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Evaluation of Non-Surgical Management of Intracranial Meningioma

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ABSTRACT

Background: Meningiomas are common extra-axial primary brain tumors, which originate from the arachnoid cap cells. It's possible that intracranial meningiomas can be managed non-surgically.

Objective: The aim of the current study was to evaluate non-surgical management of intracranial meningiomas to better guide the management decision-making.

Patients and methods: A retrospective analytical study was conducted at the Department of Neurosurgery in the Faculty of Medicine at Zagazig University. A total of 53 patients, with 57 meningiomas were enrolled in the current study. Patients were divided into 2 groups based on symptomatic and radiological progression; *Group A* included 42 patients who continued non-surgical management, and *Group B* included 11 patients who required surgical intervention. **Results**: During the follow-up period, 19.3% of patients needed surgical intervention. The mean age of cases was of 54.1 (SD 9.7) years. *Group A* patients had significantly older ages at diagnosis than *Group B* patients (P<0.05). The tumor size in *Group A* was <25mm (64.4%), ranged from 25-40mm (35.6%), and >40 mm (0%) versus 25%, 66.7%, and 8.3%, respectively in *Group B* (P=0.014). Increased size at diagnosis was a significant predictor for surgical intervention (P<0.05). In *Group A*, the rate of growth/year was 1.94 (SD 0.74) mm with the range 0.22-3.94 mm/year versus 4.92 (SD 1.3) mm with the range 3.1-6.75 mm/year in *Group B* (P=0.0001).

Conclusion: Our results contribute to predicting the growth pattern of intracranial meningioma and thus select the optimal management.

Keywords: Meningioma, Conservative, Growth rate, Non-surgical management.

INTRODUCTION

About a third of all 1ry brain tumors are meningiomas. The incidence of intracranial meningiomas is 2.3 per 100,000. The peak age is between the ages of 60 and 69, and the majority of them are women [(1)]. Based on histologic criteria, the World Health Organization divided meningiomas into 15 subgroups across 3 grades. About 80.5% of meningiomas are WHO grade 1, which have benign histology and indolent behavior. In contrast, grade 2 (17.7%) and grade 3 (1.7%) meningiomas have atypical to malignant histology and are more aggressive. Only ionized radiation exposure stands out as a potential environmental risk factor for meningioma, which has been linked to increases in the risk of 6-10 times [(2)].

Understanding the individual's goals for therapy and weighing those against the potential short- and long-term benefits and dangers is crucial [(1)].

About 2% of cranial MRIs will reveal an asymptomatic meningioma. More people are getting cranial imaging and with that come a rise in the number of patients diagnosed with meningioma by chance. Waiting to observe if the lesion progresses is a common treatment option, because of its' benign nature, modest size, and lack of compression on surrounding structures [(3)]. Increasing neurologic deficit and radiographic evidence of a surgically curable tumor make surgery an obvious indication in many individuals. In other cases, it may be best to simply observe the patient and assess them clinically and with MRI scans regularly. Patients who have no symptoms and minimal or no edema in the surrounding brain areas are good candidates for observation, as are those with minimal symptoms or a long history, those who are elderly and whose symptoms are progressing slowly, those whose life expectancy is short and/or whose clinical condition is poor due to their age, and those for whom surgery carries a significant hazard [(1)].

The aim of the current study was to evaluate non-surgical management of intracranial meningiomas to better guide the management decision-making.

PATIENTS AND METHODS

A retrospective analytical study was conducted at the Department of Neurosurgery in the Faculty of Medicine at Zagazig University. A total of 53 patients, with 57 meningiomas were enrolled in the current study.

Inclusion criteria: Patients with non-surgically treated brain meningiomas who presented to the Department of Neurosurgery at Zagazig University Hospitals from January 2015 to November 2022.

Exclusion criteria: Patients lost during the follow-up period.

Patient evaluation: All patients involved were subjected to clinical assessment by general and neurological examination, in addition to laboratory and radiological assessment.

a) Clinical assessment:

- **History taking**: Personal history, onset, and course of any complaint.
- **General examination**: Paying particular attention to the symptoms of systemic illness.

