Original Article

Functional Outcome of Operated Patients with Skull Base Meningioma in a Tertiary Care Center in Nepal: A Retrospective Analysis

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Abstract

Introduction: Surgery for skull base meningiomas (SBM) has been a challenge to neurosurgeons owing to their location and intimate relation with adjacent neurovascular structures. Many studies have shown higher approach-related morbidity as surgeon's affinity towards radical surgery. There are only few studies focused on SBM and its functional and neurological outcome. In this study, we have attempted to probe the demographics, histopathology, location, extent of resection and functional outcome of SBM after surgery.

Methods: This is a three-year retrospective analysis of SBM surgery performed at our hospital from July 2019 to June 2022.Clinical manifestations, neurological deficits, tumor characteristics, Karnofsky Performance score (KPS) and Medical Research Council Neurological Performance score (MRC-NPS) before and after surgery were analyzed by collecting patient data from hospital medical records, telephone questionnaire and hospital pathological records. Statistical analysis of functional outcome using preoperative and postoperative KPS and MRS-NPS scores was done using Paired t-test.

Results: We analyzed 65 patients with SBM who underwent craniotomy. Common histopathological subtype was found to be transitional (20) and meningothelial (19). On the basis of WHO CNS tumor classification, majority of cases (55/65, 84.6%) belong to grade 1. Complete excision rate in our series was 58.5%. Mortality rate in our series was 3.1%. Regarding functional outcome, there was significant improvement in KPS (72.46 vs. 81.69; p=0.0001) and MRC-NPS (2.89 vs. 2.31; p=0.0001) before and 3 months after surgery.

Conclusion: SBM excision is associated with significant improvement in functional and neurological status after surgery based on preliminary data. However larger retrospective series is required for validation. However one should be cautious to avoid approach related morbidity.

Keywords: *Meningioma, skull base, functional outcome, neurological outcome, KPS, MRC-NPS*

Introduction

Meningiomas constitute 13–26% of all intracranial tumors[1] and approximately 30 % of them arise from the skull base.[2] The most widely used definition as mentioned by Dr Al-Mefty as-"meningioma with dural attachment in the base of anterior, middle or posterior cranial fossa including foramen magnum and tentorium".[3] The primary treatment modality for these tumors is surgical resection.[4]Though functional outcome depends on numerous factors, it is dependent on the morbidity owing to involvement of adjacent neurovascular structures and safe resection of these complicated tumor.[5]Therefore, for attaining the optimal result of surgery, the cardinal goal should be focused on safe maximal resection rather than gross total resection as in case of convexity meningioma.(6) Radical surgery is often associated with high morbidity and

poor overall outcome in these patients. Complications are approach-related; and, hence, should be seriously considered while tailoring approach for surgery.[7] Over the recent years surgical safety has increased owing to a more understanding of surgical corridors, advent of high quality microscopes and improvisation of skull base reconstruction techniques, availability of intraoperative MRI, tumor fluorescence and Neuronavigation.[8]

Opinion is divided regarding skull base versus non skull base SBM on tumor biology and patient outcome Several predictive factors have been described as prognostic factors in SBM like age at diagnosis, preoperative Karnofsky Performance Score (KPS), extent of resection.[9] All these factors might have an implication on the functional outcome of the patient. Among them, KPS score has been widely used as a tool to assess functional status in glioma,[10] and in meningioma.[11]Another modality is a five point prognostic index, namely Medical Research Council-Neurological Performance status (MRC-NPS), which uses clinical variables to place them in different neurological outcome categories.[12] (Table 1)

Table 1. Medical Research Council-Neurological performance scale (MRC-NPS)

Grade	Performance
1	No neurological deficit
2	Some Neurological Deficit but function adequate for useful work
3	Neurological Deficit causing moderate functional impairment e.g. ability to move limbs only with difficulty, moderate dysphasia, moderate paresis, some visual disturbance
4	Neurological deficit causing major functional impairment e.g. inability to use limbs, gross speech or visual disturbances
5	No useful function-inability to make conscious responses

Original Simpson grades for meningioma excision doesn't justify the complexity of SBMs.[13] For grading extent of excision of SBM, Shinshu and Kobayashi grade addresses the microscopic excision which is done these days. It also addresses the neurovascular involvement in SBM which modifies the goal of surgery in SBM.[14] Table 2 represents grade of SBM excision.

