



# Palliative Care in Primary and Metastatic Brain Tumors

## Primer ve Metastazik Beyin Tümörlerinde Palyatif Bakım

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### Abstract

**Introduction:** Early palliative care interventions and structured advance care planning can improve symptom control and quality of life in patients with a brain tumor. In this study, we aimed to investigate symptoms, hospital discharge conditions, and the length of stay of patients with primary and metastatic brain tumors in our palliative care center (PCC).

**Material and Method:** Ninety-one patients; who had been followed-up in the PCC with the diagnosis of a primary or metastatic brain tumor were included in this retrospective study. Demographic characteristics, Glasgow Coma Scale (GCS) scores, Karnofsky Performance Scale (KPS) scores, hospital discharge status, and symptoms of the patients included in the study were compared.

**Results:** The mean age of the patients was 60.67 years; 59.3% were male, and the mean length of hospital stay was 29.26 days. The rates of PEG, tracheostomy, seizures, and paresis symptoms were significantly higher in patients with a primary brain tumor ( $p<0.05$ ). The rates of death in the hospital were significantly higher in patients with metastatic tumors and low GCS scores ( $p=0.032$  and  $p=0.00$ , respectively).

**Conclusion:** We observed differences in clinical findings and prognoses between primary and metastatic brain tumor patients during the follow-up in PCC. Further to advances in treatment methods, we believe that identifying the need for palliative care and appropriate symptom management will improve the quality of life in brain tumor patients with poor prognosis.

**Keywords:** Brain tumors, palliative care, discharge status, seizure

### Öz

**Giriş:** Erken Palyatif bakım müdahaleleri ve yapılandırılmış ileri bakım planlaması, beyin tümörü hastalarında semptom kontrolünü ve yaşam kalitesini artırabilir. Bu çalışmada palyatif bakım merkezimizde (PBM) primer ve metastatik beyin tümörü tanısı alan hastaların semptomlarını, çıkış durumlarını ve yatış sürelerini araştırmayı amaçladık.

**Gereç ve Yöntem:** Bu retrospektif çalışmada palyatif bakım servisinde primer ve metastatik beyin tümörü tanısı ile izlenen 91 hasta alındı. Çalışmaya alınan hastaların demografik özellikleri, glaskow koma skalası (GCS), Karnofsky Performans Skalası (KPS), çıkış durumu, hastanede yatış süresi ve semptomları karşılaştırıldı.

**Bulgular:** Hastaların yaş ortalaması 60,67 yıldır, %59,3'ü erkekti ve yatış süreleri ortalama 29,26 gündü. Primer beyin tümörü olan hastalarda PEG, trakeostomi durumu ve nöbet, parezi semptomu oranları anlamlı derecede fazla idi ( $p<0,05$ ). Metastatik tümörü olanlarda ve GCS düşük olanlarda çıkış durumu exitus olanlar anlamlı derecede fazla idi ( $p=0,032$ ,  $p=0,00$ ).

**Sonuç:** Primer ve metastatik beyin tümörü olan hastaların palyatif bakımda izlemleri sırasında bulgularında ve klinik prognozlarında farklılıklar olduğu görüldü. Tedavilerdeki ilerlemelere rağmen zayıf prognoza sahip beyin tümörlerinin palyatif bakım ihtiyaçlarının belirlenip, semptomların iyi yönetilmesinin, bu hastalarda yaşam kalitesini artıracaklarını düşünüyoruz.

**Anahtar Kelimeler:** Beyin tümörleri, palyatif bakım, çıkış durumu, nöbet



## INTRODUCTION

Despite major advances in cancer therapeutics over the past decade, cancer patients continue to suffer from significant morbidity. Furthermore, mortality rates in cancer remain high.<sup>[1]</sup> Brain tumors account for nearly 1.4% of all cancers.<sup>[2]</sup> Malignant gliomas are tumors of glial origin, accounting for almost 70% of primary brain cancer diagnoses. Survival in malignant gliomas is less than two years.<sup>[3,4]</sup> Cranial metastases are more common than primary brain tumors. Secondary brain tumors develop in 20-40% of systemic malignancies at a point in time during the disease course.<sup>[5]</sup> With a mean survival of 1-6 months depending on the histology and the treatment applied, brain metastases significantly shorten the average life expectancy.<sup>[6]</sup>

