Original article

Ukr Neurosurg J. 2021;27(4):30-37
doi: 10.25305/unj.242064

Recurrence rate of sphenoid wing meningiomas and role of peritumoural brain edema: a single center retrospective study

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Received: 10 October 2021
Accepted: 19 November 2021

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Objective: To evaluate the recurrence rate of the operatively treated sphenoid wing meningiomas (SWMs) in relation to other factors and role of PTBE in recurrence as a prognostic factors in a series of 67 patients.

Materials and methods: The magnetic resonance imaging (MRI), and pathology data for 67 patients with SWM, who underwent surgery at Uzhhorod Regional Neurosurgical Center between 2007 and 2021 were examined. **T**he recurrence rate and role of PTBE in recurrence in relation to: gender, age, extend of resection, histopathology, tumor volume, location and time of recurrence were evaluated. Follow-up period ranged from 6 to 168 months (median, 87 months) after surgical resection.

Results: In our study, the mean age of patients is 47 years, ranged (20-74), at the average (53.5). Male 16 (23.9%), female 51 (76.1%). Mean tumor volume was (32.8cm^3), ranged 4.2cm^3-143.7cm^3. Edema Index (EI) 1; 27 (40.3%) absent edema, and (EI) >1; in 40 (59.7%) present edema. Recurrence rate was 11 (16.4%) patients, 8 (20.0%) patients with PTBE, as compared to 3 (11.1%) patients without PTBE, (p=0,50). Female (8 patients, 15.7%), male (3 patients, 18.7%). The mean age of recurrence was 50.9 years, ranged (21-75), at the average 52.0 years. The mean age in female was 50.8 years, in male 51.0. Bivariate analysis of simultaneous effect of gender and age on SWM recurrence with logistic regression yield both main effect and interaction effect (β gender=M=7.56±6.44, P=0.24; β age=-0.034±0.031, p=0.28; β interaction term=-0.13±0.12, p=0.26).

Out of 11 recurrence cases, (2 cases, 9.5%) with small tumour volume, (5 cases, 15.6%) with medium, (3 cases, 33.3%) with large, and (one case, 20.0%) with giant tumour volume**.** The effect of tumour volume on recurrence rate is insignificant, χ^2=2.42, p=0.49.Location of SWM*;* the recurrence was in (6 cases, 25.0%) of CM location, (2 cases, 25.0%) of SOM and (3 cases, 11.5%) in lateral SWM, (p=0.19). Pathological grade*,* in the low grade (Gr.I) 7 recurrence cases (13.0%), as compared to 4cases (44.4%) in atypical Gr II, (p=0.01). Simpson grade*,* the recurrence rate was; 0% in Gr. I; 13.9% in Gr. II; 20.0% in Gr.III; and 33.3% in Gr. IV and 3 cases had died in the early post op (p<0.05).

Conclusion: The factors which had a strong impact on the recurrence rate in our study,; i) pathological grade (Gr. II, atypical type) p=0.01 and ii) Simpson grade (extend of tumor resection, p<0.05), while, PTBE (P=0.50), tumor volume (χ^2=2.42, p=0.49) and location (χ^2=3.37, p=0.19), are weak and non strong factors for recurrence. However, time of recurrence is shorter in patients with PTBE (W=20.5, p=0.092). WHO Gr. II (Spearman's p=-0.86, p=0.00063) and negligible for Simpson grade (Spearman's=-0.15, p=0.66).

Key words: *peritumoral brain edema; sphenoid wing; recurrence; tumor volume; pathological grade.*

SWM: sphenoidwingmeningiomas; **CT:** Computer Tomography; **EI:** Edema Index; **MRI:** Magnetic Resonance Imaging; **PTBE:**Peritumoral Brain Edema;**ICA:** Internal Carotid Artery; **MCA:** Middle Cerebral Artery; **SOM:** Spheno-orbital meningioma;WHO: World Health Organization; **CM:** Clinoidal Meningioma.

Introduction

Sphenoid wing meningiomas (SWM) make up approximately 10-15% of total cranial meningiomas. Meningioma possesses the ability to produce peritumoral brain edema (PTBE), despite the fact that it is extra cerebral origin, and benign, slow-growing tumor [1,2].