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- **Neurological examination**: Mental state and higher mental functions, speech, cranial nerves, motor system, sensory system, reflexes, coordination, and cerebellar evaluation.
- **Ophthalmological examination**: Complete assessment of the eye movement, visual acuity, visual field, and fundus examination.

b) Radiological investigations: All patients underwent evaluation by computed tomography (CT) scanning of the brain and skull or magnetic resonance imaging (MRI) of the brain with and without contrast administration. The diagnosis was based on findings of a uniformly enhanced extra-axial dural-based mass by CT or MRI. Both T1WI and T2WI were performed in three planes. Brain MRI was the diagnostic modality of choice in this study, it was helpful in delineating of the relationship of the tumor to the brain and it was very helpful in delineating the exact anatomical location of the tumor and its extent to nearby neurovascular structures. Magnetic resonance spectroscopy (MRS) was performed in selected cases.

Management:

All cases of meningiomas that were managed non-surgically at the initial time of presentation were included. All patients were referred to our outpatient clinic after undergoing diagnostic imaging. Their medical records and imaging data were analyzed. The endpoint for conservative treatment was the development of clinical manifestation required surgical intervention.

Patients were divided into 2 groups based on symptomatic and radiological progression; *Group A* included 42 patients who continued conservative treatment throughout the whole study duration, and *Group B* included 11 patients who required surgical intervention at any time.

The two groups were compared for the following variables: patient age and gender, manifestations, tumor location, size and calcification, MRI T2 signal, and duration of follow-up. Tumor size at the time of diagnosis was calculated according to the largest diameter in the anteroposterior, craniocaudal, or mediolateral dimension and divided into 3 groups a) <25mm, b) 25mm to 40mm, and c) >40mm. Radiological follow-up was performed 3-6 months after diagnosis and yearly thereafter.

Ethical Approval:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University (IRB Approval No. #9565/15-6-2022). Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical Analysis

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 23.0 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher's exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as mean and standard deviation (SD), and independent sample t-test/ Mann-Whitney U test was used for comparison between groups. P value ≤0.05 was considered to be statistically significant.

RESULTS

Figure 1 shows the distribution of management of the studied patients. *Group A* included patients who continued non-surgical management, and *Group B* included patients who required surgical intervention.

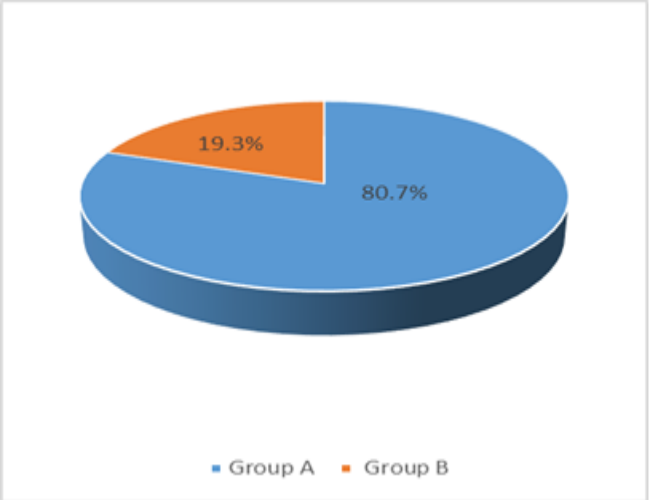

Figure (1): Frequency of the studied sample according to the outcome of follow-up.

Table 1 summarizes the demographic and clinical characteristics of the studied patients (total 53 patients with meningiomas).

Table (1): Frequency and percentage distribution of the studied sample according to demographic and clinical parameters (n.=53).

