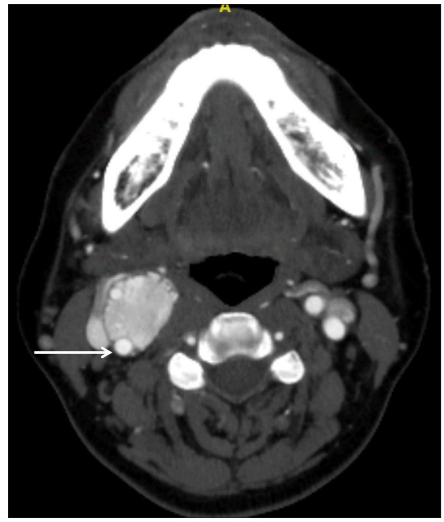

Figure 4. A 42-year-old woman with Shamblin grade I tumor (Score 3) with preserved tumor adventitia interface and angle of contact less than 180° *(white arrow)* on contrast-enhanced axial CT sections of the neck.

do not encase of the adjacent major vessels, Group II, to tumors that are adherent to or partially encase the vessels and Group III, to large tumors that encase the vessels and may require vessel replacement. The classification was based on intraoperative findings and gross specimens. The complications related to surgical excision of the lesion depended mainly on the involvement of the carotid vessels by the tumor (9).

Larger CBTs become more adherent to the carotid vessels and tumor size correlates with the Shamblin classification; hence, this classification can also be used to predict vascular morbidity. Lim et al. (9) found a higher risk of postoperative neurovascular complications in Shamblin III tumors. Meticulous presurgical planning and proper patient selection is imperative for good surgical outcomes. Thus, the importance of this classification is enhanced, if preoperative cross-sectional imaging can accurately predict the Shamblin group. Computed tomography (CT) and magnetic resonance imaging (MRI) are used for diagnosing and evaluating these tumors preoperatively. However, the need for specific imaging criteria that can predict Shamblin classification has been stressed by Van der Mey et al. (10). Arya et al. (11) proposed objective imaging criteria to correlate between the Shamblin group and the surgical outcome in a small series of patients using MRI. The purpose of the present study is to redefine the objective criteria and, hence, attempt to predict surgical outcome in CBTs.

Main points

- Carotid body tumors are highly vascular lesions located at the carotid body bifurcation.
- Large tumors and those that are adherent to the carotid vessels are known to be associated with high incidence of vascular complications and cranial nerve palsies.
- Preoperative evaluation of carotid body tumors with regard to tumor volume, angle of contact with the internal carotid artery, presence of peritumoral tuft of veins and loss of tumor adventitia interface is useful for surgical planning and prognostication.

Methods

Patients

The preoperative CT scans of the neck of patients operated for CBT in our institution over a period of 13 years (January 2004 to July 2017) were retrospectively reviewed. Approval of the institutional review board and ethics committee were obtained for this study (IRB 11534 [Retro] dated 26.09.2018). Informed consent was waived by the board due to the retrospective nature of the study. Inclusion criteria included all those with biopsy-proven CBT who underwent contrast-enhanced CT scans of the neck in our institute over the given period of time and who then underwent surgical excision. Patients who did not undergo surgery in our institute were excluded.

Imaging

Contrast-enhanced axial (3 mm slice thickness) CT scans of the neck were performed with coronal reformatted images, and the images were reviewed on our picture archiving and communication system (GE Centricity 3.2, GE Healthcare). The information recorded included axial and craniocaudal dimensions, from which tumor volume was calculated by the formula of an ellipse as the tumors were elliptical (length × breadth × height × 0.5), distance of the superior margin of the tumor to the skull base, angle of contact of the tumor with the ICA, presence or absence of a peritumoral tuft of veins, and presence or absence of a fat plane between the tumor and vessel wall adventitia (Figs. 1–3). The technique previously described by Arya et al. (11) was used to measure the angle of contact with the ICA. A score of 1 was given to angles ≤180°, a score of 2 for angles ≥181° but ≤270°, and a score of 3 for angles >270°. The presence of a peritumoral tuft of veins was given a score of 1 and its absence a score of 0. Loss of plane between the tumor and adventitia of the ICA was given a score of 1 and the presence of a clear plane was given a score of 0. By constructing a receiver operator characteristics (ROC) curve, tumor volumes were graded as 1 for tumor volume of ≤16 cc, 2 for tumor volume of ≥16.1 cc but ≤32 cc, and 3 for tumor volumes of ≥32.1 cc. The maximum possible score would be 8 and the minimum score 2. The scoring system is summarized in Table 1. These

