

RESEARCH ARTICLE

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Factors Associated with Cognitive Impairment in Brain Tumor Patients: A Cross-Sectional Study

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Abstract

Introduction: Brain tumors are the leading cause of death among all systemic tumors both primary and metastatic types. Cognitive impairment is an early symptom in approximately 58% of brain tumor patients, particularly affecting executive functions. Brain tumors can lead to physical disability, reduced hope and quality of life, and increased financial burden. However, cognitive impairment is often not recognized in its early stages and subsequently becomes a psychological burden for both patients and their families due to the resulting decline in quality of life. Early recognition of cognitive decline provides more time and opportunity to prevent further deterioration. **Methods:** This cross-sectional study was conducted from September 2024 to February 2025 at the outpatient neurology clinic of Dr. Saiful Anwar General Hospital, East Java, Indonesia. Adult patients with primary or metastatic brain tumors on contrast-enhanced MRI were enrolled. Cognitive function was assessed using MoCA-INA, and associated factors were analyzed using simple and multiple binary logistic regression. **Results:** Of 92 patients analyzed, 56 (60.8%) had cognitive impairment. In bivariate analysis, tumor type, lesion count, and several tumor locations were significantly associated with cognitive impairment. In multivariable analysis, only tumor type and lesion count remained independent predictors. Primary tumors were associated with lower odds of cognitive impairment than metastatic tumors (aOR 0.265; 95% CI 0.095–0.742; $p = 0.011$), while fewer lesions were associated with lower odds compared with multiple lesions (aOR 0.442; 95% CI 0.226–0.864; $p = 0.017$). **Conclusion:** Cognitive impairment was common in patients with brain tumors. Tumor type and lesion count were independently associated with cognitive dysfunction, with metastatic tumors and multiple lesions showing higher risk.

Keywords: Brain Tumor, Cognitive Impairment, MoCA-INA

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Introduction

Cognition is a mental action or process of acquiring knowledge and understanding through thoughts, experiences, and senses. Cognition encompasses various aspects of high-level intellectual functions and processes such as attention, memory, knowledge, decision-making, planning, reasoning, judgment, perception, understanding, language, and visuospatial functions. Cognitive impairment includes attention, language, memory, executive, and visuospatial impairments [1].

Although brain tumors are not among the three most common malignancies, they remain a major cause of cancer-related mortality among both primary and metastatic tumors. Cognitive impairment is reported as an early symptom in approximately 58% of patients

with brain tumors and most commonly affects executive function. In addition to causing physical disability, brain tumors may reduce hope and quality of life and impose a substantial financial burden on patients and their families [2, 3].

Despite the clinical importance of this issue, evidence from low- and middle-income countries remains limited. In Indonesia, studies specifically examining factors associated with cognitive impairment in patients with brain tumors are still limited [4, 5]. This represents an important gap in the literature, as local patterns of presentation, referral, diagnostic delay, and treatment access may differ from those reported in other settings. Consequently, findings from other populations may not be fully generalizable to Indonesian patients. Locally derived evidence is therefore needed to better characterize the

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burden of cognitive impairment and to identify patients at increased risk in routine clinical practice [6–8].

This study aimed to identify factors associated with cognitive impairment in patients with brain tumors treated at Dr. Saiful Anwar Hospital, East Java, Indonesia. To our knowledge, no previous study in Indonesia has specifically examined the relationship between cognitive impairment and brain tumor characteristics in this population. By identifying clinical and tumor-related characteristics associated with cognitive dysfunction, this study may contribute to improved screening strategies and earlier recognition of high-risk patients in neuro-oncological practice.

Materials and Methods

An analytical observational study with a cross-sectional design was carried out over six months, from September 2024 to February 2025, at the outpatient neurology clinic of Dr. Saiful Anwar General Hospital in East Java, Indonesia. Patients older than 18 years whose contrast-enhanced brain MRI findings indicated either a primary or metastatic tumor and who attended the neurology clinic were recruited by purposive sampling. Individuals with impaired consciousness, aphasia, or who were within eight months post-whole brain radiotherapy (WBRT) were excluded.

Independent variables comprised sex, age, tumor location (including frontal, parietal, temporal, occipital, infratentorial, or other regions), tumor type (primary versus metastatic), and lesion count (single or multiple, defined as fewer than three or three or more). The dependent variable was the presence of cognitive dysfunction, evaluated using the Indonesian version of the Montreal Cognitive Assessment (MoCA-INA). The chi-square test was selected to analyze categorical variables due to its robustness in handling non-parametric data, which is common in clinical research samples. To ensure reliability, all assessors underwent standardized training for administering the MoCA-INA, including calibration exercises to minimize inter-rater variability.

