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Original Article

Retrospective analysis of recurrence patterns and clinical outcomes in grade I–III meningiomas after surgery

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ABSTRACT

Background: The objective of this study was to evaluate the outcomes of meningioma patients with the World Health Organization (WHO) grades I–III who underwent surgical resection and identify factors influencing recurrence and survival.

Methods: This retrospective study included patients who underwent surgery for meningioma at the National Brain Center Hospital between January 2020 and December 2022. Clinical characteristics of patients with recurrence, such as gender, age, preoperative Karnofsky Performance Scale (KPS), grading, and history of radiotherapy, were recorded. The recurrence time was assessed within 2 years post-surgery. Magnetic resonance imaging or computed tomography imaging results were used to determine meningioma location, while the WHO grading was based on pathological findings. Survival analysis of recurrence across different grades was performed using Kaplan–Meier curves.

Results: Of the 184 patients who had surgical resection for meningioma, 53 (28.8%) experienced recurrence. The recurrence group consisted primarily of women (81%), with a preoperative KPS > 70% (83%), Simpson grading II–III (60.3%), WHO grade II (39.6%), and meningiomas located in the convexity (24.5%). Most patients (81.1%) had no history of radiotherapy, and 64.15% had two or more resections. The average recurrence-free period after surgery was 17.95 ± 20.39 months. Mortality due to recurrence was most common in the WHO grade II patients (11.1%). Kaplan–Meier curves showed differences in recurrence between grading subgroups, with the WHO grade III meningiomas exhibiting the highest recurrence rate and the worst prognosis.

Conclusion: Higher-grade meningiomas are more likely to recur and result in poorer outcomes. Further research is needed to investigate tumor recurrence at the molecular level. A multidisciplinary approach to treatment improves outcomes and reduces complications associated with recurrence.

Keywords: Meningioma, Outcome, Recurrence

INTRODUCTION

Brain tumors are the 19th most common type of cancer, accounting for 1.6% of cancer cases and 2.6% of all cancer-related deaths worldwide.[2] Meningioma, the most frequent primary

benign tumor of the central nervous system, makes up 40% of all primary brain tumor cases in the United States.[18] The incidence is higher in females, particularly among the elderly. While meningiomas are classified as benign, their mass effect can impair the quality of life for those affected.[10] At present, gross total resection (GTR) is recommended to remove the tumor and reduce the risk of recurrence.[8]

The World Health Organization (WHO) 2021 guidelines classify meningiomas into three grades based on histopathological findings, likelihood of recurrence, and molecular profiling.[24] Grade I tumors are slow growing, while grade II tumors have a slightly higher likelihood of progression and recurrence. Grade III tumors are the most aggressive and have the highest recurrence rate.[24] Fortunately, most meningiomas are grade I, with grade III being the least common.[18] However, 50–94% of grade III meningiomas are likely to recur even after complete removal.[5] In cases of subtotal resection, the recurrence rate for grade I and grade II meningiomas remains low, ranging from 0% to 2.36% and 7.35% to 11.46% over 5 years, respectively.[3]

Several risk factors are associated with meningioma recurrence, including high-grade meningiomas, a combination of grade II and III meningiomas, Simpson grading, tumor doubling time, younger age, tumor size, plaque lesions, and genetic factors.[13,15] As mentioned earlier, grade II and III meningiomas are more likely to recur than grade I meningiomas. The Simpson grading system assesses the extent of tumor removal [9,19], with grade I indicating complete resection. Higher Simpson grades indicate incomplete removal, increasing the likelihood of recurrence. Since meningiomas arise from the arachnoid cap of the meninges that surround the brain, they can recur in various locations, including eloquent and difficult areas, which may complicate complete resection.[17] Therefore, recurrence should be considered in these cases.

