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Original Article

The Prognostic Values of Graded Prognostic Assessment (GPA) Index In Advanced Stage NSCLC Patients With Brain Metastasis

Beyin Metastazlı İleri Evre KHDAK Hastalarında GPA İndeksinin Prognostik Değeri

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ABSTRACT

Aim: Graded Prognostic Assessment (GPA) is a new prognostic index for patients with brain metastases. Brain metastasis is a common site of metastasis in lung cancers. Lung cancer-specific GPA scoring system is used. We aimed to assess the prognostic and predictive significance of Graded Prognostic Assessment (GPA) score in non small-cell lung cancer patients with brain metastasis.

Material and Methods: This study was designed as a hospital-based retrospective observational case-series study. A total of 95 patients with brain metastatic NSCLC patients who were followed in two different oncology centers in Turkey between 2015 and 2021 have been included into this study. They were divided into 3 groups according to their GPA scores.

Results: The median age of the patients was 62 (range 44-89) years The patients were divided into 3 groups according to their GPA scores. 24 (25.2 %) patients had ''0-1'' GPA score, 54 (56,8 %) patients had ''1,5-2'' GPA score and 17 (18 %) patients had ''2,5-3'' GPA score. The median follow-up time was 11 months and 89 (93.7%) patients died during follow-up. Overall survival (OS) was 8 months. Patients in the low (0-1) GPA scores had worst overall survival than those with higher GPA scores (4.7, 12.6 and 18.5 months respectively and p=0,001).

Conclusion: In this study, we have shown that GPA score is useful in evaluating the prognosis of NSCLC patients with brain metastasis..

Keywords: GPA, Lung Cancer, Brain Metastasis

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Öz

Amaç: Derecelendirilmiş Prognostik Değerlendirme (GPA), beyin metastazı olan hastalar için yeni bir prognostik indekstir. Beyin metastazı, akciğer kanserlerinde sık görülen bir metastaz bölgesidir. Akciğer kanserine özgü GPA skorlama sistemi kullanılmaktadır. Beyin metastazı olan küçük hücreli dışı akciğer kanseri hastalarında Kademeli Prognostik Değerlendirme (GPA) skorunun prognostik ve prediktif önemini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu çalışma, hastane tabanlı retrospektif gözlemsel vaka serisi çalışması olarak tasarlandı.Bu çalışmaya 2015-2021 yılları arasında Türkiye'de iki farklı onkoloji merkezinde izlenen beyin metastatik KHDAK'li toplam 95 hasta dahil edildi. GPA puanlarına göre3grubaayrıldılar.

Bulgular: Hastaların ortanca yaşı 62 (44-89) idi. Hastalar GPA'larına göre 3 gruba ayrıldı. 24 (%25,2) hastanın GPA'sı "0-1", 54 (%56,8) hastanın GPA 'sı "1,5-2" ve 17 (%18) hastanın GPA skoru "2,5'-3" arsasındaydı. Medyan takip süresi 11 aydı ve takipte 89 (%93,7) hasta öldü. Genel sağkalım (OS) 8 aydı. Düşük (0-1) GPA skorlarındaki hastalar, daha yüksek GPA skorlarına sahip olanlara göre en kötü genel sağ kalıma sahipti (sırasıyla 4.7, 12.6 ve 18.5 ay vep=0,001).

Sonuç: Bu çalışmada beyin metastazı olan KHDAK hastalarının prognozunu değerlendirmede GPA skorunun yararlı olduğunu gösterdik.

Anahtar Kelimeler: GPAİ, Akciğer Kanseri, Beyin metastazı

Introduction

Lung cancer is the most common type of lung cancer and leading cause of cancer death worldwide [1-3]. At the time of diagnosis, approximately 50% of patients are in the metastatic stage. Metastasis to the brain is one of the most common and serious complications of this disease [4,5]. According to conservative estimates, 10% to 30% of lung cancer patients will develop brain metastases. Previously, survival after the development of brain metastases was poor and patıents wıth braın metastas represent a hıghly heterogenıc group. Prognostic scoring systems are used for patients with brain metastases. These scoring systems can be used to identify patients who are candidates for current treatments as well as predict prognostic grouping and expected survival times.