Statistical analyses were conducted using SPSS version 26.0. Cognitive impairment, assessed using the MoCA-INA, was treated as the binary dependent variable (impaired vs normal). The independent variables evaluated were age, sex, tumor type, lesion count, and tumor location categories (frontal, parietal, temporal, occipital, infratentorial, and other locations). Each variable was initially analyzed using simple binary logistic regression to evaluate its association with cognitive impairment. Variables with a p -value < 0.25 in the simple binary logistic regression analysis were entered into a multiple binary logistic regression model to determine independent predictors of cognitive impairment. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were reported. Statistical significance was set at $p < 0.05$.

Results

During the six-month study period, we enrolled 121 patient samples after applying the exclusion criteria, 29

were excluded, leaving 92 sample for analysis of patient demographics (age, sex, clinical presentation) and tumor characteristics (tumor type, number of lesions and tumor location), as detailed in Table 1.

The bivariate logistic regression analysis (Table 2) demonstrated that tumor type, number of lesions, frontal location, parietal location, and other tumor locations were significantly associated with cognitive impairment (all $p < 0.05$). Primary tumor type was significantly associated with a lower likelihood of cognitive impairment, reducing the odds by 62.1% (OR 0.379; 95% CI 0.160–0.899; $p = 0.028$). Likewise, a lower number of lesions was significantly associated with reduced odds of cognitive impairment by 57.3% (OR 0.427; 95% CI 0.243–0.751; $p = 0.003$).

By contrast, tumors located in the frontal lobe and parietal lobe were associated with significantly increased odds of cognitive impairment. Frontal lobe location increased the odds by approximately 2.6-fold (OR 2.639; 95% CI 1.112–6.262; $p = 0.028$), while parietal lobe location was associated with a 2.6-fold increase in the odds of cognitive impairment (OR 2.600; 95% CI 1.037–6.519; $p = 0.042$).

In contrast, age, sex, and temporal, occipital, and infratentorial tumor locations were not significantly associated with cognitive impairment in the bivariate analysis. Variables with p values < 0.25 in the bivariate logistic regression analysis (Table 3) were considered candidates for inclusion in the multivariable logistic regression model. Based on this criterion, tumor type, number of lesions, frontal location, parietal location, and other tumor locations were included in the multivariable analysis.

Based on the results of the bivariate logistic regression analysis, several tumor characteristics were found to be significantly associated with cognitive impairment in patients with brain tumors (Table 4). Tumor type showed a significant association with cognitive impairment (OR 0.379; 95% CI 0.160–0.899; $p = 0.028$). An OR of less than 1 indicates that primary tumors had a protective effect against cognitive impairment compared with metastatic tumors. Clinically, patients with primary tumors had approximately a 62.1% lower likelihood of experiencing cognitive impairment than those with metastatic tumors.

The number of lesions was also significantly associated with cognitive impairment (OR 0.427; 95% CI 0.243–0.751; $p = 0.003$). An OR of less than 1 indicates that patients with fewer lesions had a lower risk of cognitive impairment. In other words, an increasing number of lesions was associated with a greater likelihood of cognitive dysfunction.

Tumor location in the frontal lobe was significantly associated with an increased risk of cognitive impairment (OR 2.639; 95% CI 1.112–6.262; $p = 0.028$). This indicates that patients with frontal lobe tumors had approximately 2.6 times higher odds of cognitive impairment than those without frontal lobe involvement. This finding is consistent with the role of the frontal lobe in executive function, attention, and behavioral regulation.

Similarly, tumors located in the parietal lobe were also associated with an increased risk of cognitive

Table 1. Major Characteristics of The Studied Population

Variable	Total (n=92)	Cognitive Function				p-value
		Normal (n=36)		Impaired (n=56)		
		n	%	n	%	
Age (mean ± SD)	49.16 ± 11.365	47.54 ± 12.687		50.18 ± 10.447		0.284
< 40 years	17 (18.47%)	9	25%	8	14.28%	0.871
40-60 years	62 (67.40%)	20	55.55%	42	75%	
>60 years	13 (14.13%)	7	19.45%	6	10.71%	
Gender						
Female	62 (67.40%)	25	69.44%	37	66.07%	0.736
Male	30 (32.60%)	11	30.56%	19	33.93%	
Clinical Symptoms						
Neurological Deficit	27 (29.30%)	12	33.33%	15	26.79%	0.515
Headache	47 (51.10%)	19	52.78%	28	50.00%	
Both	18 (19.60%)	5	13.89%	13	23.21%	
Tumor Type						
Primary	54 (58.70%)	16	44.44%	38	67.86%	0.026
Metastasis	38 (41.30%)	20	55.56%	18	32.14%	
Number of Lesions						
Single	30 (32.60%)	6	16.67%	24	42.85%	0.01
Multiple (< 3)	31 (33.70%)	12	33.33%	19	33.93%	
Multiple (≥ 3)	31 (33.70%)	18	50.00%	13	23.22%	
Tumor Location						
Frontal	54 (58.6%)	16	44.40%	38	67.80%	0.026
Parietal	35 (38%)	9	25%	26	46.40%	0.039
Temporal	19 (20.6%)	7	19.40%	12	21.40%	0.819
Occipital	6 (6.5%)	1	2.70%	5	8.90%	0.244
Infratentorial	20 (21.7%)	7	19.40%	13	23.20%	0.669
Others	7 (7.6%)	6	16.60%	1	1.70%	0.009