Variables	Mean and SD/ Number (%)	
Age (years) **Mean ± SD** **(range)**	54.1 ± 9.7 (31-73)	
Gender	**N.**	**%**
Females	34	64.2
Males	19	35.8
Follow-up duration (months) Mean ± SD (range)	56.7 ± 20.4 (14-84)	
Meningioma size at diagnosis (mm) Mean ±SD (range)	23.7 ± 8.3 (9-42)	
Meningioma size, at last, follow-up (mm) Mean ± SD (range)	34.6 ±9 (21-49)	
Total growth during the follow-up period (mm) Mean ± SD (range)	10.97 ±5.4 (1-25)	
Growth rate (mm/year) Mean ± SD (range)	2.56 ±1.59 (0.22-6.75)	
Clinical manifestation at the time of diagnosis		
Non specific	30	56.7
Specific	23	43.3
Calcification		
No	31	54.4
Yes	26	45.6
MRI T2 signal		
Hyperintense	11	19.3
Hypointense	11	19.3
Iso intense	35	61.4
Follow up outcome		
Group A: patients Continued non-surgical management **Group B: patients required surgical intervention**	42 11	80.7 19.3

At diagnosis, group A was significantly older than group B (P<0.05). On the other hand, there is no difference between group A and group B regarding the distribution of gender (**Table 2**).

Table (2): Demographic characteristics of the studied groups.

Variable	Studied groups		T test	P-value
	Group A n.42	**Group B n.11**		
Age at diagnosis (years) Mean ± SD (range)	56 ± 9.1 31-73	46.9 ± 9.1 36-61	2.9	0.005*
Sex Females Males	29 (69%) 13 (31%)	5 (45.5%) 6 (54.5%)	F	0.17

T: a test of significant F: Fisher Exact test

There was a significantly higher follow-up period in group A compared to group B (P<0.05). There is no statistically significant difference between group A and group B regarding specific and nonspecific symptoms and signs at diagnosis (P>0.05).

Table (3): Follow-up duration and clinical manifestations in both groups.

Variable	Studied Groups		U test	P-value
	Group A n.42	Group B n.11		
Follow up duration (months) Mean ± SD Median (range)	 61.16 ± 19 14-84	 39.81 ± 17.5 14-60	3.370	0.001*
Follow up duration (years) Mean ± SD Median (range)	 5.1 ± 1.6 1.17-7	 3.15 ± 1.5 1.17-5	3.370	0.001*
Clinical characters Symptoms & sign	**Studied Groups**		**P-value**	
	Group A n.42	**Group B n.11**		
Nonspecific Specific	26 (61.9%) 16 (38.1%)	4 (36.4%) 7 (63.6%)	0.18	
Nonspecific: Accidently discovered Headache Numbness Fascial pain **Specific:** Changes in vision Hearing loss Convulsion Weakness	 19 (45.3%) 4 (9.5%) 2 (4.7%) 1 (2.3%) 4 (9.5%) 3 (7.14%) 7 (16.6%) 2 (4.7%)	 2 (18.18%) 2 (18.18%) 0 (0%) 0 (0%) 2 (18.18%) 3 (27.27%) 0 (0%) 2 (18.18%)	---	

T: a test of significance, U: Mann-Whitney test, F: Fisher Exact test.

Intracranial meningioma growth rates were significantly different between the two studied groups (**Table 4**).

Table (4): The growth characteristics for intracranial meningioma in the studied groups.

Variable	Studied groups		Test of significance	P-value
	Group A n.42	Group B n.11		
Size at diagnosis (mm) Mean ± SD (range)	22.18 ± 8.1 9-37	29.25 ± 6.7 19-42	2.3	0.015*
Size at last follow-up (mm) Mean ± SD (range)	32.24 ± 7.5 21-54	43.66 ± 8.9 34-59	3.3	0.001*
Total growth (mm) Mean ± SD (range)	10.05 ± 4.8 1-22.3	14.41 ± 6.1 6-25	2.4	0.015*
Growth rate (mm/year) Mean ± SD (range)	1.94 ± 0.74 0.22-3.94	4.92 ± 1.3 3.1-6.75	4.9	0.0001*

The size of intracranial meningioma in both groups was noticeably different from each other. The tumor size of cases in *Group A* was <25mm (64.4%), ranged from 25-40mm (35.6%), and >40 mm (0%) versus 25%, 66.7%, and 8.3%, respectively of cases in *Group B* (P=0.014). It means that when intracranial meningioma was less than 25 mm, it usually continues non-surgical management, while tumor equal to or more than 25 mm usually required surgical intervention (**Table 5**).

