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Analysis of functional score in adult primary brain tumor patients: A single institution study

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Abstract

Objectives: This study investigates the relationships between preoperative functional scores, tumor type, size, and location, as well as postoperative functional outcomes in brain tumor patients. *Methods*: A retrospective cohort design analyzed medical records of adult brain tumor patients at Cipto Mangunkusumo Hospital (RSCM) from 2021 to 2022. Inclusion criteria were adults aged 17 years and older diagnosed with primary brain tumors confirmed by CT or MRI imaging. Consecutive sampling was utilized for selection. Data analysis included univariate tests for descriptive statistics and bivariate hypothesis tests (Mann-Whitney, T-test, Kruskal-Wallis, ANOVA) to assess variable relationships, with significance set at $p < 0.05$. *Results*: From 456 samples, 255 met the criteria for analysis. The median age was 44 years, with a predominance of females (66.7%). Meningiomas were the most common tumor type (43.5%). The median tumor size was 27.972 cc, with 91.4% located supratentorially. Preoperative Karnofsky Performance Status (KPS) scores had a median of 80%. Significant relationships were found between tumor type and preoperative KPS scores ($p < 0.001$) and a weak negative correlation between tumor size and KPS scores (correlation coefficient = -0.194). Supratentorial tumors had higher preoperative KPS scores compared to infratentorial tumors (median 80% vs. 75%, $p < 0.05$). *Conclusion*: Tumor characteristics significantly influence functional outcomes in brain tumor patients, highlighting the importance of these factors in management strategies.

Keywords: Brain neoplasms, functional outcomes, Karnofsky Performance Status, tumor size, tumor type, tumor location

INTRODUCTION

Brain tumors are intracranial neoplasms that affect approximately 200,000 individuals globally each year. Studies have identified 4,417 brain tumors, with a male-to-female ratio of 1,900 (43%) males to 2,517 (57%) females. The incidence rates of malignant and benign tumors in men are 8.3 and 4.1, respectively, while in women, they are 6.4 and 7.2. The incidence of malignant brain tumors remains stable; however, benign tumors increase annually, with an annual percentage change (APC) of +6.2% (CI 4.5- 7.9). The primary causes of primary brain tumors (PBT) include abnormal cell division in neurons, glial cells, lymphatic tissue, blood vessels, cranial nerves, brain coverings, the skull, pituitary gland, and pineal gland. In Indonesia, the management of brain tumors lacks integration across promotional, preventive, and curative aspects, leading to delays in referrals. Surgical management can result in various complications. At Cipto Mangunkusumo Hospital (RSCM), there is currently no research analyzing the functional scores of patients pre- and post- surgery and their relationship with tumor

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type, size, location, and resectability level. This research aims to elucidate these connections to enhance the understanding and management of brain tumors.[1,2]

This study seeks to determine the relationship between preoperative functional scores and tumor characteristics such as type, size, and location. Additionally, it aims to evaluate the relationship between postoperative functional scores and tumor resectability level. Brain tumors result from abnormal cell division in the brain or central spinal canal and involve various cell types including neurons, astrocytes, oligodendrocytes, and ependymal cells. The classification of brain tumors based on WHO morphology and stage provides a comprehensive view of growth patterns and malignancy levels. Tumors can also be categorized by their location as either supratentorial or infratentorial. The epidemiology of brain tumors highlights their global impact with approximately 200,000 new cases each year, alongside gender-based differences in incidence rates. While the incidence of malignant tumors remains stable, benign tumors continue to rise annually. Data from RSCM and Dharmais Cancer Hospital in Indonesia reveal variations in patient age and common primary tumor types such as astrocytoma and meningioma.[3]

The Karnofsky Performance Status (KPS) is a standard method for measuring cancer patients' ability to perform daily tasks on a scale from 0 to 100, where higher scores indicate better functionality. KPS is utilized to determine prognosis, measure changes in patient function over time, and assess eligibility for clinical trials. The KPS assessment encompasses categories ranging from normal functioning to death. Studies indicate a strong positive correlation between KPS scores and activities of daily living (ADL), as well as a strong negative correlation with basic activities of daily living (BADL). KPS has proven to be a predictor of therapy response and survival in cancer clinical trials; evaluation parameters include daily performance activity levels, pain intensity, tumor location, number of metastases, psychological status, and survival outcomes. Although KPS is subjective in nature, the assessment relies on consistent objective values that effectively evaluate patients' abilities to perform daily activities.[4]

METHODS

This study employed a retrospective cohort design by examining the medical records of brain tumor patients treated at RSCM from 2021 to 2022. The inclusion criteria for this research encompassed adults aged 17 years and older who were diagnosed with brain tumors through CT scans or MRI imaging by a radiology specialist, with subsequent pathology verification by a pathologist. Exclusion criteria included incomplete data or cases that were not classified as primary tumors. Sample selection utilized consecutive sampling.