Table 2. Shinshu and Kobayashi Grades of SBM excision

Grade I	Complete microscopic removal of tumor and dural attachment with any abnormal bone
Grade II	Complete microscopic removal of tumor with diathermy coagulation of its dural attachment
Grade IIIA	Complete microscopic removal of intradural and extradural tumors without resection or coagulation of tits dural attachment
Grade IIIB	Complete microscopic removal of intradural tumor without resection or coagulation of its dural attachment or any extracranial extension
Grade IVA	Intentional subtotal removal to preserve cranial nerves and/or blood vessels with complete microscopic removal of attachment
Grade IVB	Partial removal leaving tumor less than 10% in volume
Grade V	Partial removal leaving tumor more than 10% or decompression with or without biopsy

In this study, we have attempted to analyze the demographics of SBMs, histopathology, tumor location, extent of resection and functional status and outcome before and 3 months after surgery.

Methods

This is a descriptive retrospective observational study conducted at the Department of Neurosurgery, Tribhuvan University Teaching Hospital, Kathmandu, Nepal. A total of 65 patients with SBM who were operated from July 2019 to June 2022 were analyzed. In our study, Al Mefty's classification[3] was used to define SBM. The study was conducted after approval by Institutional Review Board. The demographics and clinical data including contacts was retrieved from the hospital registry and discharge records. The surgery was performed by a team of qualified neurosurgeons. Operative notes were studied to document blood loss, surgical duration, and intraoperative complications. Intraoperative findings, bony invasion and neurovascular involvement were also obtained. For grading extent of resection we have used Shinshu and Kobayashi Grading of SBM excision.[15] Grade I and II excision was considered complete resection while grade IIIA and higher as incomplete resection. Incompletely resected tumors were subjected to standard radiotherapy regimen. The clinical data, including clinical history, neurological examination, KPS, cranial nerve involvement, tumor size and location and MRC-NPS were evaluated using medical records. Furthermore, telephone questionnaire was used for confirmation. Histopathological information was retrieved from pathology department records. Tumor grading has been done as per WHO

CNS tumor classification 2016 (4th Edition).

Statistical analysis was done using SPSS Version 25. Inferential statistics was used to see association between independent variables using Chi square analysis. Difference in KPS score and MRC-NPS score before and after surgery was analyzed using paired t-test. Pearson correlation was evaluated between age, tumor size, and histological grade with KPS and MRC-NPS grade in a bivariate analysis.

Results

During the study period, 395 intracranial neoplasms were operated at our hospital. Out of them, 148(37.6%) were meningiomas. Out of 148 meningiomas, 65 (43.9%) were SBMs. The mean age of the patients was 45.6 years, ranging from 24 to 74 years. In regards to gender distribution, there was a female preponderance, with 55 (84.6%) patients being female. The summary of anatomical location of SBMs is described below (Table 3). The most frequent location was found to be in the cerebellopontine angle (23.8%) followed by sphenoid ridge (21.5%).

Table 3. Location of SBMs

Location	(Frequency(percent
Cerebellopontine angle	(23.1)15
Sphenoid ridge	(21.5)14
Olfactory groove	(13.8)9
Sella	(12.3)8
Planum sphenoidale	(10.8)7
Tentorium	(9.2)6
Petroclival region	(6.2)4
Foramen magnum	(1.5)1
Clinoid	(1.5)1

Mean tumor size was 4.3 cm (range 1.9-8cm). Figure 1 represents the variation in tumor size which has been categorized into less than 3cm, 3-6 cm and >6cm.