According to the WHO classification, meningioma can be of type I, which is the benign form, type II usually

referred to as the atypical meningioma and type III, which is the malignant meningioma [3].

Surgical intervention in intracranial meningioma patients aims for complete resection, which produces an improved long-term recurrence rate [4, 5]. However, Meningioma recurs in about 20–30% of cases [6]. Studying factors that cause tumor recurrence is important because meningioma can be cured with the proper surgical intervention. Factors that determine recurrence of meningioma include the extent of tumor resection according to the Simpson grading system; which is the most important factor, age, gender, histology of the tumor, location of meningioma, vascularity of the tumor, the shape of the tumor surface, the arachnoid plane between the tumor and the brain surface as well as the presence of preoperative PTBE [7-9].

This study aims to establish the factors were linked to recurrence and role of PTBE in recurrence of SWM.

Materials and methods

We retrospectively reviewed 76 of patients with SWMs were treated between 2007 and 2021, at Uzhhorod Neurosurgical Center. 9 patients were lost to follow up and were thus excluded from statistical analysis.16 male (23.9%) and 51 female (76.1%) patients were included in our study, with an age range of 20–74 years (mean, 47 years), at the average 53.5 years. Mean age in the female group was 53.0vs 57.0 in the male group.

MRI were done in all patients prior surgery, and radiological data included tumor volume and PTBE. After surgery, histo pathological and immune histochemical analysis was performed.

Radiological examination and follow-up

In our study, the tumour volume and PTBE were measured using preoperative contrast enhanced and T2-weighted MRI films. Tumor volume was measured in three maximal diameters, using axial (a) sagittal (b) and coronal (c) scans; V = a x b x c /2. ***(Fig. 1).*** Tumour volume in this study, was classified in 4 groups,; group (A), small volume tumour (<13.5 cm^3, size of tumour <3cm), group (B), medium volume tumour (>13.5-62.5 cm^3; size of tumour 3 - < 5 cm), group (C), large (62.6-108 cm^3, size 5-6 cm),and group (D), giant (> 108 cm^3, size more 6 cm).

The formula for PTBE index **(**EI) is: EI= (V tumor + V edema) / (V tumor), ***(Fig. 2).***

An EI of 1 (absent PTBE), and EI more than 1.0 (present PTBE), andthe degree was classified as (EI) >1 - < 2 (mild),;2–<3 (moderate),;3 and more (severe).

Regarding *anatomical location,* 26 (38.8%) cases with lateral SWM, middle SWM 9 (13.2%) cases, CM 24 (36%) cases, and SOM 8 (12%) cases, with mean volume 30.7cm^3range (4.5-78.6 cm^3).

All patients had CT and MRI scans postoperatively with and without gadolinium.

The appearance of new enhanced lesions after total resection or gross total resection, or re-growth of tumor after subtotal resection in the follow-up MRI with enhancement was considered as tumor recurrence.

Surgical Techniques

In our data, all patients were operated electively, none patient was operated emergency.

The surgical approaches included in our study were performed classic Pterional Approach, skin incisions and craniotomies were fashioned according to the exact anatomical location of the lesions, determined by the pre-operative CT scan & MRI images. Extended Pterional Approach was mainly chosen in some cases for large SWMs with skull base bone invasion or severe edema. In all 24 cases of MSWM with or without CS involvement, skull base approach, with extra dural anterior clinoidectomy was done either by high speed drill or bone forceps, for early optic nerve unroofing and decompression, and for early identification and control of key neurovascular structures. Other approach was used in this study was FTOZ in single case.

Extend of tumor resection based on Simpson Grade; total resection (Gr. I-II) was achieved in 43, GTR (Gr. III) in 15 and STR (Gr. IV) in 9 patients.

