

## Survival Analysis of Brain Tumor Patients: One Year after Surgery

Tika Dwi Tama\*<sup>1</sup>, Nada Syifa<sup>1</sup>, Erni Astutik<sup>2</sup>

<sup>1</sup>Universitas Negeri Malang, Jl. Semarang No. 5, Malang, East Java, 65114, Indonesia

<sup>2</sup>Universitas Airlangga, Mulyorejo, Surabaya, East Java, 60115, Indonesia

\*Authors correspondence, Email address: tika.dwi.fik@um.ac.id

ARTICLE INFO	ABSTRACT
<b>ORCID ID</b> Author 1: <a href="https://orcid.org/0000-0003-3799-0928">https://orcid.org/0000-0003-3799-0928</a> Author 2: - Author 3: <a href="https://orcid.org/0000-0003-2934-1290">https://orcid.org/0000-0003-2934-1290</a>	Surgery is the most performed procedure to treat brain tumors. However, information about the survival of brain tumor patients after undergoing surgery is still limited in Indonesia. This study aimed to determine 1 year survival in brain tumor patients after undergoing surgical procedures and factors associated with patient survival. A retrospective cohort study was conducted in March until April 2023 with subjects of 46 brain tumor patients who were registered at the Gatot Soebroto Army Hospital and underwent surgical procedures in 2018 until 2022. Data on respondent characteristics (gender and age), clinical conditions (tumor location, stage, and tumor classification), date of surgery, and date of death were obtained from medical records. Kaplan Meier was used to determine the 1 year survival of brain tumor patients after surgery, while Cox Proportional Hazard Regression was used to determine factors associated with its survival. Kaplan Meier analysis showed that 1 year survival in post-operative brain tumor patients reached 80.5 percent. Secondary tumor was known to increase the risk of death in post-operative brain tumor patients (aHR 11.432; 95 percent CI 1.394 until 93.767). There was no significant relationship found between sex, age, tumor location, and tumor stage with brain tumor patients's survival (p-value more than 0.05). Identification of tumor classification needs to be done correctly and as early as possible so that the patient's prognosis becomes better. The therapeutic approach needs to pay attention to the condition of each patient, especially in cases of secondary brain tumors.
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### 1. Introduction

Brain tumors are known as one of the non-communicable diseases that are currently a health burden in almost all parts of the world (Ferlay et al., 2024). Although the case is rare, this type of tumor has a significant contribution to morbidity and mortality in all age groups. Among the malignant tumors suffered by humans, brain tumors are classified as one of the most malignant types of tumors (Pichaivel et al., 2022). The Global Cancer Observatory reported that in 2022, new cases of brain and central nervous system (CNS) tumors that were diagnosed reached 321,731 cases. This number placed brain and CNS tumors in the 19th place as the type of tumor with the most cases (Ferlay et al., 2024). For mortality, as many as 248,500 cases of brain tumors were reported to have died in 2022 (Ferlay et al., 2024).

The trend of new cases of brain tumors shows a significant increase in the last two decades across WHO regional areas, both in men and women (Ilic & Ilic, 2023). Countries in the Asian region reported a rapid increase, ranging from 15% to 80% compared to 2009 data (Ferlay et al., 2024; Patel et al., 2019). In Indonesia, the incidence of brain and CNS tumors is ranked 15th as the highest number of cancer cases and 11th as the cause of death among all types of cancer (Ferlay et al., 2024). Studies conducted at several hospitals in Indonesia reported that most patients were > 40 years old and had primary brain tumors of the meningioma type (Aninditha et al., 2022; Diansari et al., 2022).