Table (5): Size of intracranial meningioma in the studied groups.

Lesion size (Maximum diameter)	Studied groups		χ^2	P-value
	Group A n.45	Group B n.12		
<25 mm **25-40 mm** **>40 mm**	29 (64.4%) 16 (35.6%) 0 (0%)	3(25%) 8 (66.7%) 1(8.3%)	8.05	0.014*

Lesion size: longest diameter in the anteroposterior, craniocaudal or mediolateral dimension, χ 2: Chi-square test.

Table 6 shows that there was no statistical difference of calcification and MRI T2 signal finding in group A and group B (P>0.05).

Table (6): Radiological and MRI T2 signal finding in the studied groups.

Variable	Studied groups		Test of significance	P-value
	Group A n.45	Group B n.12		
Calcification No Yes	22 (48.9%) 23 (51.1%)	9 (75%) 3 (25%)	**2.6**	0.11
MRI T2 signal Hyperintense Hypointense Isointense	7 (15.6%) 10 (22.2%) 28 (62.2%)	4 (33.3%) 1 (8.3%) 7 (58.3%)	2.5	0.28.

Logistic regression for predicting surgical intervention in studied patients showed that increase meningioma size at diagnosis was a significant predictor for surgical intervention, (P<0.05), with the probability of needing surgical intervention is 52.8% (**Table 7**).

Table (7): logistic regression for predicting meningioma cases needing surgical intervention (n.53).

Predictor	Significance	Exp(B)	95% CI for EXP(B)	
			Lower	Upper
Meningioma size at diagnosis	0.024*	1.120	1.02	1.24

Exp(β)= Odds ratios for the predictors. CI=Confidence interval.

DISCUSSION

Meningioma growth prediction is difficult to achieve at present. These tumors are usually asymptomatic and smaller than 2 cm in diameter. Meningiomas caused by NF2 are rare, and the few studies that have investigated the topic have found that younger age at onset, female sex, and tumor location may all be linked to more rapid tumor growth, although these studies only looked at a tiny subset of individuals [(4)].

To effectively treat meningiomas, it is crucial to understand their natural course. A review of the therapy of meningiomas has shown that those that are found incidentally and are asymptomatic at the time of diagnosis by radiology can be handled with observation until the advent of symptoms, prolonged growth, or concerns about encroachment on sensitive structures. Therefore, whether an incidental meningioma needs treatment relies on the surgeon's preference. It is often influenced by factors such as the patient's age, comorbidities, tumor size, growth rate, and closeness to important structures [(5)]**.** For intracranial meningiomas, observation has been a standard practice, although it may raise treatment risks due to tumor growth and patient age [(6)]**.**

In the current study, the age of patients ranged from 31 to 73 years with a mean of 54.1 (SD 9.7) years. At diagnosis, the age of *Group A* patients was significantly older than *Group B* patients (P<0.05). Our findings that faster tumor growth is linked to younger age were supported by the results of **Lee and colleagues** [(7)] who showed that among 232 patients diagnosed with intracranial meningiomas, the average age was 60 (SD 10) years; 82.8% were female; and 25.4% of tumors were growing rapidly. Also, **Nakamura and Colleagues** [(8)] found that rapid development is substantially correlated with younger age. However, **Abi Jaoude and Colleagues** [(9)] analyzed data from 358 patients, and of those, 16.76% had lesions with fast growth. The mean age in their study was 27.5 (SD 12) years, and the tumor growth rate did not differ significantly by either age or sex. They included only intracranial meningiomas in neurofibromatosis type 2, and this could be the possible reason for the difference in our results.

In the present study, 34 (64.2%) of the patients were females and 19 (35.8%) were males. There was no difference between both groups regarding the distribution of gender. Our findings are in line with those of **Hashiba and Colleagues** [(10)] who showed no link between gender and tumor cell proliferation. Also, **Oya and Colleagues** [(11)] claimed that there is no connection between sex and tumor development (P>0.05). However, **Janah and Colleagues** [(12)] revealed that estrogen and progesterone, which are abundant in women, are crucial to the prognosis and progression of meningioma. In contrast, according to research by **Behling and Colleagues** [(13)]**,** meningioma cells in male patients had a far higher development capacity than those in female patients.