Pathologic studies

According to WHO classification of tumors of the central nervous system, there were 54 grade I cases (80.6%) classified into endothelial type (37

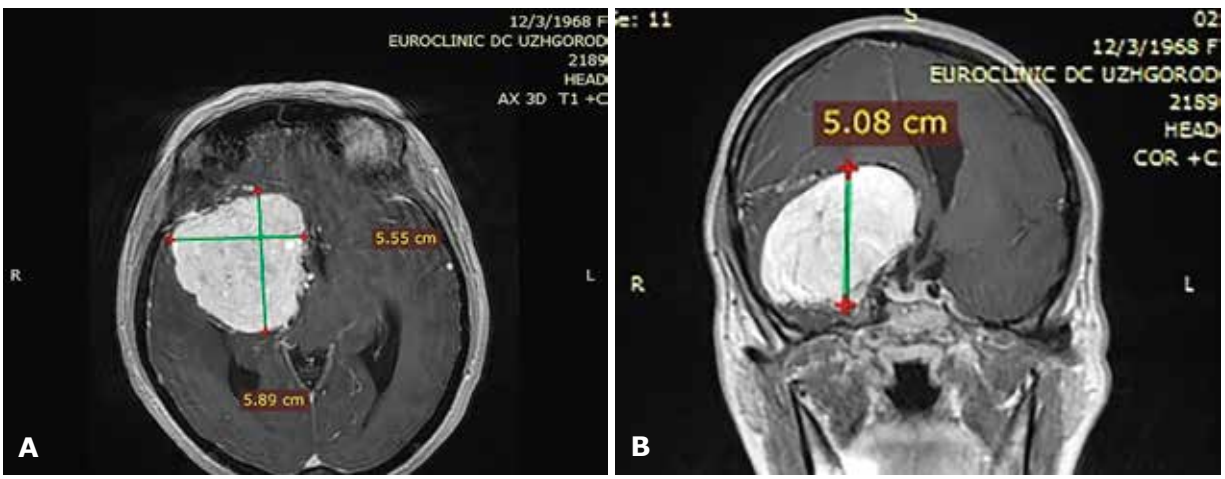

Fig. 1. Tumour volume= sagital× coronal× axial /2:5.8×5.5×5.1/2=162/2=81.3 cm^3

This article contains some figures that are displayed in color online but in black and white in the print edition

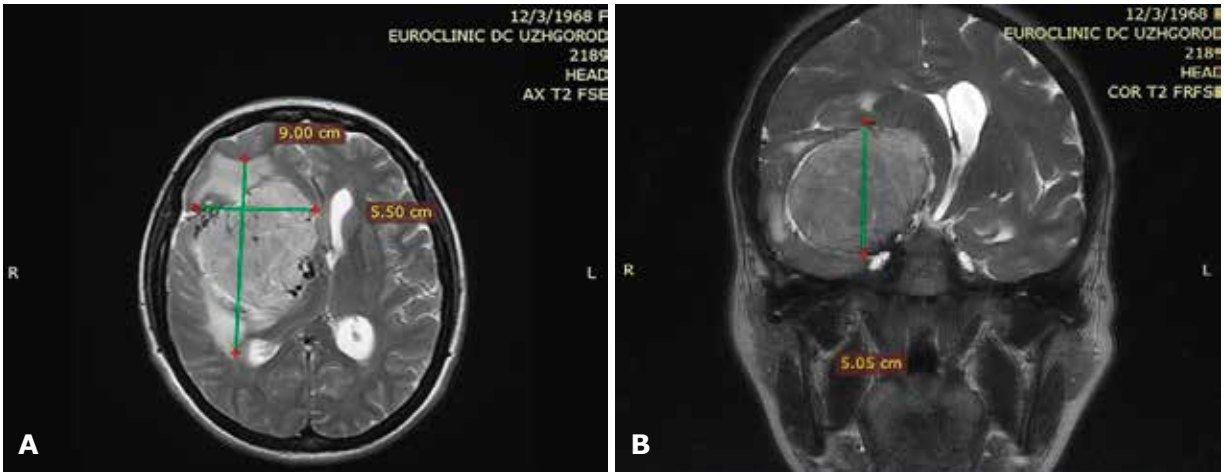

Fig. 2. PTBE volume= sagital× coronal× axial /2: 9.0×5.5×5.1 /2= 252/2=126 cm^3: EI=126/81=1.6 (mild PTBE)

cases, 68.5%), fibrous (7 cases, 12.9%), transitional (5 cases, 9.2%), angiomatous (6 cases, 11.1%) and psammomatous type found in a single patient. Grade II tumor, atypical type found in 11 cases (16.4%), and Grade III, anaplastic type found in 2 cases (3.0%).