Meningiomas are typically detected through routine brain imaging using computed tomography (CT) scans or magnetic resonance imaging (MRI), either alone or in combination.[8] High-grade meningiomas often show a dural tail at the tumor's perimeter in contrast-enhanced MRI scans. CT scans are helpful in evaluating bone hyperostosis and intraosseous tumor growth. Due to varying recurrence rates across different grades of meningioma, the European Association of Neuro-Oncology (EANO) recommends specific intervals for monitoring based on the tumor's grade.[8]

In Indonesia, the incidence and prevalence of meningioma recurrence are not well documented. Given that meningiomas have a known recurrence rate, this condition warrants attention, and documentation is essential for informing national evidence-based health policies. This study aims to evaluate the outcomes of meningioma patients after surgical resection and identify factors that may contribute to recurrence.

MATERIALS AND METHODS

Study design and patient selection

This retrospective study included postsurgical meningioma patients at the National Brain Center Hospital from January 2020 to December 2022. Patients who had received prior or follow-up radiation therapy were also included in the study. Exclusion criteria were incomplete medical records, loss of follow-up, and spinal meningiomas. Although the WHO updated its guidelines in 2021, this study used the 2016 WHO guidelines[1,17] for meningioma classification. Under the 2016 WHO guidelines, meningiomas are classified into three grades using Roman numerals, whereas the current guidelines incorporate molecular profiling, which was not included in the earlier version.[8] The board committee granted ethical approval for this study.

Data collection

Baseline data, including gender, age, preoperative Karnofsky Performance Scale (KPS), Simpson grading, meningioma location, and radiotherapy history, were obtained from medical records. The KPS was assessed preoperatively by the attending physician and classified into high and low categories, with a cutoff of 70 points. The neurosurgeon determined the Simpson grading. Meningioma location was identified using MRI or CT scans, performed according to the hospital's standard protocol. Locations were classified into convexity, parasagittal, falx, cerebellopontine angle, parasellar, tentorium, sphenoid wing, parasagittal sinus, olfactory groove, and tuberculum sellae. Locations outside these categories were classified as "other." Meningiomas involving more than one region were categorized as multiple meningiomas. As molecular profiling was not conducted in the hospital, this study could not document the molecular profile of the meningiomas. The frequency of surgeries for each patient was also recorded. Mortality data were collected based on the patient's status in the hospital, as noted in the medical records.

Statistical analysis

Data analysis was conducted using the Statistical Package for the Social Sciences Statistics version 29 by IBM Corporation. Chi-squared or Fischer's exact tests were applied to categorical data to compare the distribution between recurrent and non-recurrent meningiomas. For numerical data, normality was assessed using the Kolmogorov–Smirnov test. Skewed data were presented as median and range, while normally distributed data were reported as mean ± standard deviation. Differences in numerical data were tested using an independent *t*-test. The Kaplan–Meier plot and log-rank analysis were used to evaluate recurrence-free survival (RFS) across different meningioma grades. Statistical significance was defined as $P < 0.05$.

RESULTS

Baseline characteristics

Data from a total of 184 patients were included and analyzed in this study. Meningioma recurrence was observed in 53 patients (28.8%). The distribution of gender and age was similar between recurrent and non-recurrent meningiomas. However, the distribution of meningioma grades differed significantly between the two groups. In the recurrence group, eight out of 53 patients were classified as Simpson grade III and seven patients were histopathologically graded as WHO high-grade. Most patients in the recurrent meningioma group had more than one resection, whereas those without recurrence mostly had a single resection. The baseline characteristics of the patients are presented in Table 1.

Table 1: Patient characteristics of the meningioma patients.