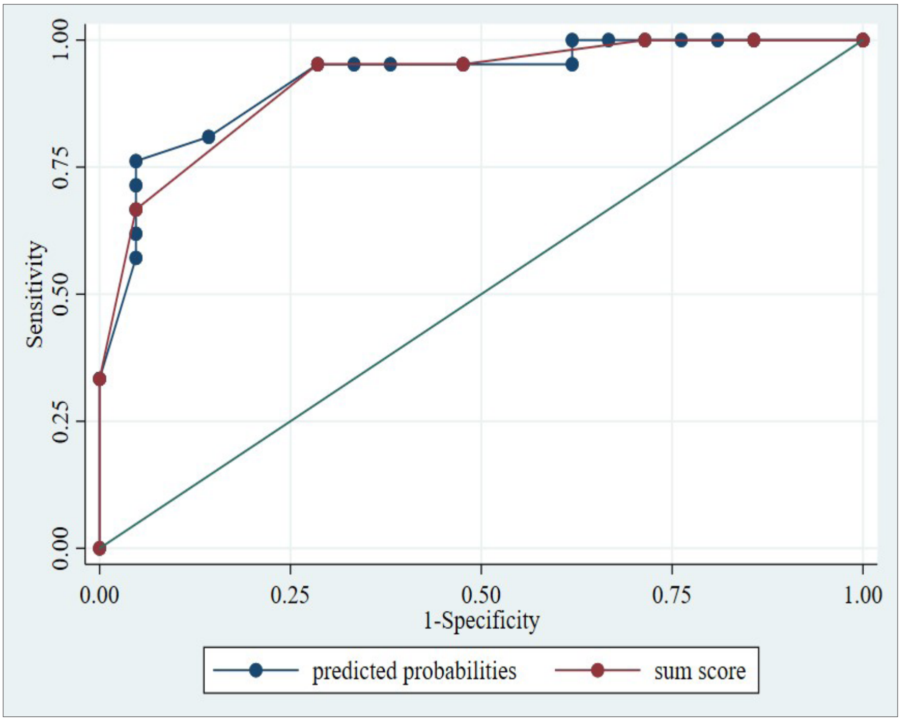

Figure 4. ROC curve determining the discriminating ability of the predicted probabilities of regression models and summative score of the training data set.