impairment (OR 2.600; 95% CI 1.037–6.519; $p = 0.042$), with approximately 2.6 times higher odds compared with tumors in other locations. This may be explained by the role of the parietal lobe in attention, sensory integration, and working memory.

In contrast, tumors classified under other locations showed a protective association with cognitive impairment (OR 0.091; 95% CI 0.010–0.791; $p = 0.030$), although the relatively wide confidence interval suggests substantial data variability.

Overall, the bivariate analysis showed that tumor characteristics particularly tumor type, number of lesions, and frontal and parietal locations played an important role in the occurrence of cognitive impairment in patients with brain tumors. Variables meeting the criterion of $p < 0.25$ were subsequently entered into the multivariable analysis to identify independent factors associated with cognitive impairment.

In the bivariate logistic regression analysis, tumor type, number of lesions, frontal location, parietal location, and other tumor locations were significantly associated with cognitive impairment ($p < 0.05$) (Table 5). However, after multivariable analysis was performed to control for the effects of other variables, only tumor type and number of lesions remained independently associated with cognitive

impairment.

Primary tumor type was shown to reduce the likelihood of cognitive impairment by 73.5% compared with metastatic tumors (adjusted OR 0.265; 95% CI 0.095–0.742; $p = 0.011$). This finding indicates that metastatic tumors carry a greater risk of cognitive dysfunction than primary tumors.

The number of lesions also remained a significant independent factor. Patients with fewer lesions had a 55.8% lower likelihood of cognitive impairment than those with multiple lesions (adjusted OR 0.442; 95% CI 0.226–0.864; $p = 0.017$). In contrast, frontal and parietal tumor locations, which were previously significant in the bivariate analysis, were no longer significantly associated with cognitive impairment after adjustment for other variables in the multivariable model. This finding suggests the possibility of confounding effects between tumor location and either tumor type or number of lesions.

The final logistic regression model had a Nagelkerke R^2 of 0.294, indicating that approximately 29.4% of the variability in cognitive impairment could be explained by the variables included in the model. Further analysis confirmed that both lesion count and tumor type significantly influenced the likelihood of cognitive dysfunction. The regression coefficients showed that

Table 2. Factors Associated with Cognitive Impairment (MoCA-INA): Bivariate Logistic Regression

	B	Sig.	Exp(B)	95.0% C.I. for EXP(B)	
				Lower	Upper
Tumor_type	-0.97	0.028	0.379	0.16	0.899
Constant	0.865	0.004	2.375		
Nagelkerke R Square	0.071				
Lesion_count	-0.85	0.003	0.427	0.243	0.751
Constant	1.353	0.001	3.87		
Nagelkerke R Square	0.134				
Age	0.021	0.278	1.021	0.983	1.061
Constant	-0.583	0.546	0.558		
Nagelkerke R Square	0.018				
Sex	0.155	0.736	1.167	0.475	2.869
Constant	0.392	0.13	1.48		
Nagelkerke R Square	0.002				
Frontal	0.97	0.028	2.639	1.112	6.262
Constant	-0.105	0.746	0.9		
Nagelkerke R Square	0.071				
Parietal	0.956	0.042	2.6	1.037	6.519
Constant	0.105	0.691	1.111		
Nagelkerke R Square	0.063				
Temporal	0.122	0.819	1.13	0.398	3.208
Constant	0.417	0.081	1.517		
Nagelkerke R Square	0.001				
Occipital	1.233	0.27	3.431	0.384	30.651
Constant	0.376	0.086	1.457		
Nagelkerke R Square	0.022				
Infratentorial	0.225	0.669	1.252	0.446	3.517
Constant	0.394	0.101	1.483		
Nagelkerke R Square	0.003				
Lainnya	-2.398	0.03	0.091	0.01	0.791
Constant	0.606	0.008	1.833		
Nagelkerke R Square	0.1				

multiple lesions carried greater odds of impairment: each step up in lesion category single, multiple fewer than three, or multiple three or more was associated with an

odds ratio of 0.347 ($p = 0.001$). Likewise, primary tumor status had a protective effect, with an odds ratio of 0.255 ($p = 0.007$), corresponding to a 74.5% reduction in the odds of cognitive impairment.