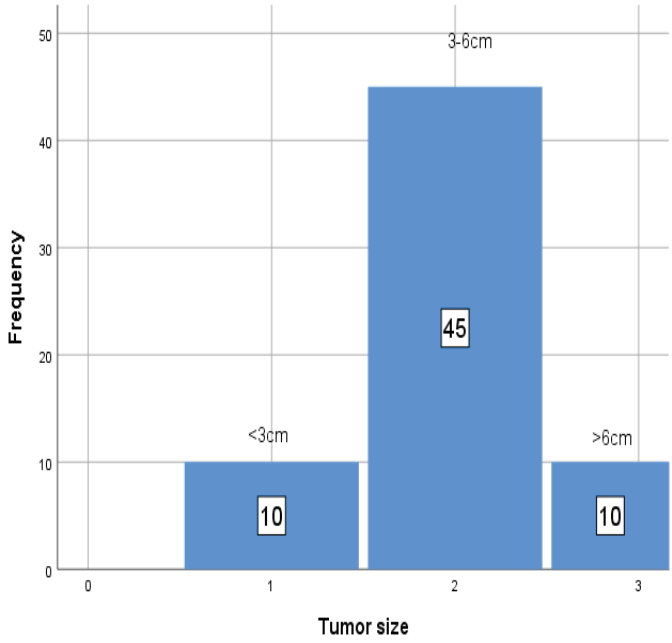

Figure 1. Bar diagram showing tumor size variation among the SBMs

Regarding clinical manifestations, spectra of symptoms were observed due to variable location and tumor size. Overall, progressive headache was present in 55(84.6%) cases. Nine out of 65 (13.8%) patients had seizure in our study. Other symptoms have been listed in Table 3. Most common neurological deficit was the optic nerve palsy [30 (46.3%) out of 65]. The summary of clinical manifestation is described in Table 4.

Table 4. Clinical symptoms in SBM

Symptoms	(Frequency(percent
Headache	(84.6) 55
Visual Deficit	(49.2) 32
Cognitive deficit	(23.1) 15
Motor Deficit	(10.8)7
Cerebellar symptoms	(26.2)17
Speech abnormality	(12.3) 8
Seizure	(13.8) 9

As shown in figure 2 Shinshu and kobayashi grade I excision was achieved in 7 (10.8%) patients. Figure 2 shown degree of excision in our series. Grade II was commonest extent of resection.

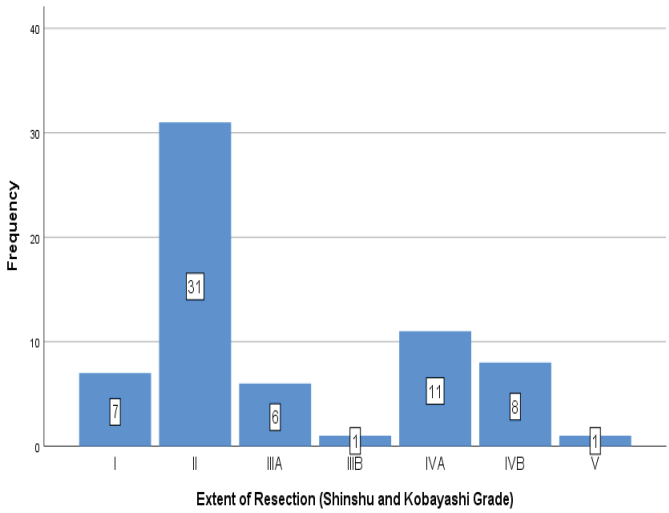

Figure 2. Shinshu and Kobayashi grade of resection in SBM

Figure 3 in one of the representative case of SBM managed at our center. She presented to us with headache and diminution of vision for one year. She underwent successful surgery for meningioma of the planum sphenoidale. Her vision improved significantly 3 months after surgery.

