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Physician-reported ECOG-PS versus patient-reported (self) ECOG-PS: Which one is a better predictor of survival in cancer?

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Abstract

The aim of this study is to determine the discrepancy and agreement between Eastern Cooperative Oncology Group Performance Status (ECOG-PS) scores evaluated by doctors and patients and examine the factors that influence the performance evaluation of doctors and patients. This study is a prospective and descriptive case-control study. General, demographic, and oncologic data of the patients were collected. e-control study. General, demographic, and oncologic data of the patients were collected. Patient-Reported Outcomes Measurement Information System (PROMIS) anxiety and depression surveys were conducted to determine patients' levels of anxiety and depression, and at the same time, both the doctors and the patients were asked to determine their performance status. As a result, the discrepancy in performance evaluation between the patient and the doctor, the factors affecting this discrepancy, and its effect on progression and survival were examined. 277 patients were included. 146 (52.7%) were male, and 131 (47.3%) were female. The most common cancers were breast cancer (17.7%, n=49) and lung cancer (17.3%, n=48). It was found that the doctors' assessment of patient performance increased the progression risk by 3.1 times (HR: 3.080, 95% CI: 1,671-5,675) in ECOG-PS 2 compared to ECOG-PS 0 and by 5 times (HR: 4.980, 95% CI 1.405-17.646) in ECOG-PS 3 compared to ECOG-PS 0. Our study determined a weak agreement between the doctor and patient in terms of performance assessment. The most significant reason for this discrepancy was found to be due to the levels of depression or anxiety in patients. In conclusion, it was demonstrated that the performance evaluations determined by doctors are more accurate and meaningful in terms of progression and survival results compared to those determined by patients.

Key words: Self-ECOG-PS, PROMIS anxiety, PROMIS depression, Charlson comorbidity index, Hollingshead index

Introduction

Numerous scales have been developed to measure the performance status (PS) of cancer patients, among which the most frequently used are the Karnofsky Performance Score (KPS) published in 1948 [1] and the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) defined in 1982 [2]. When evaluated by researchers, it has been found that ECOG-PS and KPS scores are strongly correlated with each other [3]. ECOG-PS provides general information about a patient's level of function in personal care, daily activity, and physical activity. This scale, frequently used both in clinical practice and scientific studies, is designed and approved for use by doctors. It has been demonstrated many times that this highly useful scale predicts significant clinical outcomes in cancer patients, including quality of life and PS, chemotherapy toxicity, response to chemotherapy, Progression-Free Survival (PFS), and Overall Survival (OS) [4-6]. Symptoms related to cancer can be associated with the disease and/or treatment and

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are a multidimensional phenomenon composed of physiological, sensory, emotional, cognitive, and behavioral components [7]. It has been shown that the PS graded by researchers is significantly associated with patient-reported outcomes that describe patients' subjective symptomatic experiences such as physical function, anxiety, depression, fatigue, sleep disorders, and pain in most studies [8]. Some studies in the literature assessing patients' own PS show intriguing results about the effect of the distinction in performance assessment between doctors and patients on survival outcomes. In a prospective study involving 1115 patients with solid cancer conducted by Loprinzi and colleagues, they found that the PS evaluated by the patient independently predicted mortality powerfully than the PS evaluated by the doctor [9]. In another study, it was found that discrepancies between doctors' and patients' assessments in ECOG PS increased the risk of death [10].

To re-emphasize the importance of this assessment, a correct performance evaluation in oncology practice ensures proper management of the disease. ECOG-PS is a crucial measure for prognosis, treatment toxicity, and decisions such as palliative care. However, the differences in the PS evaluations by the doctor and the patient, the characteristics of the patient and the doctor that might influence this, and whether these differences are effective in predicting significant clinical outcomes remain uncertain. In our study, we aimed to investigate whether the difference between doctors' patient performance assessments and the patients' self-assessments, and concurrently evaluated self ECOG and anxiety-depression scale results, would affect treatment and side effect management.

The aim of this study is to determine the difference and alignment between ECOG-PS scores evaluated by doctors and patients in our clinic with a high patient density, and to examine the factors affecting doctor and patient performance evaluation alongside this. In addition, it aims to determine the effect of this agreement or discrepancy on survival and treatment response situations, and to examine the relationships between survival results and patient-doctor ECOG-PS assessment through scores and indices calculated based on prognostic laboratory parameters.

Material and Methods

This study is a prospective and descriptive case-control study. Between the dates of 15.02.2022 and 02.06.2022, adult oncology patients undergoing active oncological treatment and who consented to participate in the study were included. Demographic and oncological information was noted from the answers to the survey questions posed to the patients, oncology archive records, and data obtained from the hospital automation system. For this purpose, patients' age, gender, marital status, smoking and alcohol use, family cancer histories, oncological diagnoses, diagnosis dates, comorbidities, and general oncological information, as well as their education status, professions, places of birth, places of residence, and the duration of their residence at these places were noted. In addition, hemoglobin, albumin, neutrophil, lymphocyte, platelet, C-reactive protein (CRP), and lactate dehydrogenase (LDH) values, which were checked at the time of diagnosis, were also noted.

From these demographic details, patients were grouped according to their places of birth, places of residence, educational statuses, occupational statuses, and comorbidities. Accordingly, based on the characteristics of the places they were born and lived, patients were divided into four separate groups; city, district, town, and village. In terms of geographical regions, they were grouped into seven regions; Marmara, Aegean, Black Sea, Central Anatolia, Mediterranean, Eastern Anatolia, and Southeastern Anatolia. As most of the patients lived in the province of Antalya, those residing in Antalya were grouped separately by districts, and patients living in the center of Antalya were further grouped according to the districts in the city center. The duration of living in their current residence was divided into five groups: 0-1 year, 2-5 years, 6-10 years, 11-20 years, and over 20 years. Apart from this, education status was divided into six groups; being illiterate, primary school graduate, middle school graduate, high school graduate, university graduate, and postgraduate. Lastly, occupational groups were divided into nine separate groups; unemployed, Farmer/Fisherman, Cleaning Staff/Janitor/Tea Maker/Driver, Clerk/Secretary/Office Worker, Worker/Motor Mechanic/Technician, Nurse/Health Officer, Tradesman/Business Owner, Teacher/Police/Soldier, and Lawyer/Engineer/Doctor.

Using these data, the patients were grouped according to their marital status, whether they were employed or not, their educational status, and occupation. These groups were then scored and divided into four groups in accordance with the Four-Factor Index of Social Status by Hollingshead. The Four-Factor Index of Social Status by Hollingshead is a survey designed to measure an individual's social status based on four domains: marital status, retirement/employment status, level of education, and occupational status. While marital and employment status are grouped as yes/no, education status is graded on a seven-point scale, and occupational status on a nine-point scale. Education status is grouped as follows: 7=postgraduate, 6=university graduate, 5=partial college, at least one year of vocational specialty training, 4=high school graduate, 3=partial high school-unfinished, 2=middle school, 1=elementary school or incomplete middle school, 0=no education or unknown. Occupational status is evaluated on a nine-point scale, which provides a more detailed list. The grouping of people by profession is as follows: 9=high-level executives, owners of large businesses (>250.000 Turkish Liras), large professionals, 8=managers, less professional, owner of a medium-sized business (50.000-250.000 Turkish Liras), 7=small business owners (20.000-50.000 Turkish Liras), farm owners, managers, small professionals, 6=technicians, semi-professionals, owners of smaller businesses (business value 5.000-20.000 Turkish Liras), 5=office and sales workers, small farm and business owners (business value 2.000-5.000 Turkish Liras), 4=owners of even smaller businesses (<2.000 Turkish

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Liras), skilled manual workers, craftsmen, tenant farmers, 3=machine operators and semi-skilled workers, 2=unskilled workers, 1=farm workers, small service workers, students, housewives, (dependent on welfare, no regular profession), 0=unemployed or unknown [11]. In this way, the total social status score can be calculated. The compatibility of our patients with the occupational classification was determined according to the grouping defined in a more detailed and longer list under the HI, and after scoring, their socioeconomic status (SES) was divided into four different score groups.

The comorbidity status was classified according to the Charlson Comorbidity Index (CCI) by considering the presence of diabetes, history of coronary artery disease, reduced ejection fraction, history of cerebrovascular event and transient ischemic attack, history of lung disease, chronic kidney disease, peripheral arterial disease, history of peptic ulcer, dementia, liver disease, and hemiplegia. The CCI, developed in 1987, has become a widely used index and is often considered the gold standard for assessing comorbidity in clinical research [12]. The CCI was calculated as follows: Age <50 years=0 points, 50-59 years=1 point, 60-69 years=2 points, 70-79 years=3 points, ≥80 years=4 points, presence of myocardial infarction (MI) history=1 point, presence of moderate to severe (Severe=in dialysis, post-kidney transplant status, uremia, moderate=creatinine >3 mg/dl) chronic kidney disease=2 points, presence of solid tumor local=2 points if metastatic=6 points, presence of AIDS=6 points. Each patient's CCI score was calculated accordingly.