Studies have shown that early integration of palliative care acts favorably on the quality of life, survival, mood of the patient, caregiver burden, and treatment.<sup>[7]</sup> The life-limiting nature of gliomas and secondary brain tumors and the presence of specific symptoms due to neurological impairments require an early and multidisciplinary palliative care approach.<sup>[8,9]</sup> Studies investigating whether differences exist in the palliative care needs of such patients are scarce and patients need to be evaluated more thoroughly in order for their specific needs to be addressed.<sup>[10]</sup>

In this study, we aimed to investigate the rates of percutaneous endoscopic gastrostomy (PEG), tracheostomy, pressure ulcers (PU); Glasgow Coma Scale (GCS) and Karnofsky Performance Scale (KPS) scores, and the effects of symptoms such as seizures, paresis, pain, and depression on the length of hospital stay (LOS) and discharge statuses in patients diagnosed with primary or metastatic brain tumors, who had been under follow-up in our palliative care center (PCC).

## MATERIAL AND METHOD

This retrospective study was approved by the Ethics Committee of Dışkapı Yıldırım Beyazıt Training and Research Hospital (date: 06/04/2020; approval no: 85/03). All procedures were carried out in accordance with the principles of the Declaration of Helsinki. The files of 99 patients followed-up in our hospital's PCC with the diagnosis of a primary or metastatic brain tumor in the period between 1 January 2014 and 1 January 2020 were reviewed retrospectively. Eight patients; who had missing data in patient files and who had been hospitalized for one day or shorter, were excluded from the study. The symptoms observed in the patients were classified as pain, paresis, seizures, and depression. The ages and gender of the study patients; the presence of percutaneous endoscopic gastrostomy (PEG), tracheostomies, and pressure ulcers (PU); LOS in the hospital, the patient status at the time of hospital discharge [to home or to the intensive care unit (ICU) or the patient's death in the hospital], and symptoms (seizure, paresis, pain, and depression) of the patients included in the study were compared.

The diagnosis of depression was made by a psychiatrist according to the criteria of the classification of psychiatric disorders, the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).<sup>[11]</sup> The severity of pain was evaluated using the Visual Analogue Scale (VAS).<sup>[12]</sup> VAS is a continuous scale comprising a horizontal or a vertical line, usually 10 centimeters (100 mm) in length. Patients with a VAS score between 0 and 2 cm were considered pain-free.<sup>[13]</sup>

GCS was used for neurological evaluation and determining the consciousness level of the patient. GCS is evaluated according to the verbal response, motor response, and the eye-opening reaction of the patient. A calculated total score of 15 indicates the best response, whereas a score of 3 indicates the poorest response that can be obtained from the patient.<sup>[14]</sup> The Karnofsky performance scale was used to rate functional impairment in the study patients.<sup>[15,16]</sup> The Karnofsky performance scale scores range from 0 to 100. A score between 80 and 100 indicates that the patient is able to carry on normal activities; a score between 50 and 70 indicates that the patient is unable to work but can meet most of the personal needs, and a score between 0 and 40 indicates that the patient is unable to carry on self-care.

## Statistical Analysis

The study data were transferred to the SPSS Statistics 23 package program to perform the statistical analyses. Data were summarized as frequencies (numbers and percentages) for the categorical variables. Descriptive statistics (mean, standard deviation, median, minimum, and maximum) were used for the numerical variables. The Kolmogorov-Smirnov normality analysis revealed that the numerical variables did not conform to a normal distribution. For this reason, non-parametric statistical methods were used in the study. The differences between two independent groups were assessed by the Mann-Whitney U analysis. The Kruskal-Wallis analysis was used to evaluate the differences between more than two independent groups. The relationships between two independent categorical variables were assessed using the Chi-Square analysis. The relationships between two independent numerical variables were interpreted using Spearman's rho correlation coefficient. A value of 0.05 was considered to indicate statistical significance.

## RESULTS

Eight patients; who had incomplete records and who had been hospitalized for one day or for a shorter period, were excluded from the study. A total of 91 patients; of which 37 (40.7%) were women and 54 (59.3%) were men, were included in the study. The mean age of the patients was 60.67 years and the mean LOS was 29.26 days. Of the patients; 69.2% had a primary brain tumor, 30.8% had a metastatic brain tumor, 56% had a PEG, 46.2% had a tracheostomy, and 51.6% had PU. Death occurred in 51.6% of the patients; 30.8% of the patients were discharged to home, and 17.6% of the patients were transferred to ICU. Seizures, paresis, pain, and depression

were found in 80.2%, 78%, 64.8%, and 34.1% of the patients, respectively. The mean GCS score of the patients was 8. The mean KPS score was 10-40 points in 82 (90.1%) patients and 50-70 points in 9 (9.9%) patients (**Table 1**).