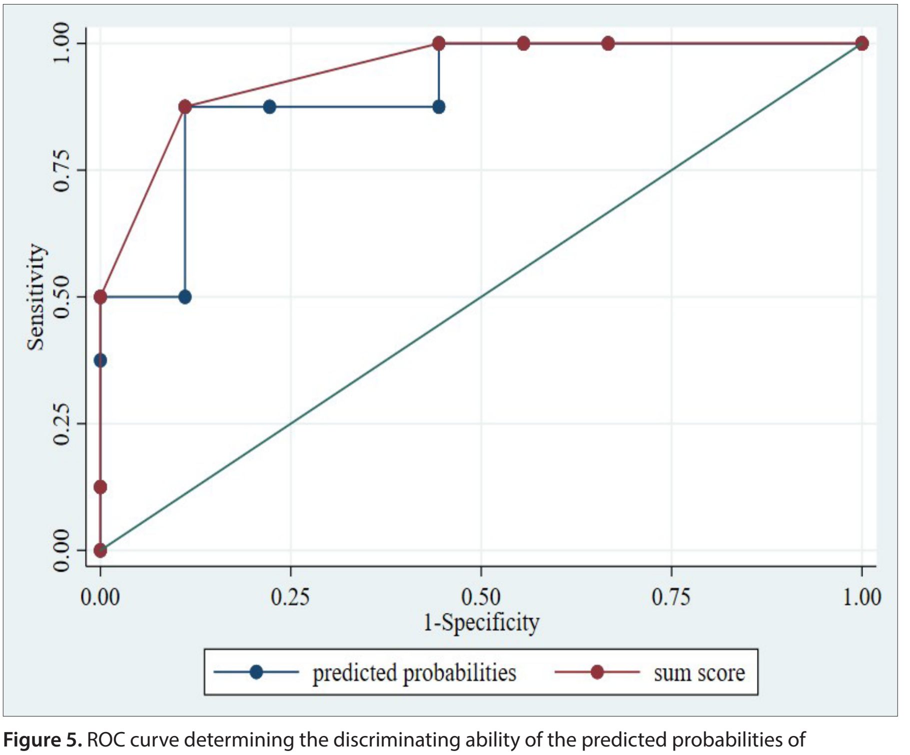

Figure 5. ROC curve determining the discriminating ability of the predicted probabilities of regression models and summative score of the test data set.

variables (angle of contact, presence/absence of peritumoral tuft of veins and loss of tumor adventitia plane) were measured independently by two radiologists with more than 5 years of experience who were blinded to the surgical grade and final record was made on consensus. The intraclass correlation between the two observers was 0.789 for the angle of contact measurement and 0.908 for the total score.

Electronic patient records were reviewed to obtain surgical details. The Shamblin grade as entered by the operating surgeon was documented.

Statistical analysis

Data were summarized using mean (SD)/ for normal distributed and median (IQR) for non-normally distributed continuous variables and the categorical data were expressed as frequency and percentages. Normality was assessed visually using p-p plot and histograms with normal curve. The continuous variables among the grades were initially tested using ANOVA with Bonferroni correction as post hoc analysis, and the categorical variables were associated using chi-square statistics. Ordinal logistic regression was used to determine various parameters as predictors with the Shamblin grades. The variables retained in ordinal logistic regression were used for creating the scores. ROC curve analysis was used to define the cutoff of all the clinical variables discriminating the surgical grade. For all the scoring analysis, grade I and II tumors were grouped in one category and grade III as another category, due to the small number of grade I tumors. A logistic model was employed with recoded surgical grades and the discrimination of the model was assessed by constructing ROC curves for the predicted values. Calibration of the model was given with Hosmer–Lemeshow statistics (Fig. 4). Similarly, a ROC curve was constructed for the total scores to find out the cutoff value which would differentiate between the surgical grades, and a score of ≥6 was obtained as an optimal cutoff to define grade III tumors. A sample of 17 tumors was used to validate the scoring system by a radiologist with more than 15 years of experience who was blinded to the surgical grade. A ROC curve was constructed to check the discriminating ability and diagnostic accuracies with 95% CI was present for the same (Fig. 5). All analysis were done using STATA IC/15.0 software.

Results

Out of the 64 tumors evaluated, 22 were excluded as surgical resection was not performed in our institution. Forty-two tumors in 40 patients were included in the study. Patient age ranged from 20 to 67 years, with a mean age of 38.8 years. Patient details and tumor characteristics are summarized in Table 2.

Table 1. Scoring system	
Parameters	Score
Tumor volume (cc)	
≤16	1
16.1–32	2
≥32.1	3
Angle of contact (°)	
≤180°	1
181°–270°	2
>270°	3
Peritumoral veins	
Absent	0
Present	1
Loss of tumor adventitia interface	
Absent	0
Present	1

Table 2. Patient demographics and tumor characteristics	
Patient demographics	
Age (years), mean±SD	38.83±11.27
Male/Female, n (%)	22 (55)/ 18 (45)
Tumor characteristics, n (%)	
Right	22 (52.39)
Left	18 (42.85)
Bilateral	2 (4.76)
Surgical grade, n (%)	
I	6 (14.29)
II	15 (35.71)
III	21 (50)
Volume of tumor (cc), mean±SD	63.94±137.79
Distance from skull base (cm), mean±SD	3.37±1.14
Angle of contact (°), mean±SD	241.67±88.52
Presence of peritumoral veins, n (%)	31 (73.81)
Loss of tumor adventitia interface, n (%)	35 (83.33)

SD, standard deviation.