In the whole studied group, meningiomas manifested at the time of diagnosis with specific symptoms in 43.3% of patients (such as changes in vision, hearing loss or ringing in the ears, convulsion, weakness, and language difficulty). Nonspecific symptoms included (accidentally discovered lesions during performing investigations for other non-related conditions such as head injury or TIA, headache, dizziness, numbness, and fascial pain). Regarding symptoms among the studied groups, it was found that there was no statistically significant difference between the studied groups regarding specific and nonspecific symptoms and signs at diagnosis (P>0.05). In accordance with the current study, **Oya and Colleagues** [(11)] reported that the occurrence of symptoms was not correlated with tumor progression. Eighty-seven percent of the 238 tumors studied were asymptomatic. When comparing tumors that caused symptoms to those that occurred by chance, there was no difference in incidence rates (P=0.36). However, a substantial correlation was observed between the pace of annual growth and the prevalence of symptoms.

In our study, the size of meningioma at diagnosis ranged from 9 to 42 mm with a mean of 23.7 (SD 8.3) mm. The follow-up duration ranged from 14 to 84 months with a mean of 56.7 (SD 20.4). The size of meningioma at the last follow-up ranged from 21 to 44 mm with a mean of 23.7 (SD 8.3) mm. The total growth during the follow-up period ranged from 1 to 25 mm with a mean of 10.97 (SD 5.4) mm and the growth rate ranged from 0.22 to 6.75 mm/year with a mean of 2.56 (SD 1.59) mm/year. There was a significantly higher follow-up period in group A cases compared to *Group B* cases (P<0.05). This was predictable as group B cases needed immediate intervention in contrast to *Group A* cases giving significant differences in the follow-up period.

Our results were consistent with **Lee and Colleagues** [(7)] who found striking differences in the development features between the two groups. The slow-growth group had an annual absolute growth rate of 0.4 (SD 0.5) cm^3, while the rapid-growth group grew at a rate of 7.3 (SD 6.0) cm^3. While 67.1% of tumors in the slow-growth group expanded linearly, the remaining tumors remained stable at a rate of 0.1 cm^3 each year. Most of the tumors (67.8 %) in the fast-growing group likewise grew linearly. Although 22% of tumors (n=13) grew exponentially, 6 tumors grew linearly or

exponentially at first but then leveled off during the follow-up period. Research also showed that the slow-growing group was followed for far longer than the fast-growing group. In contrast, **Rubin and Colleagues** [14] reported no statistically significant association between follow-up time and tumor growth rate, this finding runs counter to ours; nonetheless, it is possible that the different results from the cases they examined were not treated. After monitoring 60 patients for an average of 30 months, **Olivero and Colleagues** [15] found that 16.7% had expansion without identifying any characteristics that could have predicted this outcome.

In the current study, the size of intracranial meningioma in both groups was noticeably different from each other. We divided the lesions at the time of diagnosis according to the longest diameter in the anteroposterior, craniocaudal, or mediolateral dimension into 3 groups: <25mm, 25-40mm, >40mm. In *Group A*, 64.4% of cases had tumor sizes less than 25mm, 35.6% ranged from 25-40mm, and 0% more than 40mm while in *Group B*, 25.0% of cases had tumor sizes less than 25mm, 66.7% ranged from 25 to 40 mm and 8.3% more than 40 mm (P=0.014). We advise continuing non-surgical management when the maximum diameter is less than 25mm at diagnosis. When it is more than 25 mm, the meningioma needs to be observed more closely. Intracranial meningioma growth rates were significantly different between the two groups. *Group A* case's rate of growth was 1.94 (SD 0.74) mm/year with the range from 0.22 to 3.94 versus 4.92 (SD 1.3) mm/year (range = 3.1-6.75) in *Group B* cases (P=0.0001).