Characteristics	Recurrence *n* (%)	Without recurrence *n* (%)	*P*-value
Gender			
Men	10 (31.2)	22 (68.8)	0.737
Women	43 (28.3)	109 (71.3)	
Age (mean±SD)	46.8±15.5	47.1±11	0.881
Preoperative KPS			
≤70	9 (47.4)	10 (52.6)	0.059
>70	44 (26.7)	121 (73.3)	
Simpson grade[a]			
I	8 (100.0)	-	-
II–III	32 (22.1)	113 (77.9)	
IV–V	13 (44.8)	16 (55.2)	
WHO grading			
I	23 (19.5)	95 (80.5)	<0.001
II	21 (39.6)	32 (60.4)	
III	9 (69.2)	4 (30.8)	
Location			
Convexity	13 (28.9)	32 (71.1)	-
Falx	11 (44.0)	14 (56.0)	
Cerebellopontine angle	6 (50.0)	6 (50.0)	
Parasella	8 (34.8)	15 (65.2)	
Tentorium	5 (62.5)	3 (37.5)	
Sphenoid wing	2 (12.5)	14 (87.5)	
Parasagittal sinus	3 (15.8)	16 (84.2)	
Olfactory groove	2 (15.4)	11 (84.6)	
Tuberculum sellae	1 (14.3)	6 (85.7)	
Multiple	2 (20.0)	8 (80.0)	
Others	2 (25.0)	6 (75.0)	
Radiotherapy			
Yes	10 (100.0)	-	-
No	43 (24.7)	131 (75.3)	
Number of resections			
Single resection	19 (13.6)	121 (86.4)	<0.001
≥2 resections	34 (77.3)	10 (22.7)	
Recurrence-free months (mean±SD)	17.95±20.39	-	-

[a]Missing two data, *n*=182. SD: Standard deviation, KPS: Karnofsky Performance Scale, WHO: World Health Organization

Meningioma recurrence rate and mortality

The recurrence rate was significantly higher in the WHO grade II and III meningiomas compared to WHO grade I meningiomas [Table 2]. Mortality due to meningioma recurrence was not linked to either the WHO grade or the Simpson grade. However, patients with higher Simpson and WHO grades had mortality rates of 11.1% and 13.3%, respectively, as shown in Table 3.

RFS varied across the meningioma subgroups [Figure 1]. The WHO grade III meningiomas had the shortest RFS, followed by WHO grades II and I [Figure 1]. The Kaplan–Meier plot showed differences in RFS among patients in each WHO meningioma grade**.** Patients with the WHO grade III meningiomas had the lowest and shortest RFS compared to others. However, the differences in RFS were not statistically significant ($P = 0.798$).

DISCUSSION

This study presents the clinical characteristics of recurrent meningioma in Indonesia. The age and gender distribution were similar, and the preoperative KPS score did not influence meningioma recurrence. As anticipated, high-grade meningiomas (WHO grades II and III) were the most likely to recur within 2 years after resection, even when GTR was performed. Therefore, additional surgical resections are often required to manage clinical symptoms in cases of recurrent meningioma.

Although meningiomas are classified as benign tumors, they have a high likelihood of recurrence, particularly in high-grade cases. The recurrence rate for meningiomas in the literature ranges from 7.7% to 32.7%.[22,25] While meningioma cases tend to increase with age, the recurrence rate does not necessarily follow this pattern. However, progression-free survival (PFS) and overall survival are generally lower in patients over 65 years old, likely due to comorbidities or the location of the tumor, making it unresectable.[14] Notably, preoperative functional status does not appear to be linked to meningioma recurrence, as shown in this study and by Tosefsky *et al.*[23] In addition, since meningiomas are more commonly found in females, the recurrence rate is also higher in females. Consistent with previous studies, this analysis observed a higher recurrence rate in females compared to males, although the difference was not statistically significant. Unlike the recurrence rates reported in previous studies, the present study did not find a significant difference in RFS among the meningioma grades, although WHO grade III meningioma had the lowest RFS compared to the other grades. In comparison with other epidemiological and clinicopathological studies in high-income countries, the findings of this study are similar. Nowak *et al.*[16] observed a higher PFS rate in grade I meningioma than in grade II meningioma in Poland. In America, Hwang *et al.*[14] reported a lower recurrence rate of grade I meningioma than grade II/III meningioma. Chohan *et al.*[5] and Han *et al.*[11] did not find a significant difference in gender distribution between recurrent and non-recurrent meningioma cases. However, Hwang *et al.*'s[14] analysis indicated that male gender was associated with a higher likelihood of high-grade meningioma (odds ratio [OR] 3.46; 95% confidence interval [CI] 1.15–10.4). They found that males had a 1.1 times higher probability of experiencing meningioma recurrence within

Table 2: Relationship between meningioma grade and recurrence.