In our study, as stated above, the Systemic Immune-Inflammation Index (SII) and Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) scores were calculated from the laboratory results recorded at the time of diagnosis, which are among the calculated inflammatory and prognostic indices. The HALP score was first used by Chen et al. and has been shown as a prognostic index [13]. The SII score was first proposed by Hu and colleagues in 2014 to predict the prognosis of patients with hepatocellular carcinoma who underwent surgical resection [14]. The calculation of these scores: SII=platelet count×neutrophil count/lymphocyte count, while HALP score is calculated as hemoglobin (g/L)×albumin (g/L)×lymphocyte (/L)]/platelet(/L).

Simultaneously with chemotherapy treatment, doctors and patients were asked to assess their ECOG-PS (Eastern Cooperative Oncology Group Performance Status). For both doctors and patients, the self-ECOG-PS assessment was designed to be understood by patients or their relatives as follows: 0- Fully active, able to carry on life without performance restriction just like pre-illness, 1- Unable to perform physically strenuous activities. Can walk and perform light work. (for example, light housework, office work), 2- Can walk and is capable of all types of personal care, but cannot engage in any work activity. More than 50% of awake hours can be spent standing, 3- Only has limited personal care ability, spends more than 50% of awake hours in bed or in a chair, 4- Completely disabled. Cannot perform personal care. Can only live in bed or in a chair. They were asked to mark the PS that was appropriate for them.

While the patient determined their own PS, they were also asked to answer a survey with Patient-Reported Outcomes Measurement Information System (PROMIS) depression and anxiety questions to determine their current anxiety and depression status. Patients' anxiety and depression statuses were determined based on the t-scores calculated from this survey. The PROMIS®; [15,16] has been determined for the last seven days, with the Diagnostic and Statistical Manual of Mental Disorders (DSM 5) and level 2 Turkish validated PROMIS depression and anxiety survey. The Turkish validation of the anxiety survey was performed by Aşık and colleagues [17], while the depression validation was validated by Dikici and colleagues [18].

The PROMIS depression-related questions consist of eight questions, each with five choices, while the PROMIS anxiety-related questions consist of seven questions, also with five choices each. Answers to PROMIS depression and anxiety questionnaire questions were rated on a 5-point scale ranging from 1 ("Never") to 5 ("Always"). The calculated raw scores were a minimum of seven and a maximum of 35 for the anxiety questionnaire, and a minimum of eight and a maximum of 40 for the depression questionnaire, in line with DSM 5 and Level 2 survey. If more than 75% of the questions were answered, a preliminary calculation of the raw score was made and converted in the T-score table. The formula for obtaining the total score in partial raw scores is: (Total raw score x Number of items in the short form)/Number of items answered. If the result is a fraction, it was rounded to the nearest whole number. Raw scores were calculated based on patient responses, and the corresponding T-score and Standard Error (SE) values were determined from the table. The depression and anxiety ratings based on these resulting T-scores and SE values were determined as: less than 55 points=None-mild, 55-59.9 points=Moderate, 60.0-69.9 points=Moderate-Severe, 70 and above=Severe. Additionally, the ECOG-PS results that doctors set for patients were similarly grouped from 0 to 4 and the answers were recorded. Since the number of patients at the outpatient clinic on the day the ECOG-PS was evaluated could affect the patient performance score evaluated by the doctors, this number of patients was recorded. Then these patient numbers were grouped according to increasing intensity from 1 to 5.

Finally, the impact of patient and doctor performance evaluations on survival and oncological outcomes, the relationship between laboratory results and calculated prognostic-inflammatory scores with oncological responses, and the relationship between the ECOG-PS evaluation results set by the doctor and the patient, which are the main components of the study, were statistically examined. Analyses related to the CCI score, PROMIS depression and anxiety scores, Hollingshead SES score and grouping, which may affect this, were performed.

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Statistical analysis method

SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics; numbers and percentages were used for categorical variables, while for numerical variables mean, standard deviation, minimum, maximum, median were provided. Since numerical variables do not meet the normal distribution condition, independent two-group comparisons were made with the Mann Whitney U test, and independent comparisons of more than two groups were made with the Kruskal Wallis test within groups. Subgroup analyses in more than two groups were conducted with the Mann Whitney U Test and interpreted with Bonferroni Correction. The relationships between numerical variables were analyzed by Spearman Correlation Analysis since parametric test conditions were not met. Survival rates were examined using the Kaplan Meier Analysis. Risk factors were examined with Cox Regression Analysis. The statistical alpha significance level was accepted as $p<0.05$.

Ethical approval: This study was approved by Clinical Trial Ethics Committee of Antalya Training and Research Hospital (No:4/21- Date:17.02.2022).

Results

A total of 277 patients were included in our study between February 15, 2022, and June 2, 2022. Of our patients, 146 (52.7%) were male, and 131 (47.3%) were female. The average age was determined as 60.6±8.9 (min: 29-max: 81) years. 63.1% of the patients (n=175) were over the age of 60, and 12.3% (n=35) were over the age of 70.

When marital statuses were examined, married individuals were in the first place (68.6%, n=190), while the second most common were widowed (29.3% (n=81). In terms of education level, the highest percentage was high school graduates (58.1%, n=161), and the second most common education level was university graduates (23.1%, n=63). The two most common groups in terms of occupational grouping were the patient group without a profession (22.7%, n=63) and the group of office workers/secretaries (21.3%, n=59). Smoking and alcohol usage rates were 47.7% (n=132) and 22% (n=61), respectively. In the light of this data, when scoring was done according to marital status, education level, whether working or not, and professional categorization in a way that conforms to Hollingshead's Four Factor Index of Social Status as explained in the method section above; The HI score of the patients was 26.1±15.9 (0-57). When divided into four groups from the lowest to the highest score according to the HI score, the highest number of patients was in group 1 (43.7%, n=121), while the least number of patients was in group 4 (9.4%, n=26).

In addition, the patients' demographic information was examined in terms of their places of birth and residence. These data are summarized in Table 1.

At least one comorbidity was present in 77.3% (n=214) of the patients. The most common comorbidity was hypertension (HT) (66.4%, n=184), while the second and third most common comorbidities were peptic ulcer disease (30%, n=83) and diabetes mellitus (DM) (27.1%, n=75), respectively. From this point of view, the CCI was calculated as described in the method section. According to this, the average CCI of the patients was 6.57±2.69 (min: 2-max: 13).

To evaluate whether the number of patients seen at the polyclinic on the day of the study affects the ECOG-PS determined by the doctors for the patients, the patients were divided into five groups in this regard. Accordingly, the polyclinic intensity; the first group was between 0-30 patients, the second group was between 31-60 patients, the third group was between 61-70 patients, the fourth group was between 71-80 patients, and the fifth group was the group where 81-100 patients were seen. From this perspective, the most intense polyclinic patient number group was the polyclinic where 80 to 100 patients were seen, where 15 patients (15.4%) were evaluated in terms of their performances. The majority of patients in the study were in the polyclinic where between 30 and 60 patients were seen, where there were 162 patients (58.5%).

The general information of the patients was examined from an oncological perspective. While 73.3% (n=203) of patients had no family history of cancer, 26.7% (n=74) reported a family history of cancer. There were 17 different oncological cancer diagnoses among the participants in the study. These data are summarized in Table 1.

The results of the PROMIS depression and anxiety survey conducted at the beginning of the study were evaluated. According to the score analysis based on the survey responses, the raw score of the PROMIS depression was determined to be 18.3±6.9 (8-36). When the patients were grouped according to the T-score level calculated for each patient, it was determined that there were 122 people (44.0%) with no depression or mild level, 77 people (27.8%) with moderate level, 71 people (25.6%) with a middle level, and 7 people (2.5%) with severe depression. The PROMIS anxiety raw score was determined to be 17.1±6.2 (6-34). When the patients were grouped according to the T-score level calculated for each patient, it was determined that there were 105 people (37.9%) with no anxiety or mild level, 87 people (31.4%) with a moderate level, 74 people (26.7%) with a middle level, and 11 people (4.0%) with severe anxiety. At the time of diagnosis, laboratory values and two prognostic inflammatory scores derived from these, namely the SII and HALP scores, were calculated for each patient. The laboratory parameters (average and minimum-maximum values) were; Neutrophils 4.35±0.92 (10^3xmm^3) (2.81-6.17), Lymphocytes 1.55±0.37 (10^3xmm^3) (0.98-2.55), Platelets 355.12±68.17 (10^3xmm^3) (195-564), CRP 27.17±21.23 mg/L (6-197) and LDH 260.51±50.13 U/L (152-391). The calculated average and minimum-maximum values for the SII and HALP scores were 1077.00±464.52 (292-2358) and 1.76±0.86 (0.63-5.02), respectively. In addition to this, detailed subgroup results for other oncological data and the general characteristics of the above-mentioned patients are given in Table 1.