In agreement with our study, **Yoneka and Colleagues** [16] had results that indicate that high initial size is related to rapid expansion. They came to the conclusion that, especially for smaller tumors, an increase in diameter of 2 mm may imply a significant proportional increase in volume. In addition, **Lee and Colleagues** [7] reported that tumor size and mean annual growth rate, were significantly higher, and mean tumor doubling time, was significantly lower in the fast-growing group. The mean annual growth rate was 0.4 (SD 0.5) cm^3/year in the slow group versus 7.3 (SD 6.0) cm^3 /year in the fast-growing group. This came in agreement with **Oya and Colleagues** [11] who reported that an initial tumor diameter greater than 25 mm (P=0.0004), was associated with a short time to progression and the need for surgery after conservative treatment. Results showed that a larger tumor size upon diagnosis (more than 25 mm) was correlated with a more rapid yearly growth rate (P<0.0001).

In disagreement with our study, **Jadid and Colleagues** [17] demonstrated that patient gender or tumor size had no bearing on tumor progression. Possible explanations for the dissimilarity include the lack of overt symptoms in their situation.

The current study showed that there was no statistically significant difference between the studied groups in calcification and MRI T2 signal finding (P>0.05). In tests of statistical significance, the p-value for the reduced progression rate in calcified tumors was just 0.11. Unfortunately, the small number of individuals with calcified tumors in our study reduced the strength of this comparison. Previous research has typically yielded contradictory findings. For example, **Abi Jaoude and Colleagues** [9] revealed that in multivariate analysis, the lack of calcifications (P<0.0001) and hyperintense or isointense signal on T2-weighted MRI (P<0.005) were both significantly related to rapid tumor growth. There were 97 meningiomas that had calcifications, and these were significantly linked to a more gradual rate of growth (P<0.0001). The same results were reported by **Oya and Colleagues** [11]. Also, **Zeng and Colleagues** [18] reported that Tumor calcification was inversely associated with meningioma tumor growth rate (P<0.001) but positively associated with MRI T2 signal intensity (P<0.001).

As far as we know, only 2 studies show similar results regarding the correlation between tumor behavior and calcification and T2 signal MRI. **Lee and Colleagues** [7] reported that patients distributed with MRIT2 signal as 13.3% hyperintense, 20.4% hypointense, and 66.4% isointense. Hypointensity was higher in the slow group, but hyperintensity and isointensity were comparable between the 2 groups. Also, **Jadid and Colleagues** [17] reported that there was no significant correlation between growth differences associated with calcification (P=0.09).

Logistic regression for predicting surgical intervention in studied patients showed that increase meningioma size at diagnosis was a significant predictor for surgical intervention, (P<0.05), with the probability of needing surgical intervention is 52.8%**.**

During the follow-up period, 19.3% of patients developed an indication for surgical intervention. Our results were supported by **Abi Jaoude and Colleagues** [9], who found that 18% of patients needed surgical intervention during the follow-up period. The rate at which tumors were removed surgically was noticeably greater in the fast-growing and thus larger-sized tumors group. Surgery was significantly more common in patients with faster-growing tumors than those with slower-growing ones (39/60 faster-growing tumors were operated on compared to 27/298 slower-growing tumors, P<0.0001). As may be expected, grade II tumors were more common among those with rapid tumor development that underwent surgery, while grade I tumors were more common among those with slower tumor growth that underwent surgery (P=0.031).

Limitations of the current study:

It is a retrospective analysis of intracranial meningioma patients from a single center with a relatively small number of patients, and we did not include follow-up of patients after surgical intervention. Prospective randomized trials are needed to examine the hypothesized increased risk of late treatment of

asymptomatic growing meningiomas compared to early treatment. In the current study, we used the maximum linear diameter in any direction as a measurement of the tumor size, because the volumetric measurement requires image analysis software to track down the lesion contour in each slice image. This facility was not available in most cases. Moreover, **Zeng and Colleagues [18]** show that both methods can effectively detect tumor growth.