Table 3. Variable Selection for Multivariable Logistic Regression Analysis

Variabel	p-value	Candidate
Tumor type	0.028	YES
Lesion count	0.003	YES
Age	0.278	NO
Sex	0.736	NO
Frontal	0.028	YES
Parietal	0.042	YES
Temporal	0.819	NO
Occipital	0.27	NO
Infratentorial	0.669	NO
Others	0.03	YES

Note: based on cutoff $p < 0.25$

Discussion

Characteristics of the Study Participant

Participants in this study were diagnosed with brain tumors based on contrast-enhanced brain MRI

Table 4. Variable Selection for Multivariable Logistic Regression Analysis

Variable	Crude OR	95% CI	p-value
Tumor type	0.379	0.160–0.899	0.028
Lesion count	0.427	0.243–0.751	0.003
Frontal location	2.639	1.112–6.262	0.028
Parietal location	2.6	1.037–6.519	0.042
Other locations	0.091	0.010–0.791	0.03

Table 5. Bivariate and Multivariable Logistic Regression Analysis of Factors Associated with Cognitive Impairment

Variable	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Tumor type	0.379 (0.160–0.899)	0.028	0.265 (0.095–0.742)	0.011
Lesion count	0.427 (0.243–0.751)	0.003	0.442 (0.226–0.864)	0.017
Frontal location	2.639 (1.112–6.262)	0.028	1.854 (0.672–5.113)	0.233
Parietal location	2.600 (1.037–6.519)	0.042	1.642 (0.589–4.579)	0.343
Other locations	0.091 (0.010–0.791)	0.03	0.307 (0.028–3.345)	0.332

Note: Nagelkerke R² (Final Model) = 0.294

and subsequently underwent cognitive screening using the Indonesian version of the Montreal Cognitive Assessment (MoCA-INA). MoCA-INA was selected because it has demonstrated good sensitivity (90%) and specificity (87%–100%) for cognitive screening in Indonesia and is practical for routine clinical use [9]. Histopathological confirmation was not available for all patients because of prolonged surgical waiting times at our center and the limited study period; therefore, MRI-based diagnosis was used to allow inclusion of a sufficient number of participants. In addition, patients within eight months after whole-brain radiotherapy were excluded to minimize the influence of treatment-related cognitive decline, as previous evidence suggests that neurocognitive deficits after whole-brain radiotherapy are most pronounced during this period before later stabilization or improvement [10].

In this study, most participants were aged 40–60 years (mean 49.16 ± 11.37), female, and presented predominantly with headache (51.1%). However, age and sex were not significantly associated with cognitive impairment. These findings suggest that, in this cohort, demographic characteristics were less important determinants of cognitive dysfunction than tumor-related factors. These findings suggest that, in this cohort, demographic characteristics were less important determinants of cognitive dysfunction than tumor-related factors [11]. This is consistent with previous reports indicating that cognitive outcomes in brain tumor patients are more strongly influenced by disease burden, lesion characteristics, and treatment-related factors than by demographic variables alone [3, 10, 12]. Nevertheless, the absence of association in the present study should be interpreted cautiously, as the relatively modest sample size and the concentration of participants within a limited age range may have reduced the ability to detect smaller effects.

Cognitive Dysfunction in Brain Tumors

Cognitive impairment was common in this study, affecting 60.8% of patients with brain tumors. This prevalence is comparable to previous literature reporting cognitive dysfunction in approximately 58% of patients with intracranial tumors, supporting the view that cognitive impairment is a frequent and clinically important manifestation of brain tumors. The relatively high prevalence observed in our cohort may reflect the characteristics of a tertiary referral population, in which patients are more likely to have advanced or clinically complex disease [13]. In addition, the use of MoCA-INA

may have facilitated detection of mild cognitive deficits during routine screening [11, 14].

Cognitive domains such as memory, attention, language, executive function, and visuospatial skills may all be affected [15]. A previous study by Miotto, et.al (2011) identified a 91% prevalence of cognitive deficits in frontal and temporal tumors, predominantly impacting executive function [16]. In metastatic disease, lesion burden rather than lesion count drove impairment. Gondi, et.al (2012) reported cognitive deficits in 90% of brain metastasis patients at initial presentation, likely due to microinfiltrative growth and diaschisis, with memory as the most vulnerable domain [17].