Data analysis involved univariate tests for descriptive statistics, normality tests for numerical data, and frequency calculations for categorical data. Bivariate hypothesis tests, such as the Mann-Whitney test, independent T-test, Kruskal-Wallis test, and ANOVA, were employed to evaluate relationships between relevant variables. Correlations between numerical data were analyzed using either the Pearson or Spearman tests, depending on the distribution of the data. This research obtained ethical clearance from the RSCM-FKUI Health Research Ethics Committee, with approval letter number: KET- 306/UN2.FI/ETIK/PPM.00.02/2023.

RESULTS

Univariate analysis aimed to explain and describe the characteristics of each variable. The data were sourced from medical records, operation reports, and postoperative summaries of patients undergoing primary brain tumor surgery at RSCM during the 2021-2022 period. Out of a total of 456 samples, 255 samples met the inclusion and exclusion criteria and were included in the analysis. This analysis provides a general overview of the characteristics of patients undergoing primary brain tumor surgery and aids in the initial understanding of the distribution of variables involved in this study. The age distribution of the sample was assessed using the Kolmogorov-Smirnov test, yielding a non-normal distribution with a p- value of 0.043. The age of the sample is presented as median (44 years) with a range (18-83 years) due to the non-normal distribution of the data.

The distribution of samples based on gender and health insurance during surgery can be observed. Out of 255 samples, 170 (66.7%) were female, while 85 (33.3%) were male. The most commonly used health insurance was the National Health Insurance (JKN), covering 251 out of 255 samples (98.4%), while none used Regional Health Insurance (JAMKESDA), and only 4 samples (1.6%) were covered by public health insurance.

The types of primary brain tumors are grouped

Table 1: Sample characteristic distribution

Variables	Frequency (n)	Percentage (%)
Gender		
Female	170	66.7
Male	85	33.3
Health insurance coverage		
Public	4	1.6
(Jkn)	251	98.4
Jamkesda	0	0

into seven categories: meningioma, glioma, schwannoma, craniopharyngioma, central neurocytoma, adenoma, and others, as assessed based on expert reports from pathological examinations. The samples diagnosed with meningioma reached 111 samples (43.5%), glioma comprised 34 samples (13.3%), schwannoma accounted for 12 samples (4.7%), craniopharyngioma had 7 samples (2.7%), central neurocytoma had the fewest samples at 4 samples (1.6%), adenoma reached 60 samples (23.5%), and there were 27 samples with diagnoses other than these six categories.

The distribution of tumor sizes in the sample was also measured using the Kolmogorov-Smirnov test due to the sample size exceeding 50. A significant result of <0.001 indicates a non-normal distribution of the data, with the median tumor size measured at 27.972 milliliter, ranging from a minimum value of 0.077 milliliter to a maximum value of 425.386 milliliter.

The location of primary brain tumors is categorized into two groups: supratentorial (above the cerebellar tentorium) and infratentorial (below the cerebellar tentorium). The majority of samples, comprising 233 (91.4%), had tumors located in the supratentorial region, while 22 samples (8.6%) were found infratentorially.

The resectability level of brain tumors in this study was classified into two categories: Subtotal Resection (STR) and Gross Total Resection (GTR). Based on operation reports and postoperative summaries, most samples underwent subtotal resection surgery (214 samples; 83.9%), while gross total resection was performed in 41 samples (16.1%).

The distribution of Karnofsky Performance Status (KPS) scores in the sample was also assessed using the Kolmogorov-Smirnov test due to a sample size exceeding 50; significant results (<0.001) for both preoperative and postoperative KPS scores indicated a non-normal distribution of data as well. The preoperative median KPS score was found to be 80%, with values ranging from a minimum of 40% to a maximum of 100%; similarly, for postoperative KPS scores, the median was also recorded at 80%, with values ranging from 0% to 100%.