CONCLUSION

While asymptomatic, incidental intracranial meningiomas are rather prevalent, there is no consensus on the best way to treat them. Old age, small tumor size, and slower growth rate/year <1.9mm are predictors for non-surgical conservative management while the risk factors for the rapid growth of meningiomas are younger age, larger tumor size >25mm at diagnosis, and rapid annual growth rate >4.2mm. The current study aids in evaluating and counseling patients regarding prognosis and timely management of their intracranial meningiomas. The findings aid in determining the best course of treatment for patients with asymptomatic meningiomas.

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REFERENCES

1. **Abdelsamea M, Kamal A, Abdelaal M *et al.* (2017):** Management of Intracranial Meningioma. Sohag Med J., 21(2):185-91.
2. **Ogasawara C, Philbrick B, Adamson D (2021):** Meningioma: A Review of Epidemiology, Pathology, Diagnosis, Treatment, and Future Directions. Biomedicines, 9(3):319. doi: 10.3390/biomedicines9030319.
3. **Kalasauskas D, Keric N, Abu Ajaj S *et al.* (2021):** Distress and quality of life do not change over time in patients with operated and conservatively managed intracranial meningioma. Acta Neurochir (Wien), 163(12):3417-24.
4. **Hashimoto N, Rabo C, Okita Y *et al.* (2012):** Slower growth of skull base meningiomas compared with non-skull base meningiomas based on volumetric and biological studies. J Neurosurgery, 116(3):574-80.
5. **Behbahani M, Skeie G, Eide G *et al.* (2019):** A prospective study of the natural history of incidental meningioma—Hold your horses! Neuro-oncology Practice, 6(6):438-50.
6. **Nakasu S, Nakasu Y, Fukami T *et al.* (2011):** Growth curve analysis of asymptomatic and symptomatic meningiomas. Journal of Neuro-oncology, 102(2):303-10.
7. **Lee E, Kim J, Park E *et al.* (2017):** A novel weighted scoring system for estimating the risk of rapid growth in untreated intracranial meningiomas. J Neurosurgery, 127 (5):971-80.
8. **Nakamura M, Roser F, Michel J *et al.* (2003):** The natural history of incidental meningiomas. Neurosurgery, 53(1):62-71.
9. **Abi Jaoude S, Peyre M, Degos V *et al.* (2020):** Validation of a scoring system to evaluate the risk of the rapid growth of intracranial meningiomas in neurofibromatosis type 2 patients. Journal of Neurosurgery, 134(5):1377-85.
10. **Hashiba T, Hashimoto N, Izumoto S *et al.* (2009):** Serial volumetric assessment of the natural history and growth pattern of incidentally discovered meningiomas. J Neurosurg., 110:675-84.
11. **Oya S, Kim S, Sade B *et al.* (2011):** The natural history of intracranial meningiomas. Journal of Neurosurgery, 114(5):1250-6.
12. **Janah R, Rujito L, Wahyono D (2022):** Expressions of Progesterone Receptor of Orbital Meningiomas in Indonesia. Asian Pacific Journal of Cancer Prevention, 23(12):4137-43.
13. **Behling F, Fodi C, Wang S *et al.* (2021):** Increased proliferation is associated with CNS invasion in meningiomas. Journal of Neuro-oncology, 155(3):247-54.
14. **Rubin G, Herscovici Z, Laviv Y *et al.* (2011):** Outcome of untreated meningiomas. Isr Med Assoc J., 13:157-60.
15. **Olivero W, Lister J, Elwood P (1995):** The natural history and growth rate of asymptomatic meningiomas: a review of 60 patients. Journal of Neurosurgery, 83(2):222-4.
16. **Yoneoka Y, Fujii Y, Tanaka R (2000):** Growth of incidental meningiomas. Acta Neurochirurgica, 142(5):507-11.
17. **Jadid K, Feychting M, Höijer J *et al.* (2015):** Long-term follow-up of incidentally discovered meningiomas. Acta Neurochirurgica, 157(2):225-30.
18. **Zeng L, Liang P, Jiao J *et al.* (2015):** Will an asymptomatic meningioma grow or not grow? A meta-analysis. Journal of Neurological Surgery Part A: Central European Neurosurgery, 76(05):341-7.