These findings reinforce the importance of early cognitive assessment in brain tumor patients, particularly because cognitive decline may substantially affect functional independence, treatment adherence, and quality of life. At the same time, because MoCA-INA is a screening tool rather than a comprehensive neuropsychological battery, the results should be interpreted as evidence of global screening-detected dysfunction rather than detailed domain-specific impairment.

Relationship Between Tumor Location and Cognitive Impairment

In the bivariate analysis, frontal and parietal tumor locations were associated with cognitive impairment, but these associations were no longer significant after adjustment in the multivariable model. This pattern suggests that the initial association between tumor location and cognitive dysfunction may have been confounded by other tumor characteristics, particularly tumor type and lesion burden. Previous studies have shown that frontal and parietal lesions are often linked to deficits in executive function, attention, and memory, so the direction of the bivariate findings in the present study is biologically plausible [18]. However, our adjusted analysis indicates that location alone may not independently explain cognitive dysfunction once broader disease-related factors are considered.

Each region of the brain plays a distinct role in regulating specific cognitive functions; thus, tumors located in particular areas may disrupt the cognitive domains governed by those regions. Lesions involving multiple lobes, or even a single large lesion, are more likely to result in pronounced cognitive impairment. The type of cognitive deficit often corresponds to the lobe affected for instance, tumors in the frontal lobe are typically associated with impairments in executive functioning, while lesions in the parietal lobe tend to affect

visuospatial abilities, attention, and memory. Meanwhile, involvement of the temporal lobe may compromise long-term memory, language comprehension, and emotional processing [19].

Previous studies have shown that frontal and parietal lesions are often linked to deficits in executive function, attention, and memory, so the direction of the bivariate findings in the present study is biologically plausible [14, 19]. A study by Taphoorn, et.al (2004) who emphasized that tumors located in the frontal and parietal lobes are more frequently associated with global cognitive deficits, whereas lesions in other regions tend to produce more focal and specific impairments [2]. Additionally, Duffau et al. [20] highlighted the critical role of the frontoparietal network in supporting neuroplasticity and cognitive compensation in patients with brain tumors. Cognitive deficits observed in patients with non-dominant or infratentorial lesions are often not a direct consequence of the lesion's location but rather result from extensive edema, which exerts a mass effect on adjacent cortical or subcortical circuits, potentially leading to secondary complications such as hydrocephalus [21]. However, our adjusted analysis indicates that location alone may not independently explain cognitive dysfunction once broader disease-related factors are considered [14, 19].

The discrepancy between the unadjusted and adjusted findings may also reflect methodological limitations. Several location subgroups were small, reducing statistical power, and the study did not account for hemisphere dominance, tumor size, or peritumoral edema, all of which may influence the neurocognitive impact of lesion site. Therefore, the present findings suggest that tumor location may contribute to cognitive impairment, but its effect appears to be less robust than that of tumor type and lesion burden in this cohort.

Relationship Between Tumor Type and Cognitive Impairment

Tumor type remained independently associated with cognitive impairment after multivariable adjustment, with primary tumors showing significantly lower odds of cognitive dysfunction than metastatic tumors. This finding is consistent with previous studies indicating that patients with brain metastases frequently experience substantial neurocognitive impairment at presentation [18]. A plausible explanation is that metastatic brain tumors are more likely to be multifocal, more diffusely distributed, and associated with greater peritumoral edema, resulting in broader disruption of neural networks involved in cognition. In contrast, many primary brain tumors may initially remain more localized, although their cognitive impact may still be substantial depending on size, growth pattern, and location [14].

Primary brain tumors may contribute to cognitive dysfunction through multiple direct and indirect pathophysiological mechanisms. Cognitive impairment may arise even before the tumor is clinically diagnosed. One important mechanism is the mass effect of the tumor, which can compress adjacent brain regions involved in cognitive processing, particularly within the frontal, temporal, and parietal lobes, thereby disrupting regional

cognitive networks and impairing cognitive function [14].

The stronger association observed for metastatic tumors in this study may therefore reflect greater overall intracranial disease burden rather than tumor origin alone. This interpretation is supported by the fact that lesion count was also independently associated with cognitive impairment in the final model [22]. A study has described brain metastases as having a microinfiltrative nature and the potential to induce diaschisis, a condition in which dysfunction occurs in regions distant from the lesion itself. Furthermore, metastatic lesions exhibit a more rapid angiogenic process, leading to the formation of immature neovasculature that contributes to extensive perifocal edema. This perifocal edema is generally more severe in metastatic tumors than in primary brain tumors due to these underlying pathophysiological mechanisms. As a result, the mass effect tends to be more pronounced in metastatic lesions, often producing multidomain cognitive impairments [23].