WHO grading	Recurrence		*P*-value
	Yes	No	
I	23 (19.5)	95 (80.5)	<0.001
II and III	30 (45.5)	36 (54.5)	

WHO: World Health Organization. Figures in brackets denote the percentage

Table 3: Meningioma grade and mortality in patients with recurrent meningioma.

Grade	Mortality		*P*-value
	Yes	No	
Simpson grade			1.000*
I	1 (12.5)	7 (87.5)	
II–III	5 (11.1)	40 (88.9)	
WHO grading			0.687*
I	2 (8.7)	21 (91.3)	
II–III	4 (13.3)	26 (86.7)	

*Fisher's exact test, WHO: World Health Organization. Figures in brackets denote the percentage

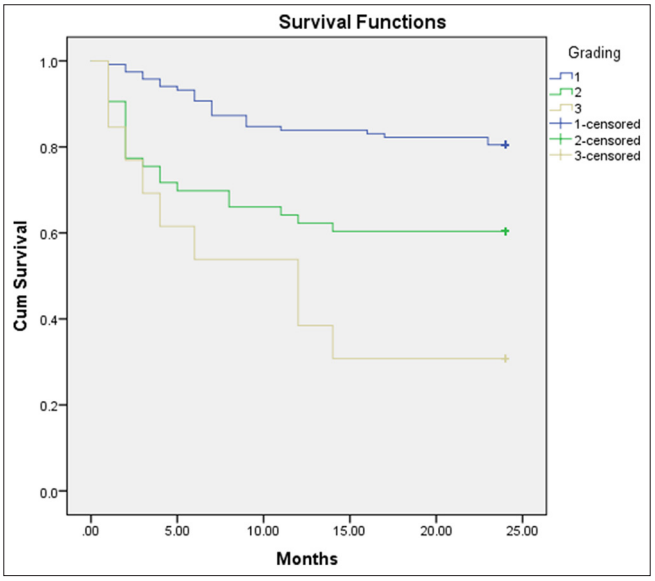

Figure 1: Kaplan–Meier plot of World Health Organization meningioma grade and recurrence within 2 years.

5 years than females, although this result was not statistically significant. Thus, the role of gender in meningioma recurrence remains unclear.

Except for WHO grade I, the other grades have a higher likelihood of recurrence. Ogasawara *et al.*[17] estimated recurrence rates of 7–23%, 50–55%, and 72–78% for WHO grade I, II, and III meningiomas worldwide, respectively. Interestingly, this study found that WHO grade I had a higher recurrence proportion than other grades, although this difference was not statistically significant. As noted earlier, GTR is the preferred treatment option since complete removal of the meningioma reduces the likelihood of recurrence, although this may not apply to WHO grade III.[8] However, not all meningiomas can be completely resected. Simpson grading is a system that classifies the extent of meningioma resection, with Simpson grade I indicating complete removal and higher grades reflecting a greater percentage of meningioma remaining in the brain cavity.[9,19,20] Consequently, Simpson grade I is associated with a lower recurrence rate compared to other grades. Similarly, a higher Simpson grade was more common in recurrent meningioma cases, although all Simpson grade I cases had recurrence. In contrast, Ehresman *et al.*[6] did not find an association between Simpson grading and recurrence, while Simon *et al.*[20] and Gousias *et al.*[9] did. However, as this study did not assess the interaction between WHO grade and Simpson grade in predicting recurrence, no conclusions can be made, and further research is needed.

According to the 2021 EANO guidelines, radiation therapy is recommended as an alternative treatment for small meningiomas (≤3 cm) or as an adjunct in pre- and postsurgical situations, regardless of the WHO grade.[8] Fatima *et al.*[7] found that radiotherapy and radiosurgery yielded similar outcomes in 4–10 years of PFS, with results of 89% and 88.8%, respectively. Since brain parenchyma is sensitive to ionizing radiation, stereotactic radiosurgery is preferred over conventional radiotherapy, as recommended by the EANO.[8] Soyuer *et al.*[21] reported a 91% PFS in patients who received postsurgical radiotherapy, compared to 38% PFS in those who did not receive radiotherapy. Since our hospital does not have radiosurgery, conventional radiotherapy is still used to manage some aggressive meningioma subtypes. In this study, radiotherapy was administered to ten patients (18.86%) with recurrent meningioma, while the other 43 patients did not receive radiotherapy.