In 1997 Gaspar at al demonstrated for the first time a scoring system for patients with brain metastases [6]. A newer prognostic index for patients with brain metastases is the Graded Prognostic Assessment (GPA) [7]. This prognostic index was originally developed from a database of study patients with different tumor types with brain metastases [8,9]. The original GPA was validated and refined with diagnosis-specific prognostic indices [10]. A series of GPA studies have revealed that survival and the factors that predict survival differ greatly depending on the diagnosis. Age, KPS, extracranial metastases, and the number of brain metastases were significant prognostic factors for survival in lung cancer with brain metastases. The aim of this study was to evaluate the prognostic and predictive importance of GPA scores in non small cell lung cancer patients with brain metastases.

Material and Methods

This study was designed as a hospital-based retrospective observational case-series study. Total of 95 patients were included into the study from Radiation Oncology Departments of Okmeydani Research and Training Hospital and Dr. Ersin Arslan Research and Training Hospital between the years of 2015 and 2021. Non small cell lung cancer patients with brain metastasis were included to the study. Demographic features and treatment modalities were recorded from patient electronic files. Variables considered included the 4 used by the existing DS-GPA (patient age, KPS, extracranial metastases, and the number of brain metastases) and was shown in table-1.

Table 1. GPA Scoring Criteria

Prognostic Factor	0 Point	0.5 Point	1 Point
Age, y	≥70	<70	NA
KPS	<70	80	90-100
ECM	Present		Absent
Brain metastases, No	>4	1-4	NA

Abbreviations
KPS: Karnofsky Performance Status
ECM: Extracranial metastasis

Statistical Analysis

All results were presented as the rate for categorical values or mean and median for continuous variables. Clinical and statistical significant correlation between continuous

variables was calculated by Spearman's rank correlation test, rs (spearman's correlation coefficient) and p value (2-tailed) were noted. Overall survival (OS) was defined as the time from diagnosis time to the date of death. Survival curves were estimated according to the Kaplan-Meier method, and log-rank tests were used for univariate statistical comparisons. Adjusted Hazard Ratio (HR) and 95% confidence interval (95% CIs) were used for estimation. All statistical data were analyzed using the SPSS version 17.0, and a p value of <0.05 was considered statistically significant.

Results

The median age of the patients was 62 (range 44-89) years and 74 (77.9%) patients were male. All of the patients (n: 95) had brain metastasis. Majority of patients had Karnofsky Performance Status 80 and 90 (n=44, 46,3% and n=35, 36,8 % respectively). 55 (57.9 %) patients had extracranial metastasis. While 60 (63,2 %) patients had a single brain metastasis, 35 (36,8 %) patients had more than 1 brain metastasis. The patients were divided into 3 groups according to their GPA scores. 24 (25.2 %) patients had "0-1" GPA score, 54 (56,8 %) patients had "1,5-2" GPA score and 17 (18 %) patients had "2,5-3" GPA score. Patient characteristics and GPA scores are shown in table 2.

Table 2. Patient characteristics and GPA Scores

Characteristics	N %
Median age	62 (44-89) years old
Gender	
Men	74 (77.9)
Women	21 (22.1)
KPS	
60	4 (4.2)
70	12 (12.6)
80	44 (46.3)
90	35 (36.8)
Cranium Metastasis Count	
Single Lesion	60 (63.2)
>1	35 (36.8)
Extracranial Metastases	
Yes	55 (57.9)
No	40 (42.
Bone Metastases	
Yes	74 (59.2)
No	51 (40.1)
GPA Score	
0-1	24 (25.2)
1,5-2	54 (56,8)
2,5-3	17 (18)
Final Status	
Alive	6 (6.3)
Exitus	89 (93.7)

The median follow-up time was 11 months and 89 (93.7%) patients died during follow-up. Overall survival (OS) was 8 months (Figure 1). Patients in the low (0-1) GPA scores had worst overall survival than those with higher GPA scores (4.7, 12.6 and 18.5 months respectively and p=0,001). Survival rates by the 3 prognostic classes are detailed in Table 3 and illustrated in the Figure-2