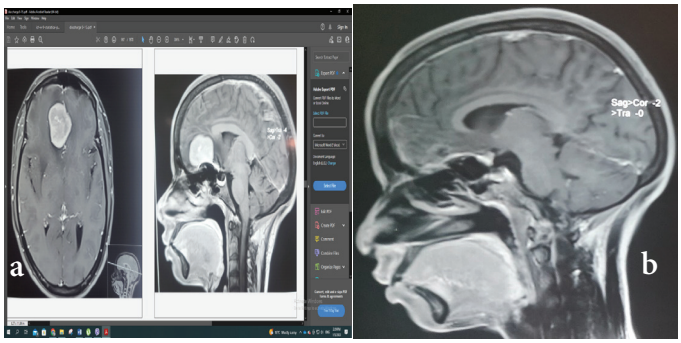

Figure 3. a.T1 sagittal MRI image of 30 years old female showing extra-axial intensely enhancing tumor in the region planum sphenoidale b. Postoperative T1 weighted sagittal post contrast MRI obtained in 2 months showing complete excision of the tumor. MRI=Magnetic Resonance Imaging

Regarding WHO grading of these tumors, majority (84.5%) were classified as WHO grade 1 while 7(13.8%) were classified as WHO grade 2. There were 3 cases of WHO grade 3 meningioma. Most common histological types were transitional (20) and meningothelial (19) which together constitute 62.9% of the tumor (Figure 4). Six out of 14 sphenoid wing meningiomas were meningothelial type while 7 out of 15 cerebellopontine meningiomas were of transitional type. There was no statistical significance of tumor grade or type (p= 0.56) with location. Bone invasion was present in 11(16.9%) patients based on preoperative imaging and intraoperative findings. Fourteen (21.5%) cases developed recurrence after surgery. Mortality in our series was 2(3.1%).

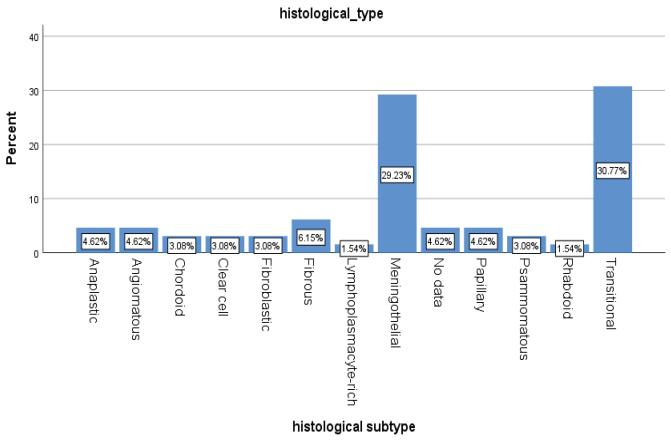

Figure 4. Histological subtypes of SBM

As shown in table 4 the difference between the KPS score and MRC-NPS pre and postoperative status in 3 months was analyzed using paired samples t-test There was a significant improvement from preoperative to postoperative status based on MRC-NPS scores (2.89 Vs 2.31; p=0.0001). KPS score significantly improved in the postoperative period (72.5 Vs 81.7; p=0.0001)

Table 4. Paired Samples Test [d(KPS)= Difference between preoperative and postoperative KPS score; d(MRC-NPS)= Difference between Preoperative and postoperative MRC-NPS score]

Mean		Paired Differences					Sig. (2-tailed)
		Std. Deviation	Std. Error Mean	Confidence Interval of the Difference 95%			
				Lower	Upper		
	d(KPS)	9.23077	12.66241	1.57058	6.09318	12.36836	.0001
	d(MRC-NPS)	0.58462	0.89952	0.11157	0.36173	0.80751	.0001

On analyzing, neurological deterioration and functional outcome after surgery, functional impairment occurred in 8 patients; and neurological deterioration observed in 5 cases. There was no change in functional status in 10 (15%) patients while the neurological deficits were unchanged in 30 (46 %) patients after surgery. In bivariate analysis, tumor size had significant low correlation with MRC-NPS (r=0.337; p=0.006) and KPS (r=-0.28; p=0.02). This reflects higher neurological and functional deterioration caused by the larger tumor. Tumor grade had significant low correlation with KPS(r=0.34; P= 0.005) and postoperative MRC-NPS (r=0.31; p=0.014) but not with preoperative MRC-NPS (p=value 0.47).