Although most meningiomas are not fatal, some may display aggressive behavior that can lead to mortality. Holleczek *et al.*[12] reported that tumor-associated mortality rates varied by gender, age, and WHO grade of the meningioma, while Chiba *et al.*[4] highlighted that Simpson grading, skull base location, and the MIB-1 index are significant factors related to meningioma mortality over 15 years. In this study, mortality was not linked to either the WHO grade or the Simpson grade, indicating that meningioma-related death was low in this cohort. However, further research with a larger sample size is needed to identify the factors contributing to meningioma-related mortality in Indonesia accurately.

This study offers insights into the clinical characteristics of recurrent meningioma patients compared to non-recurrent cases in Indonesia. As a single healthcare facility study, it can assist physicians in managing meningioma patients and detecting recurrences, enabling referrals to higher-level healthcare facilities for timely treatment. However, since this study relies on data from only one healthcare center, it does not fully represent the recurrence rates of meningioma across Indonesia. In addition, the follow-up period was limited to 2 years, which is shorter than in previous studies. Molecular profiling was not conducted at our hospital, preventing the analysis of meningioma's molecular profile. Finally, as a retrospective study, selection bias may be present.

This study provides valuable insights into the incidence and recurrence rates of brain tumors in Indonesia. However, it is essential to consider these findings in the broader context of global epidemiological trends. Comparative studies from different geographic regions reveal variations in the incidence and recurrence rates of brain tumors, which genetic predispositions, environmental factors, healthcare accessibility, and treatment availability may influence. Understanding how these factors differ across regions can provide a more comprehensive perspective on the challenges faced in managing brain tumors in Indonesia. One of the critical challenges in Indonesia is the disparity in access to diagnostic and treatment facilities. In several regions, basic neuroimaging modalities such as CT scans are either unavailable or insufficient, leading to delayed diagnoses and, consequently, larger tumor sizes at the time of presentation. This late-stage diagnosis significantly impacts treatment outcomes and recurrence rates. Limited access to MRI, which is crucial for precise tumor characterization, further exacerbates these challenges. Surgical and oncological practice patterns also vary across different areas of Indonesia. While major urban centers may have access to experienced neurosurgeons and advanced surgical facilities, rural and underserved regions often lack specialized care. The availability of adjuvant therapies, including radiotherapy and chemotherapy, remains inconsistent, with some patients having to travel long distances to receive necessary treatments. This geographical disparity in access to comprehensive care likely contributes to differences in recurrence rates when compared to more developed healthcare systems.

Further research exploring the impact of treatment and characteristics on meningioma in Indonesia is needed. The molecular characteristics of meningiomas are considered

important indicators for meningioma classification which is not analyzed in this study. Hence, the molecular profiling of meningiomas in multicenter studies should be considered, as this design may represent a comprehensive molecular characteristic of meningiomas in Indonesia. In addition, a longer follow-up time should be considered. Finally, the impact of additional therapy, such as adjuvant and neoadjuvant radiotherapy or radiosurgery, should be investigated.

This study is crucial in shedding light on the current status of brain tumor management in Indonesia and underscores the necessity for further action. Strengthening the healthcare infrastructure by improving access to diagnostic tools, expanding radiotherapy services, and enhancing surgical expertise in peripheral regions are essential steps toward reducing the burden of brain tumors. Furthermore, establishing national cancer registries and conducting multi-center studies will help refine treatment strategies and ultimately improve patient outcomes.

CONCLUSION

Recurrence patterns after meningioma surgery are crucial for evaluating patient prognosis. Higher-grade meningiomas are linked to an increased risk of recurrence.

Ethical approval: The research/study was approved by the Institutional Review Board at Rumah Sakit Pusat Otak Nasional, number DP.04.03/D.XXIII.9/298/2024, dated December 2, 2024.
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