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Table 1. Demographic information

		n	%
Gender	Female	131	47.3
	Male	146	52.7
Age Mean±SD (Min-Max)		60.6±8.9 (29-81)	
Age group	<50 years	37	13.36
	50-59 years	65	23.47
	60-69 years	140	50.54
	70-79 years	34	12.27
	≥80 years	1	0.36
Marital status	Married	190	68.6
	Single	6	2.2
	Widow	81	29.2
Education	Illiterate	3	1.1
	Primary school	20	7.2
	Secondary school	29	10.5
	High school	161	58.1
	University	64	23.1
Occupational grouping (HI).	No occupation	63	22.7
	Farmer/fisherman	25	9.0
	Housekeeper/janitor/tea seller/driver	34	12.3
	Officer/secretary desk officer	59	21.3
	Laborer/motor mechanic/technician	15	5.4
	Nurse/health officer	10	3.6
	Tradesman/business owner	25	9.0
	Teacher/police/military	27	9.7
	Lawyer/engineer/doctor	19	6.9
Occupational grouping for hollingshead	0	64	23.1
	1	32	11.6
	2	23	8.3
	3	28	10.1
	4	10	3.6
	5	54	19.5
	6	7	2.5
	7	33	11.9
	8	21	7.6
	9	5	1.8
Smoking		132	47.7
Alcohol usage		61	22.0
Hollingshead index Mean±SD (Min-Max)		26.1±15.9 (0-57)	
Hollingshead index group	1	121	43.7
	2	88	31.8
	3	42	15.2
	4	26	9.4
Place of birth	Province	48	17.3
	District	163	58.8
	Village	64	23.1
	Town	2	0.7
Region of birth	Marmara	11	4.0
	Aegean	26	9.4
	Mediterranean	123	44.4
	Central Anatolia	39	14.1
	Black Sea	15	5.4
	Eastern Anatolia	35	12.6
	Southeastern Anatolia	28	10.1

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Table 1. Demographic information

		n	%
Place of residence	Province	179	64.6
	District	68	24.5
	Village	29	10.5
	Town	1	0.4
Localization of the place of residence according to Antalya	District of Antalya to the East	46	16.6
	Neighboring Province of Antalya to the West	3	1.1
	Southeast Neighborhood of Antalya	13	4.7
	Northeast District of Antalya	3	1.1
	District of Antalya to the West	22	7.9
	District of Antalya to the North	6	2.2
	East Neighborhood of Antalya	42	15.2
	West Neighborhood of Antalya	24	8.7
	Central Neighborhood of Antalya	86	31.0
	North Neighborhood of Antalya	12	4.3
	Neighboring Province of Antalya to the North	17	6.1
	Neighboring Province of Antalya to the East	3	1.1
Length of time living in the place of residence (years)	0-1 year	36	13.0
	2-5 years	38	13.8
	6-10 years	41	14.9
	11-20 years	51	18.5
	20-81 years	110	39.9
Comorbidity	Absent	63	22.7
	Present	214	77.3
Comorbidities	HT	184	66.4
	DM uncomplicated	65	23.5
	DM with complications	10	3.6
	CAD	37	13.4
	Low EF	10	3.6
	SVO TIA	12	4.3
	Asthma/COPD	48	17.3
	CRF	22	7.9
	Autoimmune disease	7	2.5
	Peripheral vascular disease	9	3.2
	Peptic ulcer	83	30.0
	Dementia	4	1.4
	Liver disease	8	2.9
	Hemiplegia	6	2.2
Charlson Comorbidity Index Avg±SD (Min-Max)		6.57±2.69 (2-13)	
Status of solid malignancy in comorbidity index	Local/localities	156	56.3
	Metastatic	121	43.7
Family cancer history	Absent	203	73.3
	Present	74	26.7
Diagnosis group	Lung	48	17.3
	Breast	49	17.7
	GI (Gastrointestinal system)	84	30.3
	GU (Genitourinary system)	78	28.2
	Others	18	6.5
Stage at diagnosis	Stage 1	5	1.8
	Stage 2	69	24.9
	Stage 3	84	30.3
	Stage 4	119	43.0
Operation	No	135	48.7
	Yes	142	51.3

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Table 1. Demographic information

		n	%
Groups based on the time passed since included in the study	1	56	20.2
	2	2	0.7
	3	11	4.0
	4	12	4.3
	5	8	2.9
	6	26	9.4
	7	20	7.2
	8	34	12.3
	9	64	23.1
	10	44	15.9
Latest oncologic treatment	Only surgery	3	1.1
	Metastatic immunotherapy		10.5
	Metastatic hormone therapy	34	12.3
	Metastatic targeted therapy	26	9.4
	Palliative radiotherapy	4	1.4
	Induction chemotherapy	1	0.4
	Metastatic maintenance	13	4.7
	Radiotherapy	2	0.7
	Chemoradiotherapy	6	2.2
	Consolidation chemotherapy	8	2.9
	Adjuvant endocrine therapy	14	5.1
	Adjuvant chemotherapy	42	15.2
	Adjuvant targeted therapy	5	1.8
	Neoadjuvant chemotherapy	6	2.2
	Metastatic chemotherapy	84	30.3
Number of treatments received so far	New diagnosis	140	50.5
	Second line	89	32.1
	Third line	44	15.9
	>4 and above*	4	1.4
Active treatment received	Absent	39	14.1
	Adjuvant hormonal therapy	14	5.1
	Maintenance Anti Her2 therapy	4	1.4
	Maintenance Bev/Cetux	4	1.4
	Metastatic TKI (Tyrosine kinase inhibitor)	23	8.3
	Maintenance Bev/Cetux +5-FU		2.2
	Consolidated CT (Chemotherapy)	3	1.1
	Metastatic hormone therapy	37	13.4
	Adjuvant chemotherapy	1	0.4
	Neoadjuvant chemotherapy	6	2.2
	Metastatic chemotherapy	109	39.4
	Metastatic immunotherapy		10.5
	Chemoradiotherapy	2	0.7
RT (radiotherapy) history	Absent	142	51.3
	Receiving	6	2.2
	Received	129	46.6
Reason for receiving RT	Absent	142	51.3
	Palliative	50	18.1
	Curative CRT (Chemoradiotherapy)	49	17.7
	SBRT (Stereotactic Body Radiation Therapy)	8	2.9
	Adjuvant	28	10.1

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Table 1. Demographic information

		n	%
Brain RT history	Absent	248	89.5
	Active Present	29	10.5
Time of brain RT	Not received	248	89.5
	Still receiving	1	0.4
	Within 1 month of study	3	1.1
	1-3 months before study	8	2.9
	3-6 months before study	8	2.9
	6-12 months before study	8	2.9
	More than 12 months before stud	1	0.4
Groups based on the number of patients seen in the clinic that day	0-31	12	4.3
	31-61	162	58.5
	61-71	27	9.7
	71-81	61	22.0
	81-100	15	5.4
PROMIS depression raw score Avg±SD (min-max)		18.3±6.9 (8-36)	
	None, mild	122	44.0
	Moderate	77	27.8
	Mid	71	25.6
	Severe	7	2.5
PROMIS anxiety raw score Avg±SD (min-max)		17.1±6.2 (6-34)	
	None, mild	105	37.9
	Moderate	87	31.4
	Mid	74	26.7
	Severe	11	4.0
Laboratory parameters at diagnosis Avg±SD (Min-Max)			
	Neutrophil (count/mm^3)	4.35±0.92 (2.81-6.17)	
	Lymphocyte (count/mm^3)	1.55±0.37 (0.98-2.55)	
	Platelet (count/mm^3)	355.12±68.17 (195-564)	
	CRP (mg/L)	7.17±21.23 (6-197)	
	LDH (U/L)	260.51±50.13 (152-391)	
	SII score	1077.00±464.52 (292-2358)	
	HALP score	1.76±0.86 (0.63-5.02)	

An analysis was conducted on the relationship between general patient information and SII and HALP scores. The SII score showed a very weak level of positive correlation with age, a moderate level with the CCI, and a good level with the stage at diagnosis. On the other hand, a weak level of statistically significant negative correlation was found with the time elapsed from diagnosis to inclusion in the study (respectively; p=0.014 p<0.001 p<0.001 p<0.001). As for the HALP score, a very weak level of positive correlation was found with age, while a moderate level of negative correlation was detected with the CCI and the stage at diagnosis. Moreover, a weak level of statistically significant positive correlation was found with the time elapsed from diagnosis to inclusion in the study (respectively; p=0.003 p<0.001 p<0.001 p<0.001). The relationship between these parameters and the PROMIS depression and anxiety scores was examined. A moderate level of negative correlation was found between the PROMIS depression and anxiety scores and age, and a weak level of negative correlation with the CCI, while a weak level of positive correlation was found with the HI. In the relationship with the stage at diagnosis, a very weak level of statistically significant positive correlation was found with the PROMIS anxiety score (p<0.001 p<0.001 p<0.001 p<0.001 p<0.001 p=0.001 p=0.027).

Statistically significant differences were detected in the levels of SII and HALP scores with the stage at diagnosis (both p<0.001). The SII score was statistically significantly higher in stage 4 patients compared to stages 1, 2, and 3, whereas the HALP score showed the exact opposite relationship, with the lowest values in stage 4 patients compared to other stages (HALP score Stage 4 vs. other early stages p=0.001, other comparisons p<0.001). The SII score level of patients who underwent surgery was statistically significantly lower, while the HALP score was higher, compared to those who did not have surgery (both p<0.001). The relationships with PROMIS depression and anxiety scores were also examined. The average PROMIS depression and anxiety scores at diagnosis were statistically significantly higher in females compared to males (both p<0.001). The PROMIS anxiety score was higher in patients who had surgery (p=0.002). Statistically significant differences were detected in the levels of PROMIS depression scores in diagnosis groups (p<0.001). The score level of the breast cancer patient group was statistically significantly higher than the lung and gastrointestinal system (GIS) cancer patient groups (p<0.001 p=0.001).