Statistical Analysis

Descriptive statistics in the study is reported with percentage, mean and standard deviation or median with lower (LQ) and upper (UQ) quartiles considering the inherent nature of each studied variable. The hypothesis about the between-groups difference in proportions and rate was tested with Yates- corrected chi-squared test or Fisher's exact test where appropriate. Wilcoxon-Mann-Whitney test has been utilized to compare age and PTBE index between two groups, since the available data violates normal distribution. Spearman's correlation coefficient has been preferred over the Pearson's one due to the same reason. Ordinal data like WHO tumor grade has been studied with ordinal logistic regression. Statistical significance of regression models was assessed with Likelihood-ratio test of nested models. All computations were performed in R4.0.0.

Results

Incidence of SWM in relation to gender and age

This study showed female had higher tendency 51 (76.1%) as compared to male 16 (23.9%), the ratio F/M was 3.2:1.

Age in the female group was 53.0±8.3 vs 57.0±11.7 in the male group (W=508.5, p=0.14), the difference is insignificant.

PTBE in relation to gender and age

The edema was found in 40 (59.7%) cases with rather even distribution across gender. PTBE occurrence in females was 62.7%, in males -50.0% (χ^2 =0.38, p=0.54) ***(Table 1).*** Mild EI was in 24 (60.0) patients, moderate in 5 (12.5%) patients and severe in 11 (27.5%) patients.

Recurrence Rate

Incidence

Recurrence rate in this study was 11 (16.4%) patients, 8 (20.0%) patients among 40 cases with PTBE, as compared to 3 (11.1%) patients among 27 cases without PTBE, median f/u 87 months, range 6 to 168 months, (Table-2). There is weak and insignificant

Table 1. Incidence of PTBE according to age and gender (n=67)

Edema cases and age of SWM patients	Gender		Statistical significance
	Male (n=16)	Female (n=51)	
Age (median; quartiles)	58; 55.25-60.75	53; 48-60	W=293, p=0.13
<40	1 (6.3%)	5 (9.8%)	
40-49	1 (6.3%)	11 (21.6%)	
50-59	9 (56.2%)	19 (37.2%)	
60-69	5 (31.2%)	13 (25.5%)	
>70	-	3 (5.8%)	
Edema	8 (50.0%)	32 (62.7%)	χ^2=0.38, p=0.54
Mild	5 (62.5%)	19 (59.4%)	χ^2=0.91, p=0.34
Moderate	1 (12.5%)	4 (12.5%)	
Severe	2 (25.0%)	9 (28.1%)	

association between PTBE and recurrence OR=1.98, 95% CI 0.42-12.8, P=0.50.

Recurrence Rate and Gender

Out of 11 recurrent cases, female (8 patients, 15.7%) male (3 patients, 18.7%) ***(Table 2)***. The difference has been found to be slightly above in male patient, OR=1.2, 95% CI 0.18-6.2, p=0.72. However, there was no strong association between patients gender and recurrence (Me rec.+ =55, Me rec.-=55. W=380. P=0.23).

Recurrence Rate and Age

The mean age of recurrence in this study was 50.9 years, ranged (21-75), median 52.0 years. The mean age in female was50.8 years ranged (21-75), median 51.0 years. The mean age in male was 51.0 years ranged (37-62) years, median 54 years. We could not find difference in age between female (median 51.6 years) as compared to male (median, 54.0 years)

Bivariate analysis of simultaneous effect of gender and age on SWM recurrence with logistic regression yield both main effect and interaction effect (β gender=M=7.56±6.44, P=0.24; β age=-0.034±0.031, p=0.28; β interaction term=-0.13±0.12, p=0.26).

Recurrence Rate and Tumour Volume

Out of 11 recurrent cases, (2 cases, 9.5%) with small tumour volume, (5 cases, 15.6%) with medium, (3 cases, 33.3%) with large and (one case, 20.0%) with giant tumour volume ***(Table 3)*** Patients with large and giant tumor volume tend to show higher risk for recurrence 28.5% as compared to small volume 9.5%, though the difference in 3 times more than small tumor volume.