Having a primary or metastatic brain tumor was statistically significantly associated with age, the presence of a PEG, tracheostomy, or PU; and the presence of paresis or seizure symptoms ( $p < 0.05$ ). The age of the patients with a metastatic brain tumor was significantly higher compared to primary brain tumor patients ( $p = 0.001$ ). The rates of having a PEG, tracheostomy, and PU, and having paresis or seizures were significantly higher in primary brain tumor patients compared to metastatic brain tumor patients (**Table 2**).

**Table 1.** Demographic characteristics of patients

(n=91)	Mean±standard deviation	Median (Min.-Max.)
Age (Year)	60.67±13.528	60.0 (36.0-98.0)
Length of Stay (Days)	29.26±25.870	22.0 (6.0-180.0)
GCS	7.69±1.787	8.0 (4.0-12.0)
	Number	%
Gender		
Female	37	40.7
Male	54	59.3
PEG		
Yes	51	56.0
No	40	44.0
Tracheostomy		
Yes	42	46.2
No	49	53.8
PU		
Yes	47	51.6
No	44	48.4
Discharge Status		
Home	28	30.8
Exitus	47	51.6
ICU	16	17.6
Pain		
Yes	59	64.8
No	32	35.2
Paresis		
Yes	71	78.0
No	20	22.0
Seizure		
Yes	73	80.2
No	18	19.8
Depression		
Yes	31	34.1
No	60	65.9
Tumor		
Primary	63	69.2
Metastatic	28	30.8
KPS		
10-40	82	90.1
50-70	9	9.9

ICU: Intensive care unit, PEG: Percutaneous endoscopic gastrostomy, PU: Pressure ulcers, GCS: Glasgow Coma Scale, KPS: Karnofsky Performance Scale

**Table 2.** Examination of the relationship between tumors and variables

	Primary Tumor		Metastatic Tumor		Z	p
	Median (Min.-Max.)	Median (Min.-Max.)	Median (Min.-Max.)	Median (Min.-Max.)		
Age (Year)	55 (36-88)	68 (39-98)			-3.429	0.001*
GCS	8 (4-12)	7 (5-11)			-1.442	0.149
	Number	%	Number	%	X2	p
Gender						
Female	24	64.9	13	35.1	0.558	0.455
Male	39	72.2	15	27.8		
PEG						
Yes	43	84.3	8	15.7	12.391	0.000*
No	20	50.0	20	50.0		
Tracheostomy						
Yes	35	83.3	7	16.7	7.282	0.007*
No	28	57.1	21	42.9		
PU						
Yes	41	87.2	6	12.8	14.790	0.000*
No	22	50.0	22	50.0		
Pain						
Yes	40	67.8	19	32.2	0.162	0.687
No	23	71.9	9	28.1		
Paresis						
Yes	59	83.1	12	16.9	29.166	0.000*
No	4	20.0	16	80.0		
Seizure						
Yes	59	80.8	14	19.2	23.277	0.000*
No	4	22.2	14	77.8		
Depression						
Yes	18	58.1	13	41.9	2.752	0.097
No	45	75.0	15	25.0		
KPS						
10-40	55	67.1	27	32.9	1.812	0.178
50-70	8	88.9	1	11.1		

Z: Mann Whitney U X2: Chi-Square Analysis \*;  $p < 0.05$ . PEG: Percutaneous endoscopic gastrostomy, PU: Pressure ulcers, GCS: Glasgow Coma Scale, KPS: Karnofsky Performance Scale

LOS was statistically significantly associated with the presence of a PEG, tracheostomy, or PU; the PCC discharge status and the presence of paresis or seizures ( $p < 0.05$ ). LOS was significantly longer in patients without a PEG, tracheostomy, or PU. LOS was significantly long in metastatic tumor patients and in patients having no seizures. LOS was significantly higher in patients; who had died in the hospital, compared to patients discharged to home ( $p = 0.039$ ). A negative and low-level statistically significant relationship was found between age and LOS (**Table 3**).