From Table 3, we can ascertain that all types of brain tumors have a median KPS score of 80%. However, adenomas achieved the highest mean KPS score at 84.59, while other tumor types recorded lower mean scores (73.73). The statistical test resulted in a p-value of <0.001, indicating acceptance of H1 and rejection of H0; thus concluding that there is a significant

Table 2: The distribution of tumor types in the sample

Types	Frequency (n)	Percentage (%)
Meningioma	111	43.5
Glioma	34	13.3
Schwannoma	12	4.7
Craniopharyngioma	7	2.7
Central neurocytoma	4	1.6
Adenoma	60	23.5
Others	27	10.6
Total	255	100

Table 3: The relationship between tumor types and preoperative KPS scores

Variables	Median	Min - Max
Meningioma	80	40-100
Glioma	80	50-100
Adenoma	80	50-100
Others	80	40-100

Table 4: The relationship between tumor location and preoperative KPS scores

Variables	Median	Min - Max
Supratentorial	80	40-100
Infratentorial	75	40-90

relationship between tumor type and preoperative KPS scores.

Numeric-numeric data were analyzed to determine the strength of correlation between tumor size and preoperative KPS scores; this correlation yielded a value of - 0.194, categorizing it as weak according to SPSS reference values. The negative correlation suggests that as preoperative KPS scores increase, tumor size decreases; this supports our hypothesis regarding the relationship between tumor size and preoperative KPS scores.

The table indicates that supratentorial tumors have a median preoperative KPS score of 80%, whereas infratentorial tumors have a median score of 75%; these results suggest that preoperative KPS scores are generally higher for supratentorial tumors compared to infratentorial tumors, indicating better functional status prior to surgery for patients with supratentorial tumors.

From Table 5, it can be concluded that patients undergoing subtotal resection have a median postoperative KPS score of 80%, while those undergoing gross total resection have a median score of 85%; these results suggest an improvement in functional outcomes following gross total resection compared to subtotal resection. A comparison of pre-operative and post-operative KPS scores for the cohort was performed. While the median score remained at 80%, analysis of individual patient changes showed that the KPS score improved in 85 patients (33.3%), remained stable in 120 patients (47.1%), and declined in 50 patients (19.6%), Also a Wilcoxon signed-rank test indicated that this overall change was not statistically significant

Table 5: The relationship between the resectability level of tumors and postoperative KPS scores

Variables	Median	Min - Max
Sub total resection	80	0-100
Gross total resection	85	60-100

($p = 0.115$).

However, despite these median differences, statistical tests indicate $p > 0.05$, confirming no significant relationship between tumor resectability level and postoperative KPS scores; thus emphasizing that while functional outcomes differ between resection types, they do not demonstrate significant statistical differences regarding resectability level in patients with brain tumors.

DISCUSSION

The research analyzing the functional scores of adult primary brain tumor patients in the Department of Neurosurgery at RSCM for the years 2021-2022 has advantages in selecting a topic that has not been explored in Indonesia before, specifically concerning the relationship between functional scores and the type, location, size, and resectability level of brain tumors. Despite utilizing secondary data from medical records, operation reports, and postoperative summaries at RSCM, this study contributes by enabling a large sample size to be gathered in a short period. However, there are limitations, particularly in data incompleteness, restricting the number of analyzable samples to 255 out of the initial 456 samples. Nevertheless, the use of secondary data still provides benefits in understanding the factors influencing the functional scores of adult brain tumor patients.

This study reveals that the median age of participants is 44 years with a mean of 43.76 years, which aligns with previous research by Aninditha at RSCM from 2014-2016, showing a mean of 43.8 years.[5-7] Despite a variation shown in a study by Heng *et al*. in Sarawak, Malaysia, with the highest prevalence in the 51-60 age group, both studies are consistent with these findings regarding gender, where women have a higher percentage than men.[5-8] The RSCM study from 2014-2016 noted a female percentage of 68%, while in Sarawak, it reached 57.4%. In this study, the percentage of women is 66.7%.57-58 The majority of samples undergoing surgery in the Department of Neurosurgery at RSCM use National Health

Insurance (JKN) (98.4%), reflecting the increasing trend in JKN utilization as a step towards Universal Health Coverage (UHC) in Indonesia, reaching 83.25% of the total population in 2019.[5-7]

This study utilizes KPS scores obtained from patient assessments. The distribution of KPS score data is not normal, as confirmed by the Kolmogorov-Smirnov test. KPS scores show a median of 80% (range 40%-100%) before surgery and 80% (range 0%-100%) after surgery. Although still considered good as it reaches 80%, indicating the patient's ability to perform normal activities with some difficulty, symptoms, or signs, there are differences compared to other studies. A study by Gunawan *et al*. noted a median KPS of 50% (range 30%-80%) before surgery and 60% (range 0%-100%) after surgery, showing an increase in median scores from before to after surgery. In the context of survival, a study by Ramchandran *et al*. indicates that patients with KPS of 50% or higher have a survival rate between 50 and 90 days. KPS scores of 30% to 40% are associated with an average survival of 8 to 50 days, while KPS scores of 10% to 20% are related to survival of 7 to 16 days.[8,9] This study reveals a significant relationship between the type of brain tumor and preoperative Karnofsky Performance