Table 2. Recurrence in relation to gender (n=67)

Gender	Recurrence (n=11)	Present PTBE (n=40)	Absent PTBE (n=27)
Female (n=51)	8 (15.7%)	6 (15.0%)	2 (7.4%)
Male (n=16)	3 (18.7%)	2 (5.0%)	1 (3.7%)
Total (n=67)	11 (16.4%)	8 (20.0%)	3 (11.1%)

Table 3. Univariate analysis of various factors on Recurrence (n=67)

Variable Factors	No. of patient	No. of Recurrence/PTBE	Percentage
Females	51	8/6	15.7%
Males	16	3/2	18.8%
Extend of resection			
Simpson Gr. I-II	43	6/4	13.9%
Simpson Gr. III	15	3/2	20%
Simpson Gr. IV	9	2/2	33.3%
Pathological Grade			
WHO Gr. I	54	7/4	13.0%
WHO Gr. II	11	4/4	44.4%
WHO Gr.III	2	-	-
Tumor Volume			
Small	21	2/1	9.5%
Medium	32	5/4	15.6%
Large	9	3/2	33.3%
Giant	5	1/1	20.0%
PTBE			
Yeas	40	8	20.0%
No	27	3	11.1%
Anatomical Location			
Lateral	26	3/2	11.5%
Middle	9	-	-
Medial (CM)	24	6/4	25.0%
SOM	8	2/2	25.0%
Total	67	11/8	

However, the effect of tumor volume on recurrence rate is insignificant, χ^2=2.42, p=0.49. Despite, the positive relation was found between extend of tumor resection and tumor volume, (P= 0.01).

Recurrence Rate and Location

The recurrence was in (6 cases, 25.0%) of CM location, (2cases, 25.0%) of SOM and ?? (3cases, 11.5%) in lateral SWM, (Table 3). There was found association between recurrence and anatomical location, though, the CM and SOM show higher incidence for recurrence in twice more than lateral SWM. However, the effect of tumor location on recurrence rate is insignificant, χ^2=3.37, p=0.19. Dispite, thestrong relation between extend of tumour resection and anatomical location, lesser in CM, (p=0.10) and smaller overall total resection (Gr. I-II), (χ^2=6.24, p=0.0054).

Recurrence Rate and Pathological Grade

In the low grade (Gr.I) 7 recurrence cases (13.0%), as compared to 4cases (36.4%) in atypical Gr. II, (Table.3). The effect of pathological grade on recurrence rate is insignificant, χ^2=3.76, p=0.15, (when excluded 2 died patients with WHO grade II, the ratio will 13.0%vs44.4% and though to reach statistical significance, (p=0.01).

Recurrence Rate and Tumour Resection

The recurrence rate was; 0% in Gr. I; 13.9% in Gr. II; 20.0% in Gr.III; and 22.2% in Gr. IV (Table 3). Residual non progression tumor in 4 cases. The effect of tumour resection grade on recurrence rate is insignificant, χ^2=1.47, p=0.69.The explain of decreasedrecurrence among patients in Simpson Gr. IV due to mortality in 3 cases which died early post operative and all had PTBE. When excluded this 3 died patients, the recurrence will be 33.3% in Simpson grade IV, two and half time more than Simpson grade II, and though to be statistically significant, p<0.05.

Time of Recurrence

Median time to recurrence in recurred patients is 2 years, mean time to recurrence =2.9±2.3 years. Presence of edema was associated with shorter time to recurrence (mean=2.4 in PTBE group versus mean=4.33 in patients without prior PTBE), though the difference does not reach statistical significance (W=20.5, p=0.092). There is strong correlation of time to recurrence and WHO grade of tumor with much shorter time to recurrence in patients of grade II WHO grade (Spearman's p=-0.86, p=0.00063). The correlation between time to recurrence and Simpson grade of resection is negligible (Spearman's=-0.15, p=0.66) ***(Table 4)***.