Table 3. Comparison of radiological parameters among the Shamblin grades

Parameters	Shamblin grade I	Shamblin grade II	Shamblin grade III	*p* (Overall)	*p* (I vs. II)	*p* (I vs. III)	*p* (II vs. III)
Angle of contact (°)[a]	160.67±55.44	174.73±64.10	264.29±74.56	<0.001	>0.99	0.007	0.001
Maximum dimension (cm)[a]	3.78±1.19	4.27±0.92	6.26±2.17	<0.001	>0.99	0.010	0.004
Volume of tumor (cc)[a]	15.46±11.99	24.03±16.61	106.29±186.84	0.136	>0.99	0.460	0.230
Distance from skull base (cm)[a]	3.73±1.60	3.37±0.78	3.26±1.24	0.682	>0.99	>0.99	>0.99
Loss of tumor adventitia interface[b]	2 (33.33%)	9 (60.0%)	20 (95.24%)	0.003	-	-	-
Presence of peritumoral veins[b]	2 (33.33%)	10 (66.67%)	18 (85.71%)	0.038	-	-	-

[a]Mean±SD, ANOVA performed.
[b]n (%), chi-square performed.

All tumors demonstrated typical imaging features of CBT on contrast-enhanced CT scans with histopathological confirmation of the diagnosis.

The tumors were surgically classified as Shamblin I (14.3%; n=6), Shamblin II (35.7%; n=15) and Shamblin III (50.0%; n=21).

The mean angle of contact of the tumor with the ICA was 175.5° in Shamblin I tumors, 194.8° in Shamblin II tumors and 294.05° in Shamblin III tumors. Pairwise comparison showed a statistically significant difference between Shamblin I and Shamblin III (p = 0.003) and Shamblin II and Shamblin III tumors (p = 0.001). Tumor volumes ranged from 2.02 to 869.4 cc. No significant difference was seen between tumor volumes in the three surgical groups (p = 0.136). The distance between the superior margin of the tumor and the skull base, which is a predictor of the level of difficulty in surgical resection and available free segment of graft, ranged from 0 to 6.0 cm (mean, 3.37 cm). There was no significant difference in distance between the three surgical groups (p = 0.682). The peritumoral tuft of veins was seen in 75.8% of cases, with the maximum number having Shamblin grade III tumors (85.7%), which was significant (p = 0.038). Similarly, tumor adventitia interface was lost in 83.3% of tumors, all of which were Shamblin grade III (p = 0.001). The minimal final score considering all the parameters (tumor volume, the angle of contact, peritumoral tuft of veins, loss of tumor-adventitia interface) was 2 and the maximum was 7. A statistically significant difference was also found between the final scores among the three Shamblin groups (p < 0.001) (Tables 3 and 4).

Using ROC curves, a final score of ≥6 was found to have a sensitivity of 95.24% and specificity of 71.43% to separate the Shamblin grade I and grade II tumors from the grade III tumors. The discriminating ability was good, with an AUC value of 0.916.

The score of ≥6 was validated on a different set of 17 carotid body tumors and a good discriminating ability was obtained with an AUC of 0.944. The AUC of both the predicted probabilities from logistic model, as well as the sum scores, was good in discriminating grades I and II from grade III tumors.

Table 5 represents the results of the patient data set and the validation set. A summative score of ≥6 is predictive of Shamblin grade III tumors with good discrimination similar to the patient data set which is presented with c-statistics (AUC).