Globally, the five-year survival rate of brain tumor patients ranges from 4% to more than 70% (Girardi et al., 2023). Early detection and appropriate management allow patients to have a better prognosis and chance of survival. Brain tumor treatment involves a variety of approaches, including tumor histology, location, size, stage, age, and the patient's general health condition (Patel et al., 2019). Some treatments that are usually given to brain tumor patients include surgery, chemotherapy, radiotherapy, administration of corticosteroid drugs, targeted therapy, palliative care, or a combination (D'Andrea et al., 2017; Patel et al., 2019; Perkins & Liu, 2016). Surgical procedures are generally the first-line treatment in the management of brain tumors. Complete removal of the tumor mass (resection) is known to increase the patient's chances of recovery. The majority of patients reported experiencing an improvement in quality of life after 30 days of surgery, namely in physical, emotional, cognitive, and social aspects (Królikowska et al., 2022).

Surgical procedures are considered more beneficial than other methods because they are performed to reduce tumors massively. The brain tumor mass removed in the surgical procedure is attempted to be removed as much as possible. Thus, it can minimize the symptoms caused (Królikowska et al., 2022). A previous study reported that the removal of more than 90% of the tumor mass resulted in good outcomes for patient prognosis (Bonosi et al., 2023). However, the long-term survival of brain tumor patients remains a challenge given the risk of perioperative injury that can cause complications. Many factors are thought to be associated with post-surgery survival of brain tumor patients, such as tumor type, location, tumor size, type of therapy, patient age, and tumor molecular status (Chaichana et al., 2013; D'Andrea et al., 2017; Niedermeyer et al., 2024; Tang et al., 2008).

Previous studies have focused on investigating the long-term survival of brain tumor patients in general to identify prognostic factors. Furthermore, most studies still focus on identifying patient characteristics (Aninditha et al., 2021; Diansari et al., 2022; Rahmawaty et al., 2024). Meanwhile, studies that specifically evaluate the survival rate of brain tumor patients undergoing surgical procedures are still limited, especially in Indonesia. Therefore, this study was conducted to fill the gap by assessing one-year survival after surgical procedures in brain tumor patients and the factors associated with survival. A short-term evaluation of the effectiveness of surgical procedures on patient prognosis can contribute to the development of more effective treatment management strategies. Thus, the quality of life and survival of tumor patients can be improved.

## 2. Method

A retrospective cohort study was conducted at RSPAD Gatot Soebroto from March to April 2023. The study population was all brain tumor patients registered at RSPAD Gatot Soebroto and underwent surgical procedures in 2018-2022. The inclusion criteria were

patients who had confirmed diagnoses of brain tumors and underwent surgical procedures for the first time. Patients whose medical records were not found and had inadequate data (missing data) were excluded from this study. A total of 46 brain tumor patients who met the inclusion and exclusion criteria were taken as research samples.

All data related to the research variables, including respondent characteristics (gender and age), clinical conditions (tumor location, stage, and tumor classification), date of surgery, date of death, and patient condition after one year of surgery (dead or alive), were obtained from medical records. Data were extracted into the structured form according to the variables studied. The patient's age was categorized as pediatric patient ( $\leq 18$  years old) and adult patient ( $> 18$  years old) (Arania et al., 2022; of Health Republic Indonesia, 2023). If the location of the tumor is found in the cerebrum area, it is categorized as supratentorial, while tumors found in the cerebellum or brainstem are categorized as infratentorial (Sánchez-Sánchez et al., 2016). Patients with stages 1 and 2 are classified as low-grade, while patients with stages 3 and 4 are categorized as high-grade (Torp et al., 2022). Based on their origin, tumors are classified into primary tumors and secondary tumors. Tumors that start growing in the brain are classified as primary tumors, while tumors that grow in the brain due to metastasis from other parts of the body are called secondary tumors (Rahmat et al., 2021).

The collected data were then analyzed descriptively to determine the distribution of the characteristics of the research subjects. In addition, survival analysis using the Kaplan-Meier method was also carried out to determine the survival of brain tumor patients 1 year after undergoing surgery. To determine the factors associated with death in brain tumor patients after undergoing surgery, the Cox Proportional Hazard Regression test was carried out. This study has obtained ethical approval from Airlangga University with certificate number 292/HRECC.FODM/III/2023.