Discussion

SBMs demand optimal treatment strategy depending on the location and size. As these tumors are slow growing in nature they often has a less aggressive natural course compared to the supratentorial and convexity meningioma.[16][17] Possible explanation could be higher expression of progesterone receptors in SBM and low Ki 67 levels.[18] A subset of them might have indolent course but they are frequently the cause of significant neurological deficits.[19]) Surgery remains the mainstay of treatment for these tumors with adequate imaging evaluation of neurovascular involvement.[7] Larger tumor with intense enhancement might benefit from preoperative embolization which helps to minimize intraoperative blood loss.[20]

In our study, mean age of the patient was 45 years which is higher (56.3 years) in another study by Wang et al of SBMs.[21] Our higher female to male ratio compared to 2:1 in a study by Rohringer et al is probably explained by small sample size.[2] In a study by Bindal et al 35 out of 40 cases were female which is similar to our stusy.[19] In a study by Meling et al in 1148 cases of meningioma, gross total excision rate was 62% in SBM which is similar in this study. In our study, we were able achieve gross total resection in 38 out of 65 (58.5%) cases. However there is variable data regarding gross total resection which primarily depends on the tumor size and surrounding neurovascular involvement, availability of modern adjuncts which facilitates the resection as well as experience of surgeons. A study conducted in 2016 in Japan by Takeo et al have reported gross total resection rate of 70-100%.[22] In our series, 41.5% of cases underwent shinshu and kobayashi grade IIIA or higher extent of resection. Extensive infiltration of surrounding neurovascular structures was the major cause of incomplete resection. In a study by Adachi et al, many factors were identified which predicted the surgical risk and proposed ABC surgical risk scale to predict the extent of tumor removal. Tumor size, arterial effacement, brainstem compression, central location, and cranial nerve involvement were the factors on which the scale was based.[23]

Compared to another study by Scheitzach et al, mean tumor size was 3.5cm compared to 4.1cm in our series and mean MRC-NPS score was 2.02 compared to 2.89 in our series. Mean KPS was also higher 80.1 compared to 72.46 in our series.[11] This indicates delayed presentation with higher functional impairment. This attributes to less public awareness and inadequate access to neurosurgical care in Nepal. Our study suggests that that there is low, yet significant correlation of tumor size with pre-operative functional and neurological status. But the tumor size didn't affect the postoperative scores KPS and MRC-NPS scores. This implies that a larger size tumor can be resected with maximum safe resection strategy without causing further size related morbidity. The higher tumor grade was associated with lower preoperative KPS and higher neurological morbidity after surgery. Hence radical surgery may not be the best option. Safe maximal resection followed by adjuvant treatment may be the best option in such patients.[24] As per 5th edition of WHO Classification of CNS tumors 2021,[25] molecular analysis is necessary for accurate grading of meningioma and has highlighted that tumor with benign histology may have aggressive behavior in those tumors with TERT and CDKN2A/B mutation. Hence, adding molecular profile to histological grade will help to better prognosticate and tailor surgical approach for the management of this unique entity.[26] Perioperative mortality in our case was 3.1% which was similar to other study. [15]

In a study conducted by Scheitzach et al in 226 SBMs, mean KPS score was 81.0 (72.5 in our study) which improved to 87.4 after surgery. Similarly they have reported significant improvement on KPS score (preoperative 80.0 Vs postoperative 87.4) and MRC-NPS score (Preoperative 2.02 Vs postoperative 1.86; p<0.001).[19] We have similar improvement but we have lower mean preoperative KPS and higher mean preoperative MRC-NPS score owing to delayed presentation in our center. Improvement in neurological deficits was found in 60.1% in their series but only 30 (46.1%) out of 65 had neurological improvement after surgery in our series possibly due to delayed presentation.