Brain metastases usually disseminate hematogenously and commonly localize at the gray–white matter junction and arterial watershed regions, where they often present as multiple lesions. These lesions are frequently accompanied by substantial vasogenic peritumoral edema, which can exert mass effect on adjacent brain structures and contribute to neurological and cognitive dysfunction. In the present study, however, a small proportion of metastatic tumors presented as a single lesion (12.5%) [24]. Although lower than that reported in some prior series, this finding is consistent with the recognized heterogeneity of brain metastasis presentation, as a substantial minority of patients may present with solitary lesions. By contrast, most primary brain tumors in our cohort appeared as solitary lesions confined to a single lobe, particularly within the cerebral hemispheres, which is in keeping with the generally localized growth pattern of many primary intracranial neoplasms. Nevertheless, a considerable proportion of primary tumors involved more than one lobe, likely reflecting increasing tumor size, mass effect, and associated peritumoral edema, which may extend structural compression and functional disruption into adjacent regions [24–26]. However, this result should be interpreted with caution because tumor classification in the present study was based on MRI findings rather than histopathological confirmation, and primary tumors were not subclassified by histology or grade. As a result, the tumor-type variable may not have fully captured biological heterogeneity within the primary tumor group.

Relationship Between Number of Lesions and Cognitive Impairment

Lesion count was also independently associated with cognitive impairment, with fewer lesions showing lower odds of dysfunction than multiple lesions. This finding is in agreement with previous literature suggesting that patients with multiple brain lesions generally have poorer cognitive performance than those with solitary lesions [27]. Lesions may disrupt multiple cortical and subcortical networks simultaneously, resulting in cumulative effects on attention, memory, and executive function. In metastatic disease, multiple lesions may additionally

indicate more disseminated intracranial involvement and greater edema, both of which may worsen global cognitive performance [28].

The higher incidence of multiple brain lesions can be attributed to several factors, including the increasing prevalence of malignancies, improved detection of systemic cancers and their metastases, and advancements in cancer treatment modalities that have extended patient survival. As patients live longer, their likelihood of developing brain metastases correspondingly increases [17, 28]. Previous studies suggest that cognitive dysfunction is present from the early symptomatic stage in a substantial proportion of patients with brain metastases, likely reflecting the microinfiltrative nature of metastatic growth and the contribution of diaschisis. Nevertheless, the severity of cognitive impairment cannot be explained by lesion count alone. Prior studies have highlighted the importance of lesion location and volume as major determinants of neurocognitive outcome. Thus, even a single lesion located in a functionally critical region, including the frontal lobe, temporal lobe, hippocampus, or prefrontal cortex, may cause clinically meaningful cognitive deficits [17, 27, 28].

Nevertheless, lesion count should not be interpreted as the sole determinant of cognitive dysfunction. Prior studies have suggested that lesion volume, location, and associated edema may be equally or more important than lesion number alone. This may explain why some patients with single lesions still demonstrate clinically important impairment when lesions are located in strategically important brain regions. In the present study, data on lesion volume, edema severity, and other treatment-related factors were not available, which limits more detailed interpretation of the observed association. Even so, the persistence of lesion count as an independent factor in the multivariable model suggests that overall lesion burden is a meaningful marker of cognitive risk in this population.

Limitations of the Study

The results of this study could be impacted by a number of limitations and confounding variables. The cross-sectional nature of this study limits our ability to infer causality between tumor characteristics and cognitive impairment, warranting longitudinal studies for more definitive conclusions. Limitations of the study First, there may be bias in the results because the MoCA-INA completion was completed by a large number of people. Second, because inclusion criteria are based solely on contrast-enhanced head MRI results rather than anatomical pathology results, research variables are still perceived as being lacking in cases where tumor types are only differentiated based on primary and metastatic. Third, there is no differentiation between the dominant and non-dominant hemispheres in terms of tumor location. Fourth, samples do not distinguish between treatments that have already been administered to patients, such as radiotherapy, chemotherapy, surgery, chemoradiotherapy, or no intervention at all. Fifth, information about other clinical symptoms and therapy already received by samples, such as ASM in patients with epilepsy symptoms, other ICP increase signs, and KPS score during

examination, is not displayed. The only clinical symptoms that are differentiated in patients are headache, seizures, and other neurological deficits. Sixth, there are too many sample size differences in the distribution of primary tumor types and metastases, which could influence research findings. As a result, more research is required.