### 3. Result and Discussion

#### 3.1 Results

Of the 46 brain tumor patients at RSPAD Gatot Soebroto who underwent surgical procedures, most of the patients were male (52.2%) and adults ( $> 18$  years old) (71.7%). Based on the patient's clinical condition, the location of the tumor was most often found in the supratentorial part (71.7%), most patients (52.2%) were in stages 1 and 2 (low-grade) and had primary brain tumors (91.3%). Patient characteristics are presented in Table 1.

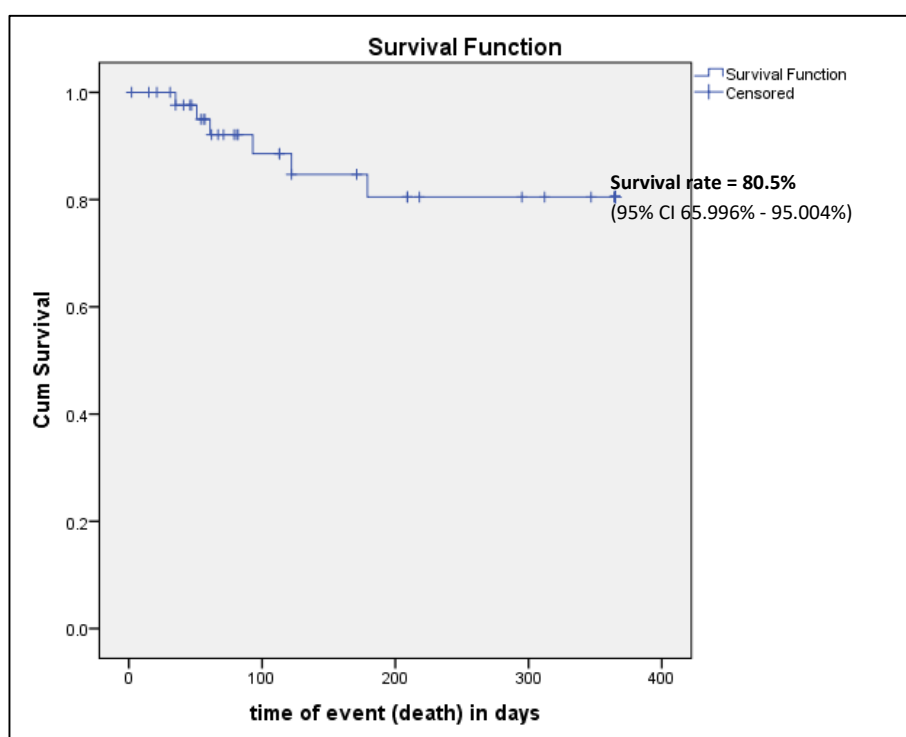
**Table 1. Characteristics of brain tumor patients undergoing surgical procedures**

Variable	Frequency (n)	Percentage (%)
<b>Gender</b>		
Male	24	52.2
Female	22	47.8
<b>Age group</b>		
$\leq 18$ years old (pediatric patient)	13	28.3
$> 18$ years old (adult patient)	33	71.7
<b>Tumor location</b>		
Supratentorial	33	71.7
Infratentorial	13	28.3

Variable	Frequency (n)	Percentage (%)
<b>Stadium</b>		
1 and 2 ( <i>low-grade</i> )	24	52.2
3 and 4 ( <i>high-grade</i> )	22	47.8
<b>Tumor classification</b>		
Primary tumor	42	91.3
Secondary tumor	4	8.7
<b>Total</b>	46	100.0

Source: Primary data, 2023

The 1-year survival rate of brain tumor patients after undergoing surgery was 80.5% with a standard error of 0.074 (95% CI 65.996% - 95.004%). It showed that 80.5% of brain tumor patients still survive after 1 year of surgery. The survival rate of brain tumor patients showed a decline over time. Figure 1 shows that cases of death in brain tumor patients often occur in the first 6 months after surgery.