The hospital discharge status was statistically significantly associated with the presence of primary or metastatic brain tumors and GCS scores ( $p < 0.05$ ). While significantly more patients with primary brain tumors were discharged to home, the mortality rate was significantly higher in patients with metastatic brain tumors. The mortality rate was significantly high in patients with low GCS scores (**Table 4**).

**Table 3.** Examination of the relationship between the length of stay and variables

	Length of hospitalization		Statistical Analysis	P
	Number	Median (Min.-Max.)		
Gender				
Female	37	58 (36-90)	Z=-1.093	0.274
Male	54	60 (43-98)		
PEG				
Yes	51	55 (36-98)	Z=-2.216	0.027*
No	40	63,5 (44-88)		
Tracheostomy				
Yes	42	53,5 (36-75)	Z=-2.980	0.003*
No	49	61 (36-98)		
PU				
Yes	47	60 (36-98)	Z=-2.021	0.043*
No	44	59 (36-90)		
Discharge Status				
1.Home	28	53 (36-88)	KW=6.484	0.039* Difference: EX-Home
2.Exitus	47	63 (36-98)		
3. ICU	16	55 (44-87)		
Pain				
Yes	59	57 (36-98)	Z=-1.129	0.259
No	32	63 (39-87)		
Paresis				
Yes	71	59 (36-98)	Z=-0.634	0,526
No	20	62,5 (36-87)		
Seizure				
Yes	73	55 (36-98)	Z=-2.621	0.009*
No	18	64 (36-90)		
Depression				
Yes	31	60 (36-98)	Z=-0.206	0.837
No	60	59,5 (36-90)		
Tumor				
Primary	63	55 (36-88)	Z=-2.081	0.037*
Metastatic	28	68 (39-98)		
KPS				
10-40	82	21.5 (6-180)	Z=-0.726	0.468
50-70	9	24 (10-56)		
	<b>Number</b>	<b>r</b>	<b>p</b>	
Age	91	-0.231	0.028*	
GCS	91	0.131	0.215	

Z: Mann Whitney U KW: Kruskal Wallis \*: p<0.05 r: Spearman's Rho Correlation Coefficient.  
PEG: Percutaneous endoscopic gastrostomy, PU: Pressure ulcers, GCS: Glasgow Coma Scale, KPS: Karnofsky Performance Scale

## DISCUSSION

The life-limiting nature of primary brain tumors and the presence of specific symptoms due to neurological impairment require an early and appropriate palliative care approach.<sup>[17]</sup> Brain metastases are the most common cerebral malignancies, in which most of the symptoms occur due to direct brain compression caused by the tumor or edema. Palliative care has an essential role in approaching patients with brain metastasis and managing their symptoms.<sup>[9]</sup> Of the patients followed-up in our palliative care center; 69.2% had been diagnosed with primary brain tumors and 30.8% had

been diagnosed with metastatic brain tumors. The mean age of the patients was 60.67 years; 59.3% of the patients were men, and the mean LOS was 29.26 days.

Studies have documented the potential value of PEG tube placement in patients with nutritional and swallowing problems such as those with head and neck cancer. In patients with cancer, enteral tube feeding is often required due to dysphagia, odynophagia, side effects during or after treatment, dehydration, and weight loss.<sup>[18]</sup> There is very little research on PEG placement in patients with brain tumors receiving palliative care.<sup>[19]</sup> The use of tracheostomy during the palliative care process in cancer patients aims to relieve symptoms, provide comfort, facilitate daily life activities, and achieve long-term optimization survival period.<sup>[20]</sup> In our study, the rates of tracheostomy (83.3%) and PEG (84.3%) were significantly high in patients with primary brain tumors. We thought that such high rates of tracheostomy and PEG could be explained by the longer-term survival of primary brain tumor patients compared to patients with metastatic brain tumors. The study by Jakobsen et al.<sup>[21]</sup> demonstrated that advanced age, proximity to death, long hospital stays, and a poor clinical condition increased the risk of PU development. In our study, PU was significantly more common in patients diagnosed with primary brain tumors compared to patients with metastatic brain tumors. We thought that this finding could result from the high rate of paresis, higher rates of discharge to home despite a longer hospital stay, and the longer survival of patients with primary brain tumors compared to metastatic tumor patients.