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In our study, the average laboratory values and SII and HALP scores at the commencement of the study were calculated. No statistically significant differences were detected in the SII and HALP score levels in diagnosis groups (p=0.214, p=0.249).

Significant differences were detected in the SII levels during the study in the active treatments received by the patients (p<0.001). The SII levels during the study were higher in those without active treatment and those receiving metastatic hormonal therapy compared to those receiving metastatic chemotherapy. The SII study level of those receiving metastatic tirozin kinaz inhibitors (TKI) was significantly higher than those receiving adjuvant hormonal therapy, metastatic hormonal therapy, neoadjuvant chemotherapy, and metastatic chemotherapy, and those receiving metastatic immunotherapy was significantly higher than those receiving neoadjuvant chemotherapy and metastatic chemotherapy (all comparisons p<0.001).

PROMIS depression and anxiety section

The factors related to the results obtained from the PROMIS depression and anxiety survey, a significant parameter of the study, were examined.

The PROMIS Depression-Anxiety Scores were significantly higher in females compared to males (p<0.001 for both).

A statistically significant difference was detected in the PROMIS Depression scores among the diagnosis groups (p=0.001). The PROMIS Depression score in breast cancer was statistically significantly higher than in patients diagnosed with lung and GIS cancers (p<0.001, p=0.002).

The PROMIS Depression score in patients who had undergone surgery was statistically significantly higher than in those who had not (p<0.001 for both).

A statistically significant difference was detected in the PROMIS Anxiety scores among the marital status groups (p=0.015). The PROMIS Anxiety scores were statistically significantly higher in married individuals compared to widowed individuals (p=0.006).

A statistically significant difference was detected in the PROMIS Depression-Anxiety scores among the education groups (p<0.001 for both). The PROMIS Depression score was statistically significantly higher in university graduates compared to illiterate individuals, primary and middle school graduates, and in high school graduates compared to primary and middle school graduates (University graduate vs. illiterate p=0.002, other comparisons p<0.001). PROMIS Anxiety scores were statistically significantly higher in university graduates and high school graduates compared to primary and middle school graduates (p<0.001 for both comparisons).

A significant difference was detected in the PROMIS Depression-Anxiety scores among occupational groups (p<0.001 for both). Apart from the depression score in patients with the occupation of Farmer/Fisherman and Tradesman/Business owner, the PROMIS Depression-Anxiety scores of all occupational groups were significantly lower compared to those without an occupation (all comparisons p<0.001). The PROMIS Depression-Anxiety scores were higher in patients who were Nurses/Health officers compared to those without an occupation, those who were cleaners/janitors/tea makers/drivers, and those who were Tradesman/Business owners, while only anxiety scores were statistically significantly higher compared to those who were Workers/Mechanics/Technicians (p<0.001, p=0.001, p=0.001, p<0.001, p<0.001, p<0.001).

A statistically significant difference was detected in the PROMIS Depression-Anxiety scores in terms of the place of birth, characteristics of the place of residence, and regions where the patients were born (p<0.001, p<0.001, p<0.001, p=0.001, p=0.001, p=0.001). The PROMIS Depression-Anxiety scores of patients who were born and reside in cities and districts were higher than those of the patients from towns and villages (District vs. Town-Village (p=0.001, p=0.003, other comparisons p<0.001). In terms of the regions of birth, the PROMIS Depression score was significantly higher in the Marmara and Central Anatolia regions compared to the Southeastern Anatolia region; the PROMIS Anxiety score was higher in the Marmara region compared to the Mediterranean, Eastern Anatolia, Southeastern Anatolia regions, and in the Mediterranean region and Central Anatolia regions compared to the Southeastern Anatolia region (p=0.001, p=0.002, p<0.001, p=0.002, p<0.001).

The PROMIS depression score was found to be moderately statistically significantly correlated with the raw Promis anxiety score (p<0.001). The PROMIS depression score was found to have a moderate level correlation with age, a weak correlation with the level of education, and a weak and negative correlation with the CCI, whereas it was found to be weakly and positively statistically significantly correlated with the HI and the number of patients in the doctor's clinic on the day of the study (p<0.001 for all comparisons). The PROMIS anxiety raw score was found to have a moderate correlation with age, a weak correlation with the level of education, a weak and negative correlation with the CCI, and a weak and positive statistically significant correlation with the stage at diagnosis and the HI (p<0.001, p=0.001, p=0.028, p<0.001 in order). Table 2 shows the level of relationship between PROMIS depression and anxiety scores and various factors.

The relationship between depression and anxiety survey results and ECOG-PS evaluation results was examined. The raw score calculated from the PROMIS depression survey had a weak and negative relationship with the performance score evaluated by doctors, a weak and positive relationship with the performance score evaluated by patients themselves, and a moderate and statistically significant relationship in a positive direction with the difference in performance scores between doctor-patient evaluations (p=0.001, p<0.001, p<0.001). The raw score calculated from the PROMIS anxiety survey had a weak and statistically significant relationship in a positive direction with the performance score evaluated by patients themselves and the difference in performance scores in doctor-patient evaluations (p=0.020, p<0.001).

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Table 2. Level of relationship between PROMIS depression and anxiety scores and various factors

	PROMIS depression score		PROMIS anxiety score	
	r	p	r	p
PROMIS anxiety raw score	0.504	<0.001		
Age	-0.462	<0.001	-0.441	<0.001
Stage at diagnosis	-0.006	0.915	0.132	0.028
Education	-0.220	<0.001	-0.172	0.004
Hollingshead index	0.238	<0.001	0.313	<0.001
Years of place of residence	0.032	0.600	0.079	0.191
Days since diagnosis till the study	0.099	0.100	-0.079	0.188
Charlson Comorbidity Index	-0.253	<0.001	-0.199	0.001
Number of patients in the clinic on the day of the study	0.287	<0.001	0.066	0.272
SII study score	-0.044	0.466	-0.089	0.141
HALP study score	-0.073	0.223	-0.005	0.937

The differences between the depression status determined according to the PROMIS depression survey and the PS evaluated by doctors, the PS in which the patients evaluate themselves, and the PS difference in doctor-patient evaluations were found to be significant (p=0.002, p<0.001, p<0.001). In those with mild depression status, the ratio of patients with an ECOG-PS 2 PS evaluated by doctors was high, in those with moderate and severe depression status, the ratio of patients with an ECOG-PS 1 was high, and in those with severe depression, the ratio of patients with an ECOG-PS 0 was high. In those with mild depression status, the ratio of patients who are active, defined as ECOG-PS 0 in the PS where patients evaluate themselves, was high, while in those with mild to moderate depression, the ratio of patients with ECOG-PS 1, defined as having physical activity limitations, was high. In those with moderate and severe depression, the ratio of patients with some limitations but can perform daily activities, defined as ECOG-PS 2, was high, while in those with severe depression, the ratio of patients who spend more than half of the day in bed and have limitations in daily activities, defined as ECOG-PS 3, was high. In those with mild depression status, the ratios of patients with a performance score difference of -1 and 0 in the doctor-patient evaluation were higher, in those with moderate depression status, the ratio of patients with a performance evaluation difference of 0 were higher, in those with moderate depression status, the ratio of patients with a performance evaluation difference of 1 were higher, and in those with severe depression status, the ratio of patients with a performance evaluation difference of 2 were higher.

The differences between the anxiety level determined according to the Promis anxiety survey and the PS evaluated by doctors, the PS in which the patients evaluate themselves, and the PS difference in doctor-patient evaluations were found to be statistically significant (p=0.033, p=0.001, p=0.002). In those with mild to moderate anxiety status, the ratio of patients who are active, as defined by ECOG-PS 0 in the PS evaluated by doctors, the ratio of patients with ECOG-PS 1, defined as having physical activity limitations in those with moderate anxiety status, and the ratio of patients with some limitations but can perform daily activities, as defined by ECOG-PS 2 in those with severe anxiety status, were higher. In those with mild anxiety status, the ratio of patients who are active, defined as ECOG-PS 0 in the PS where patients evaluate themselves, were higher, while in those with mild to moderate anxiety, the ratio of patients with ECOG-PS 1, defined as having physical activity limitations, were higher, and in those with moderate and severe anxiety, the ratio of patients with some limitations but can perform daily activities, defined as ECOG-PS 2, were higher. In those with mild anxiety status, the ratios of patients with a performance score difference of -1 and 0 in the doctor-patient evaluation were higher, in those with moderate anxiety status, the ratio of patients with a performance score difference of 0-1 were higher, in those with moderate anxiety status, the ratio of patients with a performance score difference of 1 were higher, and in those with severe anxiety status, the ratio of patients with a performance score difference of 0-1 were higher.