Source: Primary data, 2023

**Figure 1. One-year survival of brain tumor patients after surgical procedures**

The survival rate of female brain tumor patients, aged > 18 years, having tumors in the supratentorial area, and low grade (stadium 1-2) tended to have a higher chance to survive after 1 year of undergoing surgery (Table 2). The survival rate of brain tumor patients with these characteristics ranged from 69.1 to 86.6%. Nevertheless, the survival rates were not statistically different from other categories. Gender, age, tumor location, and stage did not have an association with the death status of brain tumor patients after 1 year of undergoing surgery ( $p$ -value > 0.05) (Table 2). The results of the Cox regression analysis showed that tumor classification was associated with 1-year survival of brain tumor patients after surgery (aHR 11.432; 95% CI 1.394 - 93.767). Secondary brain tumor patients had a higher risk of death compared to primary brain tumor patients. The survival rate among those patients was

37.5%, while in patients with primary tumor, the survival rate was 71.0%. Patients who are classified as having secondary tumor have an eleven times higher risk of death than primary brain tumor patients (Table 2).

**Table 2. One-year survival of brain tumor patients after surgical procedures based on patient characteristics**

Variable	Log rank (p-value)	Survival rate (%)	Cox Regression	
			p-value	aHR (95% CI)
<b>Gender</b>			0.613	
Male	0.619	68.5		Ref
Female		69.1		0.669 (0.141 – 3.179)
<b>Age group</b>				
≤ 18 years old (pediatric patient)	0.253	43.8	0.243	Ref
> 18 years old (adult patient)		75.4		0.353 (0.061 – 2.030)
<b>Tumor location</b>			0.575	
Supratentorial	0.290	75.6		Ref
Infratentorial		36.9		1.664 (0.280 – 9.869)
<b>Stadium</b>			0.185	
1 and 2 ( <i>low-grade</i> )	0.119	86.6		Ref
3 and 4 ( <i>high-grade</i> )		45.7		3.377 (0.559 – 20.414)
<b>Tumor classification</b>			0.023*	
Primary tumor	0.052	71.0		Ref
Secondary tumor		37.5		11.432 (1.394 – 93.767)

Source: Primary data, 2023

### 3.2 Discussion

This study found that 8 out of 10 brain tumor patients were able to survive after 1 year of undergoing surgical procedures. The survival probability found in this study is almost the same as studies conducted in Nigeria and the United States (Danjuma et al., 2022; Phillips et al., 2023). Studies in Nigeria and the United States reported that after 1 year of surgery, the mortality rate of brain tumor patients ranged from 23% to 25.6% (Danjuma et al., 2022; Phillips et al., 2023). In general, surgical procedures are the recommended treatment for brain tumors (Królikowska et al., 2022; Löfgren et al., 2022). The surgical process is carried out to reduce the tumor mass, either by removing all (resection) or part of it. The removal of the tumor mass aims to prevent the growth and spread of the tumor to other parts of the body. In addition, surgery also aims to help maintain nerve function and reduce damage to healthy brain tissue (Królikowska et al., 2022; Löfgren et al., 2022). Although there are risks that can be posed by surgical procedures, proper decision-making and a skilled medical team can help ensure the safety and success of this procedure. The quality of life of brain tumor patients has improved after undergoing surgical procedures, especially in physical and emotional aspects (C.-W. Kim et al., 2016; Królikowska et al., 2022). Surgical procedures have been reported to be effective in improving neurological performance and maintaining the condition in a stable state. This procedure also reduces the chances of recurrence. Thus, the patient's prognosis can be better.