In conclusion, cognitive impairment was frequent among patients with brain tumors in this study. Multivariable analysis showed that only tumor type and lesion count were independently associated with cognitive impairment, whereas tumor location was not retained in the final model. Patients with metastatic tumors and greater lesion burden had a higher likelihood of cognitive dysfunction. These findings highlight the importance of incorporating early cognitive assessment into the evaluation of high-risk brain tumor patients, particularly those with metastatic disease or multiple lesions. Further prospective studies are warranted to validate these findings and to determine their implications for risk stratification, monitoring, and early intervention in neuro-oncological practice.

Author Contribution Statement

D.R: Conceptualization, methodology, investigation, data curation, formal analysis, writing-original draft. H.A.: Investigation, formal analysis, data curation, writing- review and editing. S.B.R: Supervision, validation, writing-review and editing. Z.A: Supervision, methodology, validation, writing-review and editing.

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Availability of data

The data generated and/or analyzed during the current study are not publicly available for legal/ethical reasons but are available from the corresponding author on reasonable request. This study doesn't register in any registration dataset.

Ethical Consideration

Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Brawijaya (Approval Number: 400/302/K.3/102.7/2024). Informed consent was acquired from patient or guardians of all participants before enrolment in the study.

Conflict of Interest

There are no conflicts of interest to disclose.