ECOG-PS and associated parameters

A very weak level of compliance was determined between the doctor and patient ECOG-PS evaluation results (Kappa Compliance Coefficient 0.220). Patient ECOG-PS evaluation results were higher than those of doctors (p<0.001). The performance evaluations of 49.8% of patients were higher than the doctors' evaluations of patients' performances. 91.4% of the higher ones were 1 point higher, while 8.6% were found to be 2 points higher. The performance evaluation of 1.8% of patients was 1 point lower than the doctors' evaluations of patients' performances. 48.4% of evaluations were equal. These relationships are shown in Tables 3 and 3A.

The doctors' evaluation of patients' performance; was found to be weakly negatively correlated with the HI, HALP score at diagnosis, PROMIS depression raw score, and the SII score during the study, while it was found to be significantly positively correlated with the CCI, and the SII score at diagnosis (p=0.035, p=0.001, p<0.001, p<0.001, p<0.001).

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Table 3. Doctor-patient ECOG-PS evaluation compliance

Doctor's performance evaluation	Active	Limited physical activity	Some limitations but can perform daily activities	Spend more than half of the day in bed and have limitations in daily activities	Total n (%)
Active	**10**	18	2	0	30 (10.8)
Limited physical activity	2	**64**	99	10	175 (63.2)
Some limitations but can perform daily activities	0	2	**57**	9	68 (24.5)
Spend more than half of the day in bed and have limitations in daily activities	0	0	1	**3**	4 (1.4)
Total n (%)	12 (4.3)	84 (30.3)	159 (57.4)	22 (7.9)	277 (100)

Table 3A. Doctor-patient ECOG-PS evaluation difference

	n (%)
Patient performance>Doctor's performance evaluation	138 (49.8)
1 point	126 (45.5)
2 points	12 (4.3)
Patient performance<Doctor's performance evaluation	5 (1.8)
Patient performance=Doctor's performance evaluation	134 (48.4)

The patient performance evaluation; while it was found to be weakly negatively correlated with the HI, HALP score at diagnosis, and the SII score during the study, it was found to be statistically significantly positively correlated with the CCI, PROMIS depression raw score, PROMIS anxiety raw score, and the SII score at diagnosis (p=0.042, p<0.001, p<0.001, p<0.001, p<0.001, p=0.020, p=0.001). The parameters and analyses related to the ECOG-PS evaluation of the patient and the doctor are shown in Table 4.

The difference in Doctor-Patient ECOG-PS evaluation results; was found to be moderately correlated with the number of patients in the doctor's outpatient clinic on the day of the study and the PROMIS depression raw score, and weakly positively and statistically significantly correlated with the PROMIS anxiety raw score (p<0.001 for all).

Table 4. Parameters and analyses related to the ECOG-PS evaluation of the patient and doctor

	Doctor's performance evaluation		Patient's performance evaluation		Performance difference	
	r	p	r	p	r	p
Hollingshead Index	-0.127	0.035	-0.122	0.042	-0.009	0.880
Charlson Comorbidity Index	0.344	<0.001	0.317	<0.001	0.004	0.948
PROMIS depression raw score	-0.198	0.001	0.255	<0.001	0.503	<0.001
PROMIS anxiety raw score	-0.070	0.248	0.140	0.020	0.254	<0.001
Diagnosis SII score	0.249	<0.001	0.202	0.001	-0.034	0.576
Diagnosis HALP score	-0.253	<0.001	-0.210	<0.001	0.025	0.684
SII study	-0.278	<0.001	-0.217	<0.001	0.026	0.669
HALP study	-0.001	0.985	0.036	0.555	0.016	0.786

The detailed analyses and subgroup results of the difference between doctor and patient ECOG-PS evaluations, which form the main theme of our study, are shown in Tables 5, 5A, and 5B. The statistically significant findings related to this were as follows; the difference in performance levels evaluated by doctors and patients in female patients was higher than in male patients (p<0.001). When this difference was evaluated according to the occupational groups in the HI index; the difference in performance levels evaluated by doctors and patients was statistically significant (p=0.049). Among the occupational groups, only those who are nurses/health officers had a higher difference in performance levels evaluated by doctors and patients than those in the farmer/fishing occupation (p=0.005).

There was a statistically significant difference in the difference between doctor and patient ECOG-PS evaluations in Promis depression score interpretation groups (p<0.001). Those with moderate, middle, and severe depression had statistically significantly higher differences in performance evaluation levels compared to those with none or mild levels, and those with moderate depression had statistically significantly higher differences compared to those with mild depression (p<0.001 for all).

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There was a statistically significant difference in doctor and patient performance difference levels in Promis anxiety score interpretation groups (p<0.001). The difference in doctor and patient performance levels was found to be higher in those with moderate anxiety according to the Promis anxiety score interpretation, compared to those with none or mild levels (p<0.001).

A significant difference was found between the performance evaluations of the doctor and patient in groups determined by the number of patients in the outpatient clinic (p<0.001). Accordingly, the difference levels between the doctor and patient performance evaluations of those in the 2nd group (31-61 patients), 3rd group (61-71 patients), 4th group (71-81 patients), and 5th group (81-100 patients) were higher than those in the 1st group (0-31 patients) (p<0.001). Also, the difference levels between the doctor and patient performance evaluations of those in the 3rd group (61-71), 4th group (71-81), and 5th group (81-100) were statistically significantly higher than those in the 2nd group (31-61) (p<0.001). No statistically significant difference was found between groups with a patient count above 60 (third, fourth, and fifth groups) (p=0.832, p=0.098, p=0.049). In addition, no significant difference was found regarding performance evaluation status according to the characteristics of the patients' place of birth and residence (p=0.949, p=0.690, p=0.398, p=0.552). Tables 5, 5A and 5B show these relationships.

Survival analyses were conducted and factors affecting PFS were examined. Firstly, the relationships between ECOG-PS evaluations and their differences between the doctor and the patient, and progression were examined. It was found that the doctor's evaluation of the patient's performance increased the risk of progression 3.1 times (HR: 3.080, 95% CI: 1.671-5.675) in those with ECOG-PS 2 compared to those with ECOG-PS 0, and 5 times (HR: 4.980.95% CI: 1.405-17.646) in those with ECOG-PS 3 compared to those with ECOG-PS 0 (respectively p<0.001 p=0.013).

Table 5. Detailed subgroup analyses of the difference between Doctor and Patient ECOG-PS evaluations

		Difference in Doctor and Patient Performance					
		Avg.	**SD**	**Min**	**Max**	**Median**	**p**
Gender	**Female**	0.66	0.55	-1	2	1	<0.001
	Male	0.40	0.64	-1	2	0	
Age	**<50 years**	0.65	0.59	0	2	1	0.484
	50-59 years	0.55	0.56	0	2	1	
	60-69 years	0.48	0.61	-1	2	0	
	70 and over	0.51	0.74	-1	2	0	
Education	**Illiterate**	0.67	1.15	0	2	0	0.765
	Primary school	0.50	0.76	-1	2	0	
	Secondary school	0.41	0.63	-1	1	0	
	High school	0.54	0.60	-1	2	1	
	University	0.53	0.56	0	2	0.5	
Occupational grouping HI	**No occupation**	0.62	0.55	0	2	1	0.049
	Farmer/fisherman	0.24	0.78	-1	2	0	
	Cleaner/janitor/tea maker/driver	0.41	0.56	0	2	0	
	Officer/secretary desk officer	0.56	0.57	-1	2	1	
	Worker/motor master/technician	0.73	0.59	0	2	1	
	Nurse/health officer	0.90	0.32	0	1	1	
	Tradesman/business owner	0.48	0.77	-1	2	0	
	Teacher/police/soldier	0.44	0.64	0	2	0	
	Lawyer/engineer/doctor	0.47	0.51	0	1	0	
Hollingshead Index group	**1**	0.50	0.62	-1	2	0	0.749
	2	0.56	0.64	-1	2	1	
	3	0.57	0.59	0	2	1	
	4	0.42	0.50	0	1	0	
Family cancer history	**Absent**	0.49	0.61	-1	2	0	0.156
	Present	0.61	0.62	-1	2	1	
Rt brain history	**Absent**	0.53	0.62	-1	2	0.5	0.624
	Active yes	0.45	0.57	-1	1	0	
Stage at diagnosis	**Stage 1**	0.40	0.55	0	1	0	0.786
	Stage 2	0.48	0.50	0	1	0	
	Stage 3	0.50	0.69	-1	2	0	
	Stage 4	0.57	0.62	-1	2	1	

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Table 5. Detailed subgroup analyses of the difference between Doctor and Patient ECOG-PS evaluations

Underwent surgery?	**No**	0.48	0.61	-1	2	0	0.273
	Yes	0.56	0.61	-1	2	1	
Number of treatments received so far	**New diagnosis**	0.54	0.60	-1	2	1	0.257
	2nd round	0.54	0.62	-1	2	0	
	3rd round	0.50	0.63	0	2	0	
	>4 and above round	0.00	0.00	0	0	0	
PROMIS depression T score interpretation	**None, mild**	0.23	0.56	-1	2	0	<0.001
	Moderate	0.57	0.52	0	2	1	
	Mid	0.90	0.48	0	2	1	
	Severe	1.29	0.76	0	2	1	
PROMIS anxiety T interpretation	**None, mild**	0.35	0.62	-1	2	0	<0.001
	Moderate	0.56	0.58	0	2	1	
	Mid	0.73	0.58	-1	2	1	
	Severe	0.45	0.52	0	1	0	
Outpatient number group	**0-31**	0.17	0.39	0	1	0	<0.001
	31-61	0.30	0.51	-1	1	0	
	61-71	0.89	0.51	0	2	1	
	71-81	0.85	0.57	-1	2	1	
	81-100	1.20	0.68	0	2	1	