Previous studies have shown that the Karnofsky Performance Scale (KPS) score of brain tumor patients increased after undergoing surgery. In glioma patients, the median KPS score after surgery increased by 20%, while in glioblastoma patients, the median KPS score

was 80, an increase of 20 points compared to the score before surgery (Chambless et al., 2015; Gunawan et al., 2020). The Karnofsky Performance Scale is an indicator used to assess the prognosis of cancer patients. This indicator measures the patient's functional ability to carry out daily activities and respond to therapy. The higher the KPS score, the better the patient's condition. This condition gives patients a greater chance of survival (Frappaz et al., 2021).

Tumor classification is known to be one of the factors associated with the survival of brain tumor patients after 1 year of undergoing surgery. After undergoing surgery, patients with secondary tumors have a higher risk of death compared to patients with primary tumors. This finding is in line with a study conducted by Tang et al. (Tang et al., 2008). The survival rate of secondary brain tumor patients after 1 year of undergoing surgery was 21%, while in patients with primary brain tumors, the survival rate was 51% (Tang et al., 2008). Secondary brain tumors are tumors that grow in the brain and arise due to the spread of tumors from other parts of the body (Winther et al., 2022). Generally, secondary brain tumors originate from metastases of lung, breast, kidney, and skin cancers (J. Kim et al., 2018). Patients with secondary brain tumors show that the cancer cells in their bodies have experienced wider spread and are aggressive, causing more severe systemic impacts. Secondary brain tumor patients also tend to have more lesions compared to primary tumor patients (Aninditha et al., 2022; Winther et al., 2022). This condition causes increased intracranial pressure and causes more extensive edema. It can cause rapid neurological and brain tissue damage. The chance of complications from surgical procedures in these patients is also greater. Previous studies reported that post-surgical complications in patients with secondary brain tumors reached 29.8% (Niedermeyer et al., 2024). The most commonly reported complication is venous thromboembolism (Ene & Ferguson, 2022). Venous thromboembolism can increase the occurrence of bleeding and intravascular coagulation so that the risk of death is higher (Kabashneh et al., 2020).

Gender, age, tumor location, and stage have been reported to have no relationship with the survival of brain tumor patients 1 year after undergoing surgical procedures. It can probably be explained because the surgical procedures performed have considered various aspects of each patient. The decision on the type of surgery performed depends on case-by-case conditions (Pace et al., 2020). The medical team conducts a series of examinations to obtain accurate information about the patient's condition and the characteristics of the tumor before deciding on the most appropriate surgical procedure and the most beneficial (Kumar et al., 2022).

This study has several limitations that need to be considered. Variables such as tumor size, tumor type, comorbid conditions, type of surgical procedure, type of adjuvant therapy, molecular data, and lifestyle were not studied in this study. These factors may affect patient survival after undergoing surgical procedures. The retrospective cohort study design used in this study makes it very dependent on the accuracy and completeness of the data available in the medical records. It can affect the accuracy of the data analysis performed. The study population is also limited to one health service so the results obtained cannot describe a wider population. Therefore, it is hoped that these limitations can be controlled in further research. However, this study can provide important implications for improving strategies for treating brain tumor patients. Patient characteristics identified as causes of survival can be

used as a basis for clinicians to develop the most appropriate treatment strategies to improve patient prognosis.

#### 4. Conclusion

The survival of brain tumor patients after one year of undergoing surgical procedures is still quite good. The patient's chance of survival reaches 80.5%. Tumor classification has a significant relationship with the survival of brain tumor patients after 1 year of undergoing surgical procedures. Patients with secondary brain tumors have a higher risk of death compared to patients with primary brain tumors. The variables of gender, age, tumor location, and tumor stage are not related to the survival of brain tumor patients. The classification of tumors suffered by patients is an important basis for determining brain tumor treatment strategies. Identification needs to be done correctly and as early as possible so that the patient's prognosis is better. The therapeutic approach needs to consider the condition of each patient, especially in cases of secondary brain tumors.

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