Extent of resection clearly has implications on both recurrence rates and overall survival.[21] However, they pose a challenge of neurovascular preservation during surgery beside myriad of approach related complications. Hence, there is more inclination towards safe maximal resection owing to the indolent nature of SBM.[27] Now-a-days, the technology is rapidly evolving

which facilitates more radical excision and advent of minimally invasive surgery like endoscopic surgery in skull base arena for excision of these tumors. [28] In a 10 years study by Zhang et al in 2017, they have reported up to 94% gross total resection rate by endoscopic skull base approach.[29]

Conclusion

In our study there were altogether 65 operated cases of SBM which accounted for 16% of the cases. According to WHO grading, histopathology revealed majority (60%) were mesothelial and transitional subtype and belonged to grade 1. In regards to tumor size, over 90% were larger than 3 cm in diameter, indicating that nearly all were of large size tumors. Nearly half (47.7%) of these SBM underwent Shinsu and Kobayashi grade II resection. SBM excision helps to improve functional and neurological status of the patients. However, one should attempt to minimize approach related complications. The goal of surgery should be safe maximal resection rather than radical resection in case of neurovascular involvement.

References

1. Marosi C, Hassler M, Roessler K, Reni M, Sant M, Mazza E, et al. Meningioma. Crit Rev Oncol Hematol. 2008;67(2):153–71.
2. Rohringer M, Sutherland GR, Louw DF, Sima AAF. Incidence and clinicopathological features of meningioma. J Neurosurg. 1989;71(5 I):665–72.
3. Edition S. Al-Mefty's Meningiomas. Al-Mefty's Meningiomas. 2014.
4. Apra C, Peyre M, Kalamarides M. Current treatment options for meningioma. Expert Rev Neurother [Internet]. 2018;18(3):241–9. Available from: https://doi.org/10.1080/14737175.2018.1429920
5. Lefkowitz MA, Hinton DR, Weiss MH, Giannotta SL, Couldwell WT. Prognostic variables in surgery for skull base meningiomas. Neurosurg Focus. 2008;2(4):E4.
6. Nanda A, Vannemreddy P. Recurrence and outcome in skull base meningiomas: Do they differ from other intracranial meningiomas? Skull Base. 2008;18(4):243–52.
7. Samii M, Gerganov VM. Surgery of extra-axial tumors of the cerebral base. Neurosurgery. 2008;62(6 SUPPL.):1153–68.
8. Raheja A, Couldwell WT. Microsurgical resection of skull base meningioma—expanding the operative corridor. J Neurooncol [Internet]. 2016;130(2):263–7. Available from: http://dx.doi.org/10.1007/s11060-016-2197-7
9. Da Broi M, Borrelli P, Meling TR. Predictors of survival in subtotally resected who grade i skull base meningiomas. Cancers (Basel). 2021;13(6):1–12.
10. Stark AM, Stepper W, Mehdorn HM. Outcome evaluation in glioblastoma patients using different ranking scores: KPS, GOS, mRS and MRC. Eur J Cancer Care (Engl). 2010;19(1):39–44.
11. Scheitzach J, Schebesch KM, Brawanski A, Proescholdt MA. Skull base meningiomas: Neurological outcome after microsurgical resection. J Neurooncol. 2014;116(2):381–6.
12. Latif AZB, Signorini D, Gregor A, Grant R, Ironside JW, Whittle IR. Application of the MRC brain tumour prognostic index to patients with malignant glioma not managed in randomised control trial. J Neurol Neurosurg Psychiatry. 1998;64(6):747–50.