The clinical findings of brain tumors depend on the location, histological type, and size of the tumor. Typical symptoms include increased intracranial pressure and focal neurological findings. Seizures are frequent complications occurring in 70% of primary brain tumor patients and in 40% of patients with brain metastases.<sup>[22]</sup> Consistent with our study, Ostgathe et al.<sup>[23]</sup> found out that the symptoms of paresis and seizures were more frequent in primary brain tumors than metastatic brain tumors. It is estimated that 50% of patients with brain tumors have depressive symptoms.<sup>[24]</sup> In our study, we identified depression in 34.1% and pain in 64.8% of the palliative care patients with primary or metastatic brain tumors; however, we did not detect a statistically significant difference between the two groups.

It has been demonstrated in the literature that the mortality rate is higher in metastatic brain tumor patients compared to patients with primary brain tumors and other palliative care patients.<sup>[23]</sup> The prognosis of metastatic brain tumors is poor and the average survival is 6-12 months.<sup>[25]</sup> Similarly, the mortality rate was significantly high and the length of hospital stay was long in metastatic brain tumor patients in our study. We think that the poor clinical condition of these patients prolonged their stay in palliative care. It has been previously shown that low GCS scores are associated with a long LOS and a close proximity to death in serious diseases and injuries.<sup>[26]</sup>

**Table 4.** Examination of the relationship between discharge condition and variables

	Discharge Status						K.W.	p
	1.Home		2.EX		3. ICU			
	Median (Min.-Max.)		Median (Min.-Max.)		Median (Min.-Max.)			
Age (Year)	53 (36-88)		63 (36-98)		55 (44-87)		4.205	0.122
GCS	9 (6-12)		7 (4-10)		8 (7-11)		30.124	0.000* Difference: 2-1,3
	Number	%	Number	%	Number	%	X2	p
Gender								
Female	15	40.5	17	45.9	5	13.5	2.914	0.233
Male	13	24.1	30	55.6	11	20.4		
PEG								
Yes	18	35.3	22	43.1	11	21.6	3.448	0.178
No	10	25.0	25	62.5	5	12.5		
Tracheostomy								
Yes	18	42.9	18	42.9	6	14.3	5.353	0.069
No	10	20.4	29	59.2	10	20.4		
PU								
Yes	14	29.8	25	53.2	8	17.0	0.093	0.955
No	14	31.8	22	50.0	8	18.2		
Pain								
Yes	14	23.7	33	55.9	12	20.3	4.024	0.134
No	14	43.8	14	43.8	4	12.5		
Paresis								
Yes	21	29.6	37	52.1	13	18.3	0.260	0.878
No	7	35.0	10	50.0	3	15.0		
Seizure								
Yes	26	35.6	34	46.6	13	17.8	4.668	0.097
No	2	11.1	13	72.2	3	16.7		
Depression								
Yes	11	35.5	18	58.1	2	6.5	4.027	0.133
No	17	28.3	29	48.3	14	23.3		
Tumor								
Primary	24	38.1a	27	42.9a	12	19.0a	6.885	0.032*
Metastatic	4	14.3b	20	71.4b	4	14.3a		
KPS								
10-40	19	23.2	47	57.3	16	19.5	-	-
50-70	9	100.0	0	0.0	0	0.0		

K.W.: Kruskal Wallis X2: Chi-Square Analysis \*: p<0.05. PEG: Percutaneous endoscopic gastrostomy, PU: Pressure ulcers, GCS: Glasgow Coma Scale, KPS: Karnofsky Performance Scale

In our study, we found that the mortality rate was significantly high in patients with low GCS. Although studies have shown that performance status is an independent predictor of survival in patients with cancer, no significant relationship was found between KPS and LOS or discharge status in our study. [27]

Our study had limitations such as the small number of patients and the lack of a control group.

## CONCLUSION

In our study, we observed that there were differences in the findings and clinical prognoses in patients with primary and secondary brain tumors during the follow-up in palliative care. In patients with primary brain tumors, the rates of having a PEG, a tracheostomy, seizures, and paresis symptoms were

significantly high. While mortality was significantly high in patients with metastatic tumors and low GCS scores, the rate of "discharged to home" status was significantly high in patients with primary brain tumors. Further to advances in treatment, we are of the opinion that identifying palliative care needs and providing appropriate symptom management will improve the quality of life in brain tumor patients with poor prognosis.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee (Date: 06/04/2020, Decision No: 85/03).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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