Table 5A. The relationship between the difference in Doctor and Patient ECOG-PS evaluations and the interpretation of Promis depression and anxiety scores

		Difference in doctor and patient performance	
		PROMIS depression score interpretation	**PROMIS anxiety score interpretation**
		p	**p**
None, mild etc.	**Moderate**	<0.001	0.015
	Mid	<0.001	<0.001
	Severe	<0.001	0.505
Moderate etc.	**Mid**	<0.001	0.045
	Severe	0.009	0.610
Mid etc.	**Severe**	0.072	0.118

Table 5B. The relationship between the difference in Doctor and Patient ECOG-PS evaluations and the outpatient patient number group

Difference in Doctor and Patient Performance		
Outpatient number group		**p**
0-31 vs.	31-61	0.327
	61-71	<0.001
	71-81	<0.001
	81-100	<0.001
31-61 vs.	61-71	<0.001
	71-81	<0.001
	81-100	<0.001
61-71 vs.	71-81	0.832
	81-100	0.098
71-81 vs.	81-100	0.049

According to the doctors' performance evaluations, the median PFS (mPFS) duration was 34±2.2 months (95% CI: 29.7-38.3). In those with ECOG-PS 0, mPFS was 55 months, in those with ECOG-PS 1, mPFS was 36±2.7 months (95% CI: 30.7-41.3), in those with ECOG-PS 2, mPFS was 20±2.0 months (95% CI: 16.02-4.0), and in those with ECOG-PS 3, mPFS was 18±7.0 months (95% CI: 4.3-31.7). A statistically significant difference was found between mPFS according to the scores in doctors' performance evaluations (Log Rank p=0,009). The mPFS values of those with ECOG-PS 2 and 3 were shorter compared to those with ECOG-PS 0 and 1 (ECOG-PS 0 p<0.001 p=0.001 and ECOG-PS 2 p<0.001 p=0.0032). Performance evaluation was divided into two groups, with 0 and 1 as a group and 2 and 3 as another group, and analysis and survival graph were performed. After this separation, the m PFS of the group with ECOG-PS 0 and 1 was 38 months (SE 2.6, 95% CL: 32.9-43.1), while the m PFS of the group with PS 2 and 3 was 20 months (SE 1.9, 95% CL: 16.4-23.6). This is shown in Figure 1 and 2.

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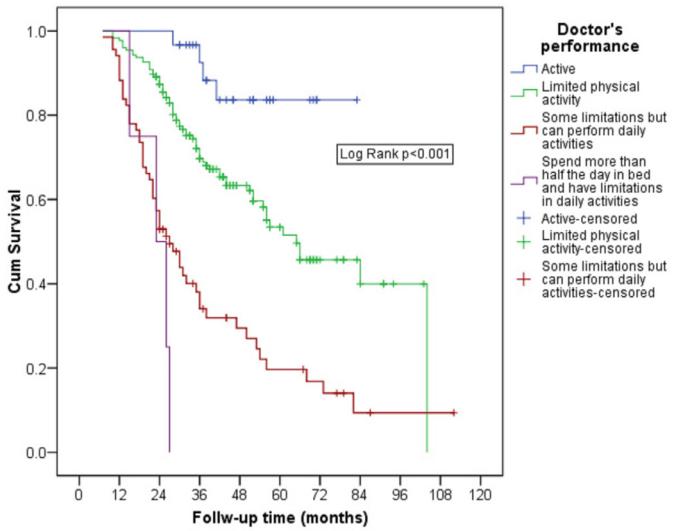

Figure 1. OS according to Doctors-assessed ECOG-PS

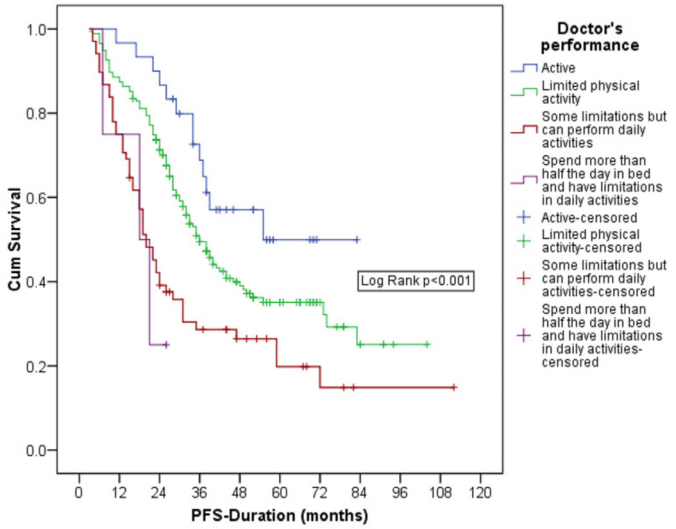

Figure 2. PFS according to Doctors-assessed ECOG-PS

In the patients' own evaluations of their ECOG-PS, no significant difference was detected in terms of progression among other ECOG-PS evaluation levels compared to those with ECOG-PS 0. However, a statistically significant difference was found between the patients' own ECOG-PS evaluation levels and mPFS (Log Rank p=0.009). The two groups that revealed this significant difference were the patient groups who evaluated their own performance as ECOG-PS 1 and 2. A statistically significantly lower mPFS was found in those with ECOG-PS 2 (28±1.9 months (95% CI: 24.2-31.8)) compared to those with EOCG-PS 1 (47±12.4 months (95% CI: 22.7-71.3)) (p=0.001). Performance evaluation was divided into two groups, with 0 and 1 as a group and 2 and 3 as another group, and analysis and survival graph were performed. After this separation, the m PFS of the group with ECOG-PS 0 and 1 was 44 months (SE 8.1, 95% CI: 28.2-59.8), while the m PFS of the group with PS 2 and 3 was 28 months (SE 1.8, 95% CI: 24.5-31.5). The relationship between the patients' own evaluations of their ECOG-PS and mPFS is shown in Figure 3 and 4.

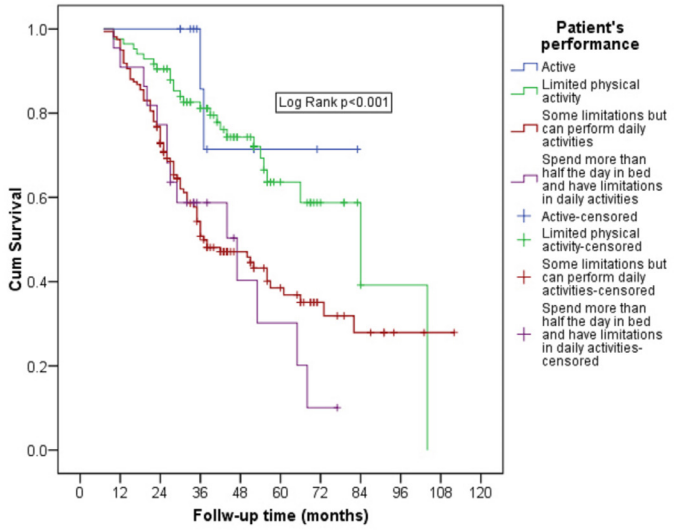

Figure 3. OS according to Patient-assessed ECOG-PS

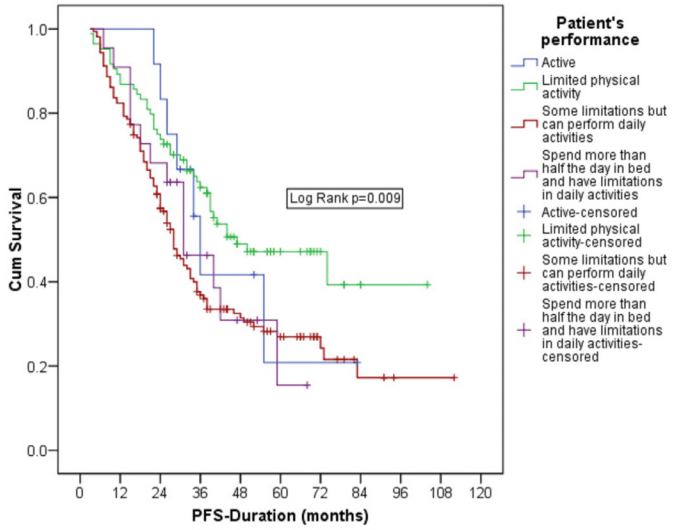

Figure 4. PFS according to Patient-assessed ECOG-PS

Being diagnosed with lung cancer compared to other cancers, being a smoker compared to non-smokers, having a high Systemic SII score at diagnosis compared to a low one, having a SII score group of 3 and above at diagnosis compared to group 1, having a HALP score group of 7 and 8 at diagnosis compared to those in group 2-3, having a high CCI compared to a lower one, coding solid cancer as metastatic in the CCI compared to local/locally advanced, having a HALP score group of 4 during the study compared to score group 1 were all found to increase the risk of progression. Being diagnosed with breast cancer compared to other cancers, and being locally advanced and advanced at diagnosis (Stage 4) were found to be protective against the risk. The risk factors for progression in the multivariate Cox Regression Analysis model were identified as lung cancer, smoking, increase in SII score, increase in CCI, while breast cancer, GIS cancer, genitoüriner system (GUS) cancer, and increase in HALP score at diagnosis were protective factors.