13. SIMPSON D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry. 1957;20(1):22–39.
14. Kobayashi S, Okudera H, Kyoshima K. Surgical Considerations on Skull Base Meningiomas. Skull Base Surg. 2015;173–4.
15. Chen CM, Huang APH, Kuo LT, Tu YK. Contemporary surgical outcome for skull base meningiomas. Neurosurg Rev. 2011;34(3):281–96.
16. Savardekar AR, Patra DP, Bir S, Thakur JD, Mohammed N, Bollam P, et al. Differential Tumor Progression Patterns in Skull Base Versus Non–Skull Base Meningiomas: A Critical Analysis from a Long-Term Follow-Up Study and Review of Literature. World Neurosurg [Internet]. 2018;112(2018):e74–83. Available from: https://doi.org/10.1016/j.wneu.2017.12.035
17. Hashimoto N, Rabo CS, Okita Y, Kinoshita M, Kagawa N, Fujimoto Y, et al. Slower growth of skull base meningiomas compared with non-skull base meningiomas based on volumetric and biological studies: Clinical article. J Neurosurg. 2012;116(3):574–80.
18. Kuroi Y, Matsumoto K, Shibuya M, Kasuya H. Progesterone Receptor Is Responsible for Benign Biology of Skull Base Meningioma. World Neurosurg [Internet]. 2018;118:e918–24. Available from: https://doi.org/10.1016/j.wneu.2018.07.100
19. Bindal R, Goodman JM, Kawasaki A, Purvin V, Kuzma B. The natural history of untreated skull base meningiomas. Surg Neurol. 2003;59(2):87–92.
20. Luther E, Kaur G, Komotar R, Ivan ME. Commentary: Concomitant embolization and microsurgical resection of a giant, hypervascular skull base meningioma: 2-dimensional operative video. Oper Neurosurg. 2021;21(2):E99–100.
21. Wang YC, Chuang CC, Wei KC, Hsu YH, Hsu PW, Lee ST, et al. Skull base atypical meningioma: Long term surgical outcome and prognostic factors. Clin Neurol Neurosurg [Internet]. 2015;128:112–6. Available from: http://dx.doi.org/10.1016/j.clineuro.2014.11.009
22. Goto T, Ohata K. Surgical resectability of skull base meningiomas. Neurol Med Chir (Tokyo). 2016;56(7):372–8.

23. Adachi K, Kawase T, Yoshida K, Yazaki T, Onozuka S. ABC Surgical Risk Scale for skull base meningioma: A new scoring system for predicting the extent of tumor removal and neurological outcome - Clinical article. J Neurosurg. 2009;111(5):1053–61.

24. Wagner A, Joerger AK, Lange N, Meyer B, Shiban E. Surgical and Functional Outcome after Resection of 57 Tentorial Meningiomas. Sci Rep. 2019;9(1):1–8.

25. WHO Classification of Tumors. Definitions. 2020.

26. Birzu C, Peyre M, Sahm F. Molecular alterations in meningioma: prognostic and therapeutic perspectives. Curr Opin Oncol. 2020;32(6):613–22.

27. Ichinose T, Goto T, Ishibashi K, Takami T, Ohata K. The role of radical microsurgical resection in multimodal treatment for skull base meningioma. J Neurosurg. 2010;113(5):1072–8.

28. Wang EW, Zanation AM, Gardner PA, Schwartz TH, Eloy JA, Adappa ND, et al. ICAR: endoscopic skull-base surgery. Int Forum Allergy Rhinol. 2019;9(S3):S145–365.

29. Zhang QH, Wang ZL, Guo HC, Kong F, Yan B, Li MC, et al. Endoscopic approach to remove intra-extracranial tumors in various skull base regions: 10-year experience of a single center. Chin Med J (Engl). 2017;130(24):2933–40.