Thirteen patients also underwent a digital subtraction angiogram (DSA) prior to surgery for preoperative planning and embolization. Eight tumors were found

Table 4. Regression analysis between the surgical grades and the various parameters

	Univariate analysis		Multivariate analysis	
Parameters	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
Angle of contact	1.02 (1.01, 1.03)	0.001	1.00 (0.99, 1.02)	0.269
Loss of tumor adventitia interface	12.09 (2.58, 56.66)	0.002	2.17 (0.31, 15.38)	0.438
Presence of peritumoral veins	5.29 (1.35, 20.70)	0.017	4.45 (0.77, 25.62)	0.094
Maximum dimension	4.15 (1.92, 8.99)	<0.001	0.85 (0.18, 4.05)	0.833
Volume of tumor	1.09 (1.04, 1.15)	<0.001	1.09 (0.99, 1.19)	0.081
Distance from skull base	0.79 (0.45, 1.38)	0.400	-	-

Table 5. Results of the patient data set and validation set presented with c-statistics (AUC)

Parameters	Patient data set	Validation set
AUC (95% CI)		
Predictive probabilities	0.921 (0.839, 1.000)	0.903 (0.076, 0.754)
Summative scores	0.916 (0.838, 0.995)	0.944 (0.047, 0.852)
Diagnostic accuracies of summative score ≥6		
Sensitivity (95% CI)	0.952 (0.762, 0.999)	0.875 (0.473, 0.997)
Specificity (95% CI)	0.714 (0.478, 0.887)	0.889 (0.518, 0.997)
LR (+)ve	3.330 (1.680, 6.600)	7.880 (1.220, 50.900)
PPV (95% CI)	0.769 (0.564, 0.910)	0.875 (0.473, 0.997)
NPV (95% CI)	0.938 (0.698, 0.998)	0.889 (0.518, 0.997)

AUC, area under the curve; CI, confidence interval; LR (+)ve, positive likelihood ratio; PPV, positive predictive value; NPV, negative predictive value.

to have prominent feeding vessels from the external carotid artery (ECA), 3 tumors had prominent feeding vessels from both the ECA and ICA, and 2 had prominent feeders from the ECA and vertebral artery (VA). Twelve of the 13 patients underwent preoperative embolization, with ≤50% reduction in tumor vascularity in 3 patients and a 60%–80% reduction in vascularity in 7 patients. One patient required a complete ICA occlusion prior to surgery. One patient, however, did not benefit from preoperative embolization.

Estimated blood loss during the surgery was documented in 9 patients. One patient had a blood loss of >1500 mL, 3 had a blood loss of >1000 mL, 3 had a blood loss of >500 mL and 2 had blood loss of <500 mL. All those with blood loss of more than 1000 mL were Shamblin Grade III tumors. One patient with Shamblin Grade III tumor had a blood loss of <500 mL. The other patients with blood loss had Shamblin II tumors.

The documented postoperative complications included hematoma at the postop bed (n=2), stroke (n=3), ICA thrombosis (n=1), and cranial nerve palsy (n=6). The lower cranial nerves (IX, X, XI) were involved in 5 patients, 2 patients had XII nerve palsies and 3 patients had VII nerve palsy, and 2 patients had involvement of the sympathetic chain. All these complications were seen in the Shamblin Group II and III tumors.

Discussion

The Shamblin grading of CBTs is a widely used surgical classification dating to 1971 and is based on intraoperative findings and postmortem specimen examination. The Shamblin grade of the tumor has been useful to predict postoperative complications, including injury to neurovascular structures and also to determine the need for arterial reconstructions (12–14). Additional parameters which have been found useful to predict surgical outcome include tumor volume and distance from the skull base (15).

Obholzer et al. (16) proposed a new classification system for paragangliomas of the neck, including both CBTs and glomus vagale tumors as they felt that the risks of surgery were similar to both groups. Unlike the classification system proposed by Arya et al. (11) which addressed only the aspect of encasement of the internal carotid artery, they included additional parameters like relationship to the skull base and cranial nerve involvement, which were also significant outcome predictors. Encasement of the internal carotid artery by >50%, distance from the skull base <2 cm and the presence of cranial nerve deficits detected by clinical examination were the parameters used by the authors to grade the tumors from Type 1 to Type 4. This classification included both clinical examination findings to detect cranial nerve deficits and imaging parameters. In our scoring system, using only criteria based on imaging findings on contrast-enhanced CT, we have been able to predict the Shamblin grade and hence the outcome.