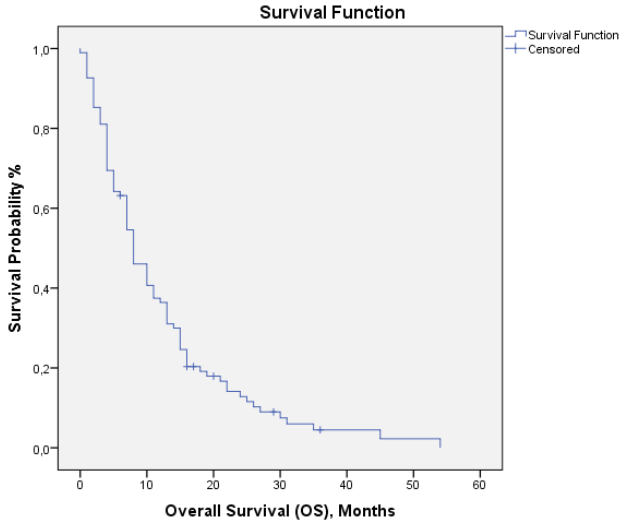

Figure 1.

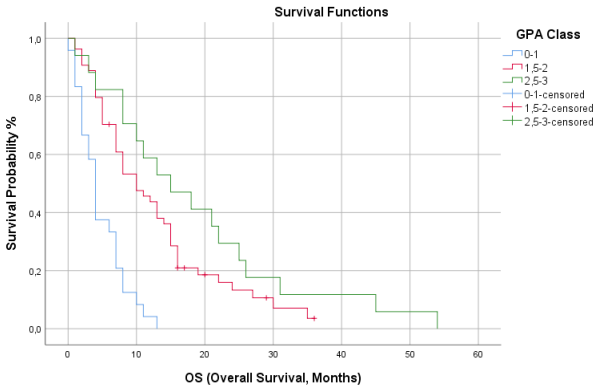

Figure 2

Table 3. Relationship between GPA Scores with Overall Survival

GPA Scores	Median OS	
	Months	p
0-1 (Low)	4	0,001a
1,5-2 (Intermediate)	10	0,001a
2,5-3 (High)	15	0,001a

Abbreviations
a Statistically Significant
GPA : Graded Prognostic Assessment
OS Overall Survival

Discussion

In this study, the GPA scores of 95 NSCLC patients with brain metastasis were analyzed retrospectively. The results showed that the GPA score was an independent prognostic factor in these patients. In our study, we showed that patients with low GPA scores had worse prognosis.

During the past 25 years, multiple prognostic models have been developed. The Radiation Therapy Oncology Group's (RTOG) Recursive Partitioning Analysis (RPA) was first used in 1997 by Gaspar et al in their foundational study on a prognostic index for patients with brain metastases [6]. In this trial, They established 3 distinct prognostic classes based on Karnofsky Performance Status, age, and control of primary and metastatic disease. Sperduto et al. devised the GPA in 2008, using data from 1960 participants in 5 phase 3 Radiation Therapy Oncology Group trials [7]. The GPA index also took into account the number of brain metastases (BM) in addition to the first three RPA criteria. Based on a second, independent, multi-institutional retrospective analysis of 4,259 additional patients with brain metastases from breast carcinoma, small-cell and non-small-cell lung carcinoma, GI cancers, melanoma, and renal cell carcinoma, the original GPA was validated and improved with diagnosis-specific prognostic indices [11,12].The diagnosis specific GPA, a later iteration released in 2012, maintained the 4-point scoring system but added sophistication and placed more attention on the primary location of origin and related criteria [13]. There were identified four illness classes, and the median survival time ranged from 3.0 to 14.8 months.

This was revised in 2017 to include molecular profiling for NSCLC, further highlighting the biologic heterogeneity of NSCLC BM [14]. The inclusion of the lung GPA based on contemporary molecular profile would be very helpful in the initial patient evaluations and aid in the creation of fresh paradigms for the choice and administration of therapeutic modalities. We also determined the prognostic importance of the GPA index in our study. however, performing these analyzes with molecular subtyping will provide a better separation of prognostic groups.

The our study has some considerable limitations. First, as with any retrospective study, unpredictable biases may have influenced our results and the number of patients was low. Second, no evaluation was made according to molecular subtypes in our study.

In conclusion, the results of our study showed that GPA score is useful and cost-effective prognostic marker in evaluating the prognosis of NSCLC patients with brain metastasis and should therefore be included in routine clinical practice for these patients.

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