Status (KPS) scores, with a significance value of <0.001, tested using the Kruskal- Wallis test due to the non-normal distribution of data. The median preoperative KPS scores for all four types of tumors are 80%, but differences emerge when looking at the mean values, where adenoma has the highest mean (84.59%) and other tumor types have the lowest mean (73.73%). Benign tumors, such as adenoma and meningioma, tend to have higher KPS scores, indicating better functional outcomes, while malignant tumors, especially gliomas, show lower KPS scores, reflecting poorer outcomes. These results indicate that the type of brain tumor can influence patient functional scores, with benign tumors tending to have better outcomes compared to malignant tumors.[10-13] This study reveals a relationship between the size of brain tumors and the outcomes of preoperative KPS scores, tested using the Spearman correlation due to the non-normal distribution of data. Although the correlation is weak (- 0.194), the results indicate that as the size of the tumor increases, KPS scores tend to be lower. This finding is consistent with other studies stating that smaller tumor sizes correlate with better patient prognosis. The research also highlights the importance of tumor size in the general staging system, where tumor size can affect the staging level and disease classification. A study by Shah *et al.* confirms a close relationship between glioma size and prognosis, indicating that tumor size strongly correlates with patient survival. Although various measurement methods (1D, 2D, TV, EV) have high levels of agreement, the research suggests that 1D measurements can be reliable in assessing tumor growth and correlate with survival. These findings support the view that the size of brain tumors plays a crucial role as an independent prognostic factor in determining patient survival, with smaller sizes tending to correlate with higher KPS scores.[14-16]

This study reveals the significant relationship between the location of brain tumors and preoperative KPS scores, with a p- value of <0.05. Utilizing the Mann-Whitney test due to the non-normal distribution of data, the research indicates that the median preoperative KPS scores in patients with tumors in the supratentorial region are higher than those located in the infratentorial region, suggesting that patients with tumors above the cerebellar tentorium have higher preoperative KPS scores. This finding differs from some other studies, such as Hamed *et al*., who found nonsignificant differences between tumor locations in the supratentorial and infratentorial regions. Nevertheless, that study also suggests that tumors in the infratentorial region tend to have a better prognosis in terms of mortality and survival. Another study by Chandra *et al*. on supratentorial glioblastoma compared to cerebellar glioblastoma in geriatric patients found nonsignificant differences in tumor location, but cerebellar glioblastoma showed slightly better prognosis. A study by Sayegh *et al.* on ependymoma also indicates that infratentorial tumors have better Progression- Free Survival (PFS) and overall survival, although supratentorial tumors are more likely to undergo total resection. The differences in these findings can be attributed to other variables such as tumor type and size, where the significance of tumor type and size to preoperative KPS scores in this study is relatively smaller compared to tumor location.[17-19]

This study reveals that although there are apparent differences in the median (KPS) scores postoperatively between total resection (Gross Total Resection/GTR) and subtotal resection (Subtotal Resection/STR), the p- value > 0.05 (0.107) indicates that these differences are not statistically significant. Thus, this finding suggests that there is no significant difference between STR and GTR in terms of postoperative KPS scores in adult brain tumor patients. Although some studies by Han *et al*., Hatoum *et al*, Tang *et al*, Kramm

et al, and Grewal *et al.* support these results by showing that GTR may provide a better prognosis than STR for gliomas and craniopharyngiomas. In this study, the nonsignificance between the resectability level and postoperative KPS scores may be due to limited sample size or differences in the types and locations of tumors that can affect KPS scores even after surgery. The importance of tailored management to the characteristics of each patient is emphasized, considering that GTR, while improving prognosis, may also carry the risk of additional complications.[20-24]

This study has several limitations. Firstly, its retrospective design relying on medical records is susceptible to missing data and documentation inconsistencies, as evidenced by the reduction of our initial sample from 456 to 255 records. Furthermore, the single-center nature of this study may introduce selection bias and limit the generalizability of our findings to other populations with different demographic or clinical characteristics. As our analysis of functional outcomes was limited to the KPS score. A more detailed analysis of the factors driving changes in postoperative KPS was not feasible within the scope of this data. While we observed a trend towards higher median KPS in the GTR group, our analysis was unable to fully elucidate the detailed trajectory of functional recovery. The binary classification of resection extent (STR vs. GTR), while standard for our clinical documentation, is a simplification. A more granular grading system, such as the Simpson Grade for meningiomas or volumetric analysis, could provide more nuanced insights into the relationship between resection degree and outcome.

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