The maximum tumor dimension was measured in our study; however, it was excluded from the scoring system as volume correlated better with the different groups. Luna-Ortiz et al. (17), in 2006, suggested an alteration of the Shamblin classification which would more accurately predict surgical and postoperative vascular and neurological morbidity, unlike the Shamblin classification which only predicted vascular morbidity. This classification was based on size of the tumor and correlated well with the original Shamblin classification; however, this was again an intraoperative classification.

Although the presence of a peritumoral tuft of veins on cross-sectional imaging has not been described in literature, this is a finding that has been quite consistently seen in many of our cases of CBT, and they are likely to represent early draining veins seen on catheter angiography (18). Peritumoral tuft of veins is an indirect indicator of tumor vascularity and its presence may be considered a triage criteria for preoperative embolization. Although it may not change the Shamblin grade of the tumor, it can contribute to intraoperative surgical blood loss and vascular complications. Thirty-one of the 42 tumors had a peritumoral tuft of veins, with the maximum number being in the Shamblin grade III group (18/31).

The presence of a plane between the tumor and the adjacent internal carotid artery is the other parameter considered in our scoring system. Surgeons have described a white line, which is an avascular plane between the tumor and the adjacent vessel, which is lost when there is infiltration of the vessel wall, making subadventitial dissection impossible (17, 15). In our study, we have used the loss of tumor adventitia interface on preoperative CT, which would indicate infiltration of the subadventitia and warn the surgeon about the need for vascular resection, reconstruction or both. Tumor adventitia interface was lost in 35 of 42 tumors, with the maximum number being in the Shamblin Group III tumors.

Kim et al. (15), in their large study of CBTs, found that a combination of tumor volume, distance from skull base and Shamblin grade were the best predictors of cranial nerve injury risk and bleeding. Every 1 cm reduction in distance from the skull base was associated with a higher risk of blood loss and higher risk of cranial nerve injury after adjusting for tumor volume and the Shamblin grade. Although, it is a very important parameter to consider while preoperatively assessing patients with CBT, in our subset of patients, the distance between the tumor upper margin and base of skull did not correlate significantly with the Shamblin grade and, hence, was not included in our scoring system.

A more recent publication by Lozano-Corona et al. (19) used three-dimensional volumetric reconstruction (3DVR) of 57 CBTs on preoperative CT angiographic studies and correlated it with surgical outcomes like the estimated intraoperative blood loss, duration of surgery, and length of hospital stay. A statistically significant positive correlation was found between the 3DVR and estimated blood loss. In our study we have included tumor volumes in the scoring system as it was found to correlate significantly with Shamblin grades; however, correlation with surgical outcomes was not assessed.

Although there are various gradings of CBTs in the literature as mentioned, there is no definite simple objective scoring system based on imaging findings alone. Hence, the authors have attempted to develop a scoring system by combining various parameters that have correlated with the Shamblin grade. By predicting the Shamblin grade preoperatively, patients may be adequately counselled regarding the surgical complications and outcome prior to the surgery.

This study has a few limitations. We did not have enough patients with Shamblin grade I tumors, as many patients in this group may have opted out of surgery. Hence, we could not separate grade I and grade II tumors using our scoring system. As the study is retrospective, some important information including estimated blood loss during surgery and postoperatively was not available for all our patients and, hence, could not be completely evaluated. Although we included only CT scans of CBTs in our study, many centers may prefer MRI for imaging evaluation and we have not validated our scoring system using MRI.

In conclusion, this study emphasizes the need for good preoperative imaging while planning surgery for a CBT. The scoring system we have suggested, which includes parameters like tumor volume, the angle of contact, the presence of a peritumoral tuft of veins and loss of tumor adventitia interface, may aid in the preoperative assessment, planning, and prognostication of CBTs.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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