Discussion

In our study, were operated upon 67 patients SWM retrospectively, females had higher tendency 51 (76.1%) as compared to males 16 (23.9%), the ratio F/M was 3.2:1, age in the female group was 53.0±8.3 vs 57.0±11.7 in the male group (W=508.5, p=0.14), the difference is insignificant.. *Magill et al.,* also found, that females had 2.8 times as compared to males and that mean age was 55.7 years among 1113 meningioma patients in their study [10].

Despite primarily extra axial locations, slow progression rates, and usually benign histological characteristics, meningiomas frequently are associated with PTBE [11]. PTBE is found in approximately 50% of meningiomas, and originates in the region of the tumour margin and travels by bulk flow through the relatively loosely interconnectedfibers of white matter [12, 13].

Meningioma is mostly a benign tumor that can be cured by total surgical excision [14, 15]. However recurrence occurs in almost 20% of cases [16, 17]. Many factors were linked to recurrence including; gender, age, shape of the tumor surface, PTBE and before all, the extent of tumor excision according to the *Simpson* grading system [18-20]. In this study we aimed to establish the factors were related to recurrence and role of PTBE inrecurrence SWM.

Recurrence rate in this study was 16.4% patients in mean f/u 87 months (range 6-168 months), with rather even distribution across gender; females (15.7%), males (18.7%) P=0.23 and age; mean age in females was 50.8 years and 51.0 years in males, (p=0.28). Similar observations were found by *R.O. Mirimnoff et al.,* who studied 225 cases and observed that was no difference in recurrence or progression rates according to age or gender within 5 and 10 years f/u [21].

Many studies have showed that PTBE was significantly associated with recurrence in meningiomas [22, 23]. Furthermore, sphenoid ridge and parasagittal meningiomas, represented the most common locations for recurrent in one study, and both of them had preoperative PTBE in all cases [24]. *Simis et al.,* provided a plausible explanation to the role of PTBE in recurrence of meningioma. He concluded that PTBE was associated with the invading potential of meningiomas [22]. In our study there is a weak and insignificant association was found between PTBE and recurrence OR=1.98, 95% CI 0.42-12.8, P=0.50. However, this does not mean that PTBE is unimportant, the presence of edema was associated with shorter time to recurrence

Table 4. Recurrence according to time/year in 67 patients, median f/u 87 months

Time of Recurrence/year	Recurrence (n=11)	Present PTBE (n=8)	Absent PTBE (n=3)
one year	4 (36.3%)	4	-
2 years	2 (18.2%)	2	-
3 years	2 (18.2%)	1	1
5 years	2 (18.2%)	1	1
8 years	1 (9.1%)	-	1

(mean=2.4years in PTBE group vs mean=4.33 years in patients without prior PTBE). This finding is also supported by other study reports that, tumours showing recurrence were associated with a higher pre-operative PTBE index and those with higher PTBE index were associated with lesser time to recur [24].

The recurrence rate in our data was 13% of WHO grade I tumors and 44.4% in WHO grade II. One study with a single series of 1799 meningiomas from 1582 patients followed for an average of 13 years showed that the recurrence rate was 7% of WHO I tumors 35% of WHO II, and 72.7% of WHO III [25]. These findings correspond with our study. Furthermore,the grading of the average recurrenceratesof these three groups by WHO 2016, was 7.0% to 20.0% in grade I, whereas, 30.0%to40.0% and 50.0%to 80.0% in grade II and grade III respectively [26].

Bivariate analysis of simultaneous effect of pathological grade and PTBE on tumor recurrence, pathological grade confirmed higher risk of recurrence in Grade II (44.4%) vs (13.0%) in Grade I, $p<0.05$,and no association between PTBE and recurrence, $p=0.50$

The relationship between histopathology and recurrence is still uncertain. [27].