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Table 6 shows the risk factors affecting patients' progression, as determined by Cox regression analysis.

When the effect of physicians' performance evaluation on progression was adjusted for Promis depression-anxiety status, those with ECOG-PS 2 were found to be 3.1-fold and those with ECOG-PS 3 were found to be 5.7-fold risk factors for progression compared to those with ECOG-PS 0 (p<0.001 p=0.009). The effects of patients' performance evaluation and the difference between doctor-patient performance evaluation on progression were analyzed by adjusting for PROMIS depression-anxiety status. When ECOG-PS 0 was taken as the reference for performance evaluation of the patients, no significant difference was found compared to patients with other performance scores. There was no statistically significant effect for progression between those with a difference in performance compared to those without a difference in doctor-patient performance evaluation.

Table 6. Single and multivariate Cox Regression Analysis of progression-related risk factors

	p	HR	95% CI (min-Max)	
Age	0.094	1.016	0.997	1.035
Gender (Ref: female) male	0.128	1.266	0.935	1.715
Diagnosis				
Lung	<0.001	4.669	3.192	6.830
Pancreas	0.437	1.351	0.632	2.885
Bile ducts	0.764	1.191	0.379	3.740
Brain	0.053	2.684	0.987	7.302
Breast	0.001	0.458	0.294	0.713
ColoRectal	0.061	0.656	0.422	1.019
Prostate	0.293	0.745	0.430	1.289
Stomach	0.117	1.634	0.884	3.023
RCC	0.530	1.166	0.723	1.880
Bladder	0.779	1.153	0.427	3.111
Melanoma	0.789	0.902	0.423	1.924
Ovary	0.843	1.086	0.480	2.458
Cervical	0.958	0.948	0.132	6.789
Ureteral	0.970	1.038	0.145	7.421
Endometrium	0.359	0.049	0.000	31.061
HCC	<0.001	16.436	3.833	70.473
NET	0.309	0.360	0.050	2.575
GIST	0.211	0.048	0.000	5.598
Sarcoma	0.625	0.613	0.086	4.377
Testis	0.490	0.500	0.070	3.576
Stage at diagnosis (Ref: Stage 4)	<0.001			
Early	0.949	0.000	0.000	
Locally advanced	<0.001	0.114	0.070	0.185
Advanced	<0.001	0.245	0.167	0.361
Alcohol	0.525	0.886	0.611	1.286
Smoking	<0.001	1.766	1.303	2.395
Hollingshead Index	0.426	0.996	0.987	1.006
Hollingshead Index (Ref: 1)	0.839			
2	0.860	1.031	0.730	1.457
3	0.589	0.882	0.559	1.391
4	0.521	0.825	0.457	1.486
SII score	<0.001	1.002	1.001	1.002

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Table 6. Single and multivariate Cox Regression Analysis of progression-related risk factors

	p	HR	95% CI (min-Max)	
SII group (Ref: 1)	<0.001			
2	0.384	1.590	0.560	4.516
3	<0.001	7.385	2.894	18.844
4	<0.001	11.503	4.496	29.430
5	<0.001	18.913	7.265	49.232
6	<0.001	15.848	6.170	40.705
7	<0.001	16.010	5.422	47.277
8	<0.001	16.553	4.990	54.913
HALP score	<0.001	0.283	0.211	0.379
HALP score (Ref: 2)	<0.001			
3	0.852	891.08		
4	0.870	379.65		
5	0.853	855.14		
6	0.838	1704.04		
7	0.816	4666.94		
8	0.802	9123.95		
Charlson Comorbidity Index	<0.001	1.225	1.161	1.294
Solid cancer status in Charlson Comorbidity Index (Ref: local/locally advanced) metastatic	<0.001	6.069	4.310	8.544
Doctor's performance evaluation (Ref:ECOG-PS 0)	<0.001			
ECOG-PS 1	0.075	1.690	0.948	3.010
ECOG-PS 2	<0.001	3.080	1.671	5.675
ECOG-PS 3	0.013	4.980	1.405	17.646
Patient's performance evaluation (Ref: ECOG-PS 0)	0.011			
ECOG-PS 1	0.692	0.850	0.382	1.895
ECOG-PS 2	0.268	1.541	0.717	3.312
ECOG-PS 3	0.492	1.375	0.554	3.410
PROMIS depression comment (Ref: none, mild)	0.243			
Moderate	0.329	0.836	0.583	1.198
Mid	0.052	0.682	0.463	1.004
Severe	0.407	0.653	0.239	1.785
PROMIS anxiety comment (Ref: none, mild)	0.578			
Moderate	0.544	1.118	0.780	1.604
Mid	0.478	1.147	0.786	1.673
Severe	0.318	0.598	0.217	1.643
SII study	0.181	1.000	1.000	1.001
SII study group (Ref:1)	0.171			
2	0.221	0.790	0.541	1.153
3	0.430	1.189	0.774	1.828
4	0.381	1.298	0.724	2.329
5	0.242	1.520	0.753	3.067
6	0.679	0.743	0.181	3.040
7	0.101	2.342	0.847	6.471
HALP study	0.244	1.094	0.940	1.273

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Table 6. Single and multivariate Cox Regression Analysis of progression-related risk factors

	p	HR	95% CI (min-Max)	
HALP study group (Ref:1)	0.272			
2	0.457	1.203	0.739	1.958
3	0.149	1.422	0.881	2.295
4	0.018	1.947	1.122	3.379
5	0.386	1.386	0.662	2.901
6	0.553	0.546	0.074	4.041
7	0.975	0.977	0.231	4.141
Risk factors for progression in multivariable Cox Regression Analysis				
Lung ca	0.039	2.190	1.042	4.605
Breast ca	<0.001	0.166	0.077	0.359
GIS ca	0.002	0.328	0.163	0.658
GUS ca	0.003	0.330	0.161	0.677
Other ca	.			
Smoking	0.022	1.524	1.063	2.183
SII score	0.007	1.001	1.000	1.002
HALP score at diagnosis	0.000	0.387	0.235	0.638
HALP score during study	0.078	0.834	0.681	1.021
Charlson Comorbidity Index	0.001	1.136	1.055	1.222
Doctor's performance evaluation (Ref: ECOG-PS 0)	0.082			
ECOG-PS 1	0.148	0.569	0.265	1.221
ECOG-PS 2	0.146	0.532	0.227	1.244
ECOG-PS 3	0.258	2.447	0.518	11.553
Patient's performance evaluation (Ref: ECOG-PS 0)	0.768			
ECOG-PS 1	0.634	0.784	0.288	2.133
ECOG-PS 2	0.804	0.879	0.319	2.422
ECOG-PS 3	0.491	0.659	0.201	2.159

The relationship between overall median survival (m OS) and ECOG-PS was also analyzed. In the physicians' assessment of the patients' performance, those with ECOG-PS 1 were 3.6 times, those with ECOG-PS 2 were 10.2 times and those with ECOG-PS 3 were 23.5 times more likely to die than those with ECOG-PS 0 (p=0.013 p<0.001 p<0.001).

There was a statistically significant difference in the duration of mOS in the performance evaluations made by the doctors (Log Rank p<0001). Those with ECOG-PS 1, 2 and 3 had lower estimated OS than those with ECOG-PS 0, and those with ECOG-PS 2 and 3 had lower estimated OS than those with ECOG-PS 1 (ECOG-PS 0 p=0.007 p<0.001 p<0.001 p<0.001 ECOG-PS 1 p<0.001 p<0.001). Performance evaluation was divided into two groups, with 0 and 1 as a group and 2 and 3 as another group, and analysis and survival graph were performed. After this distinction, the mOS of the ECOG-PS 0 and 1 group was 84 months (SE 14.6, 95% CL: 55.4-112.6), while the mOS of the PS 2 and 3 group was 26 months (SE 2.4, 95% CL: 21.3-30.7). This relationship is shown in Figure 5 and 6.