References

1. Finney GR, Minagar A, Heilman KM. Assessment of mental status. *Neurol Clin.* 2016;34(1):1-16. <https://doi.org/10.1016/j.ncl.2015.08.001>.
2. Taphoorn MJB, Klein M. Cognitive deficits in adult patients with brain tumours. *Lancet Neurol.* 2004;3(3):159-68. [https://doi.org/10.1016/s1474-4422\(04\)00680-5](https://doi.org/10.1016/s1474-4422(04)00680-5).
3. Sinha R, Stephenson JM, Price SJ. A systematic review of cognitive function in patients with glioblastoma undergoing surgery. *Neurooncol Pract.* 2020;7(2):131-42. <https://doi.org/10.1093/nop/npz018>.
4. Hapsari MY, Ilyas MF, Ristinawati I, Stepvia S, Novika RG. Profile of Cognitive Impairment in Patients with Brain Tumors in Dr. Moewardi Hospital, Surakarta. *Indonesian Journal of Medicine.* 2022;7(2):242-50. <https://doi.org/10.26911/theijmed.2022.7.2.532>
5. Sari ER, Rambe AS, Nasution IK. The Relationship between Cognitive Function and Quality of Life in Patient with Intracranial Tumors at Haji Adam Malik Hospital Medan. *J Soc Med.* 2023;2(8):254-60. <https://doi.org/10.47353/jsocmed.v2i8.73>
6. Schubart JR, Kinzie MB, Farace E. Caring for the brain tumor patient: Family caregiver burden and unmet needs. *Neuro Oncol.* 2008;10(1):61-72. <https://doi.org/10.1215/15228517-2007-040>.
7. Pöhlmann J, Weller M, Marcellusi A, Grabe-Heyne K, Krott-Coi L, Rabar S, et al. High costs, low quality of life, reduced survival, and room for improving treatment: an analysis of burden and unmet needs in glioma. *Front Oncol.* 2024;14:1368606. <https://doi.org/10.3389/fonc.2024.1368606>.
8. Liu R, Page M, Solheim K, Fox S, Chang SM. Quality of life in adults with brain tumors: Current knowledge and future directions. *Neuro Oncol.* 2009;11(3):330-9. <https://doi.org/10.1215/15228517-2008-093>.
9. Lumempouw S, Ramli Y. Montreal cognitive assessment versi indonesia (moca-ina) untuk skrining gangguan fungsi kognitif. *Neurona (Majalah Kedokteran Neuro Sains Perhimpunan Dokter Spesialis Saraf Indonesia).* 2010 Jul 1;27(4).
10. van Grinsven EE, Nagtegaal SHJ, Verhoeff JJC, van Zandvoort MJE. Impact of Stereotactic or Whole Brain Radiotherapy on neurocognitive functioning in adult patients with brain metastases: A systematic review and meta-analysis. *Oncol Res Treat.* 2021;44(11):622-36. <https://doi.org/10.1159/000518848>
11. Gempt J, Lange N, Bette S, Foreman SC, Cammardella JH, Albertshäuser J, et al. Factors influencing neurocognitive function in patients with neuroepithelial tumors. *Sci Rep.* 2017;7(1):17764. <https://doi.org/10.1038/s41598-017-17833-w>.
12. Kirkman MA, Hunn BHM, Thomas MSC, Tolmie AK. Influences on cognitive outcomes in adult patients with gliomas: A systematic review. *Front Oncol.* 2022;12:943600. <https://doi.org/10.3389/fonc.2022.943600>.
13. Parsons MW, Dietrich J. Assessment and management of cognitive symptoms in patients with brain tumors. *Am Soc Clin Oncol Educ Book.* 2021;41:e90-e9. https://doi.org/10.1200/edbk_320813.
14. Ardhini R, Aninditha T, Andriani R, Sofyan HR. Fungsi kognitif pada pasien tumor otak metastasis pasca radiasi whole brain radiotherapy di dua RS rujukan kanker Indonesia. *Neurona.* 2020;38(1).
15. Lastri DN. Neurobehaviour Dasar dan Pemeriksaannya. In: *Buku ajar Neurologi 2017.* Departemen Neurologi FKUI-RSCM.
16. Miotto EC, Junior A, Silva CC, Cabrera HN, Machado MA, Benute GR, et al. Cognitive impairments in patients with low grade gliomas and high grade gliomas. *Arq Neuropsiquiatr.* 2011;69(4):596-601. <https://doi.org/10.1590/s0004-282x2011000500005>.
17. Gondi V, Hermann BP, Mehta MP, Tomé WA. Hippocampal dosimetry predicts neurocognitive function impairment after fractionated stereotactic radiotherapy for benign or low-grade adult brain tumors. *Int J Radiat Oncol Biol Phys.* 2012;83(4):e487-93. <https://doi.org/10.1016/j.ijrobp.2011.10.021>.
18. Price M, Neff C, Nagarajan N, Kruchko C, Waite KA, Cioffi G, et al. CBTRUS statistical report: American Brain Tumor Association & NCI Neuro-Oncology branch adolescent and young adult primary brain and other central nervous system tumors diagnosed in the United States in 2016-2020. *Neuro Oncol.* 2024;26(Supplement_3):iii1-iii53. <https://doi.org/10.1093/neuonc/noae047>.
19. Pendergrass JC, Targum SD, Harrison JE. Cognitive impairment associated with cancer: A brief review. *Innov Clin Neurosci.* 2018;15(1-2):36-44.
20. Duffau H. The huge plastic potential of adult brain and the role of connectomics: New insights provided by serial mappings in glioma surgery. *Cortex.* 2014;58:325-37. <https://doi.org/10.1016/j.cortex.2013.08.005>.
21. Schellekens MMI, Li H, Wijnands M, Papounidou A, Boot EM, Verhoeven JI, et al. Lesion locations are associated with cognitive impairment after ischemic stroke in young adults. *Neuroimage Clin.* 2026;49:103930. <https://doi.org/10.1016/j.nicl.2025.103930>.
22. Ismail MS, Muis A, Asmedi A. *Buku Acuan Modul Neurovaskular [Neurovascular Module Reference Book].* 1st ed. PERDOSSI; 2009.
23. Brady ST, Siegel GJ, Albers RW, et al. *Basic Neurochemistry: Principles of Molecular, Cellular, and Medical Neurobiology.* 8th ed. Amsterdam: Elsevier, 2012.
24. Aizer AA, Lamba N, Ahluwalia MS, Aldape K, Boire A, Brastianos PK, et al. Brain metastases: A Society for Neuro-Oncology (SNO) consensus review on current management and future directions. *Neuro Oncol.* 2022;24(10):1613-46. <https://doi.org/10.1093/neuonc/noac118>.
25. Fink KR, Fink JR. Imaging of brain metastases. *Surg Neurol Int.* 2013;4(Suppl 4):S209-19. <https://doi.org/10.4103/2152-7806.111298>.
26. Smirniotopoulos JG, Jäger HR. IDKD springer series Differential diagnosis of intracranial masses. In: Hodler J, Kubik-Huch RA, von Schulthess GK, editors. *Diseases of the Brain, Head and Neck, Spine 2020–2023: Diagnostic imaging.* Cham (CH): Springer Copyright 2020, The Author(s). 2020. p. 93-104.
27. Triebel KL, Gerstenecker A, Meneses K, Fiveash JB, Meyers CA, Cutter G, et al. Capacity of patients with brain metastases to make treatment decisions. *Psychooncology.* 2015;24(11):1448-55. <https://doi.org/10.1002/pon.3753>.
28. Linnert M, Iversen HK, Gehl J. Multiple brain metastases - current management and perspectives for treatment with electrochemotherapy. *Radiol Oncol.* 2012;46(4):271-8. <https://doi.org/10.2478/v10019-012-0042-y>.



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