However, a subset of WHO grade I meningiomas with a high-risk potential were also seen to recur. Marciscano et al., gave a probable explanation to this recurrence in benign (WHO grade I) meningiomas. He emphasized that such benign (WHO grade I) tumours possessed some atypical areas which predisposed it to recur. He also proved that the chance of recurrence was higher in WHO grade III and WHO grade II meningiomas being 60-94% and 29-59%, respectively, while the chance of recurrence in WHO grade I meningiomas was found to be 7-25% only [27]. Several studies have tried to provide an explanation as to the increased risk of recurrence in WHO grade II and grade III meningiomas; higher cellularity, atypical and brisk mitosis and presence of necrosis possibly are some factors implicated in high recurrence [28, 29]. Further, among other factors that predispose to recurrence, PTBE represents a key factor [22]. Notably, in our study we observed the strong correlation of time to recurrence and WHO grade of tumor with much shorter time to recurrence in patients of grade II WHO grade (Spearman's $p=-0.86$, $p=0.00063$).

Many studies have shown that extent of resection is the most important factor influencing recurrence rate [29]. Incomplete resection of meningiomas frequently results in recurrence, but even total resection is associated with a significantly high incidence of recurrence, ranging from 3 to 32% in different series [21]. Other report by T Ouyang et al., who studied 53 SWM cases and observed 46.7% with STR (grade IV) had recurrence as compared to 7.9% with total resection (grade I-II) $p=0.004$ [30].This present study agrees with previous works in the importance of extent of resection to recurrence. In our group, 13.9% with complete removal Simpson grade (I-II) had recurrence, 20% with Simpson grade III, and 33.3% recurrence cases of the (9 patient with Simpson grade IV), 3 died early post op, and other 4 cases with residual non progression. There is a positive correlation between extend of resection according to Simpson grade and recurrence and though to be significant $p<0.05$

Multivariate analysis of simultaneous effect of Simpson grade, time of recurrence and PTBE on tumor recurrence, Simpson grade confirmed higher risk of recurrence in Grade IV (33.3%) vs (13.9%) in grade I-II. $p<0.05$, while no association was found between PTBE and recurrence. Remarkably, the correlation between time to recurrence and Simpson grade of resection is negligible (Spearman's=-0.15, $p=0.66$).

Recurrence was in 9.5% with small tumour volume,15.6% with medium, 33.3% with large and 20.0% with giant tumour volume. It was evident thatpatients with large and giant tend to show higher risk for recurrence 28.5% as compared to small volume 9.5%, though the difference is in 3 times more than small tumor volume. However, the effect of tumor volume on recurrence rate is insignificant, ($\chi^2=2.42$, $p=0.49$). Other study showed that, tumor size also an important factor for the surgical outcome [31]. In the report presented by Liu DY et al., [32] was found, a statistic significance in the extent of resection distribution between large and medium and small tumors ($p=0.032$), while tumor recurrence was not significantly corrected with the tumor size ($p=0.209$). We agree with previously works that large tumor is also a worse predictive factor for complete tumors resection ($p=0.01$),while it is not a significant factor for recurrence, (($p=0.49$).

In our study,the recurrence was in 25.0% for each of CM and SOM, while 11.5% was in lateral and 0% was in middle SWMs location. There was found the association between recurrence and anatomical location, though, the CM and SOM show higher incidence for recurrence in twice more than lateral SWM. However, the effect of tumor location on recurrence rate is insignificant, $\chi^2=3.37$, $p=0.19$. This finding also supported by other study reports thatmeningiomas that were strictly limited to the middle and lateral sphenoid wing have a recurrence rate of less than 10% [21]. Guduk et al. reported tumor recurrence in 27% among 141 of SWM cases, of which 40% were SOMs and 18% were LSWMs [33]. Bonnal J et al., in their works and experience have observed, that recurrence of lateral and middle SWMs start from anterior clinoid process, when tumor extend medially, and resection of ACP might help to reduce the recurrence rate [34].

Conclusion

Finally, the common surgical findings which had a strong impact on the recurrence rate in our study,;pathological grade (Gr. II, atypical type) and Simpson grade (extend of tumor resection),while, PTBE, tumor volume and location, are weak and non strong factors for recurrence (statistically insignificant). However, time of recurrence is shorter in patients with PTBE, WHO Gr. II and negligible for Simpson grade. Moreover, bivariate analysis of simultaneous effect of gender, and age on SWM recurrence with logistic regression,yield both main effect and interaction.

Disclosure

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical

standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

The written informed consent was obtained from each patient or appropriate family member before the surgery.

Funding

The research had no sponsor support.

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