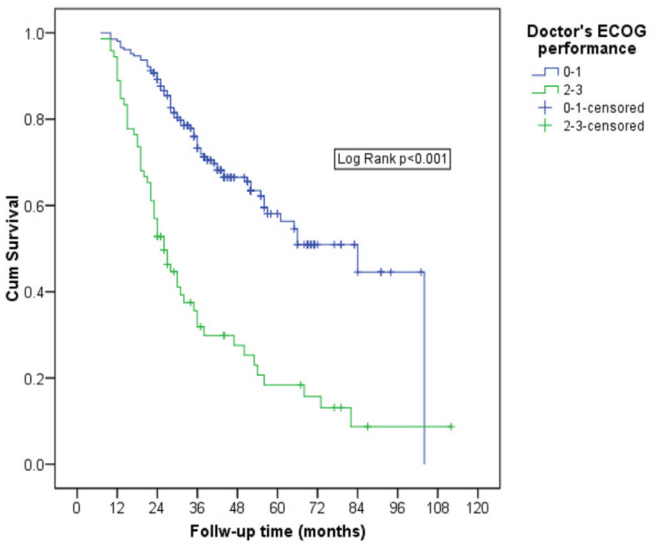

Figure 5. OS figure when doctor's evaluated ECOG-PS is divided into 0-1 and 2-3

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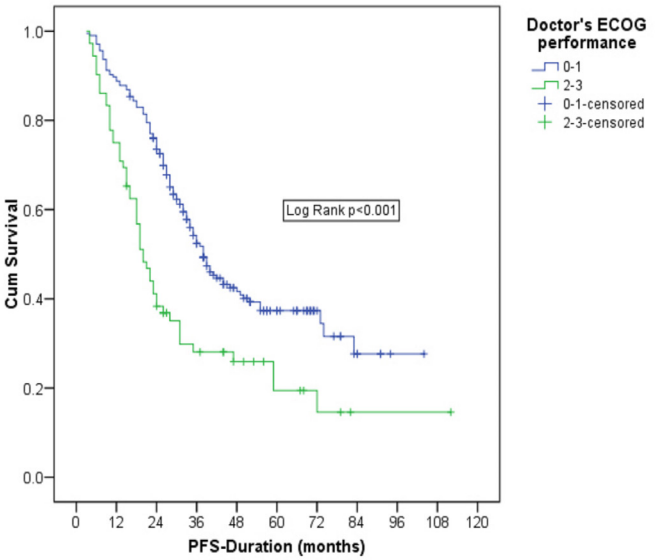

Figure 6. OS figure when doctor's evaluated ECOG-PS as 0-1 and 2-3, the simplified version

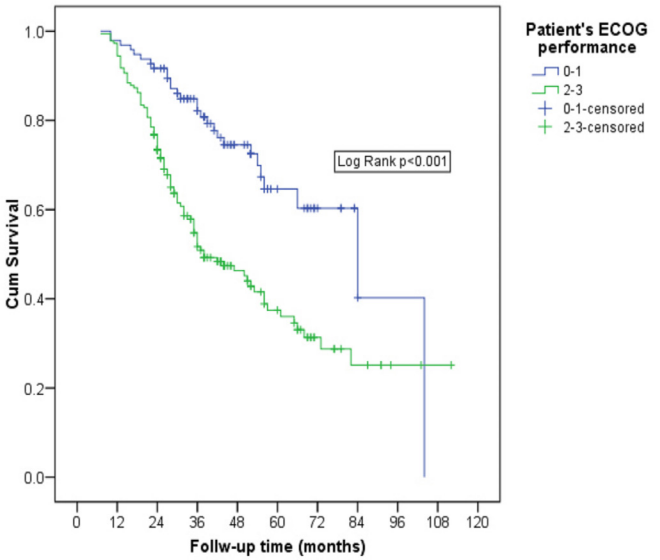

Figure 7. OS figure when patient's evaluated ECOG-PS is divided into 0-1 and 2-3

When the effect of physicians' performance evaluations on mortality was adjusted for Promis depression-anxiety status, those with ECOG-PS 1 were 3.6 times, those with ECOG-PS 2 were 9.7 times and those with ECOG-PS 3 were 20.7 times more likely to die compared to those with ECOG-PS 0 (p=0.013 p<0.001 p<0.001). When the effect of patients' performance evaluation on mortality was adjusted for Promis depression-anxiety status; ECOG-PS 2 patients were 7.8 times and ECOG-PS 3 patients were 9.1 times more likely to die than ECOG-PS 0 patients (p=0.046 p=0.032). When the effect of doctor-patient performance evaluation difference on mortality was adjusted for PROMIS depression-anxiety score status, no statistically significant effect was found compared to those without evaluation difference.

In patients' own performance assessments, those evaluated as ECOG-PS 2 had a 4.2 times higher risk and those evaluated as ECOG-PS 3 had a 5.1 times higher risk of death compared to those with ECOG-PS 0 (p=0.046, p=0.032).

Statistically significant differences were found in mOS durations in the patients' own performance assessments (Log Rank p<0.0001). The mOS durations were shorter for those evaluated as ECOG-PS 2 and ECOG-PS 3 compared to those with ECOG-PS 0 and those evaluated as ECOG-PS 1 (active p=0.025, p=0.019; physical activity limitation p<0.001, p=0.001). Performance evaluation was divided into two groups, with 0 and 1 as a group and 2 and 3 as another group, and analysis and survival graph were performed. After this distinction, the mOS of the ECOG-PS 0 and 1 group was 84 months (SE: 15.3, 95% CL: 54-114), while the mOS of the PS 2 and 3 group was 34 months (SE: 5.0, 95% CL: 28.2-47.9). This relationship is shown in Figure 7 and 8.

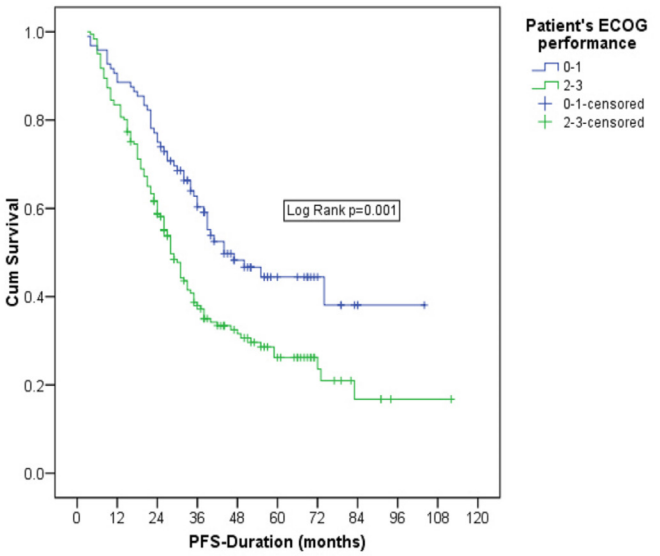

Figure 8. OS figure when patient's evaluated ECOG-PS as 0-1 and 2-3, the simplified version

In the Cox Regression analysis of the univariate effects of risk factors for mortality, the following factors were identified as posing an increased risk: advanced age, being female as opposed to male, having lung cancer as opposed to other cancers, smoking as opposed to non-smoking, having a high SII score as opposed to a low one, being in the SII score groups calculated at diagnosis 3 and above as opposed to group 1, coding the metastatic status in the solid cancer parameter of the CCI as local/locally advanced, the presence of physical activity limitation (ECOG-PS:1) in the doctor's patient performance evaluation as opposed to being active (ECOG-PS:0), having some limitations but still being able to perform daily activities (ECOG-PS:2), spending more than half the day in bed and having limitations in daily activities (ECOG-

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PS:3), as opposed to being in ECOG-PS:0 group, having HALP score group 4 as calculated during the study as opposed to group 1. All these were identified as risk factors for death. On the other hand, being diagnosed with breast cancer as opposed to other cancers, being in stage 1, 2, and 3 as opposed to stage 4, having a high HI score as opposed to a low one, being in the 3rd group in HI score grouping as opposed to the 1st group, having a high HALP score as calculated during the study as opposed to a low one, being in the HALP score groups 4-5-6 as calculated during the study as opposed to the 2nd group, having no or mild Promis depression status as opposed to moderate and severe depression status, being in group 1 of SII study groups calculated during the study, as opposed to group 2, were identified as protective factors against death. In the multivariate Cox Regression Analysis model for death risk factors, lung cancer, SII score, increase in the CCI, and ECOG-PS 3 according to Doctor's performance evaluation ECOG-PS 0 were seen as risk factors, while breast cancer was identified as a protective factor. Table 7 shows the Mortality Risk Factors Univariate and Multivariable Cox Regression Analysis.

Table.7 Mortality risk factors univariate and multivariate Cox Regression Analysis

		p	HR	95% CI (Min-Max)
Age	<0.001	1.089	1.062	1.062
Gender (Ref: female) male	0.004	1.723	1.195	1.195
Diagnosis				
Lung	<0.001	4.500	2.907	2.907
Breast	<0.001	0.146	0.064	0.064
GI (Gastrointestinal System)	0.552	1.119	0.772	0.772
GU (Genitourinary System)	0.470	1.148	0.790	0.790
Others	0.226	0.575	0.235	0.235
Stage of diagnosis (Stage 4)	<0.001			
Early	0.013	0.141	0.030	0.030
Locally advanced	<0.001	0.132	0.075	0.075
Advanced	<0.001	0.289	0.185	0.185
Alcohol	0.373	0.816	0.523	0.523
Smoking	<0.001	2.759	1.906	1.906
Hollingshead Index	0.001	0.979	0.968	0.968
Hollingshead Index (Ref: 1)	0.020			
2	0.312	0.817	0.553	0.553
3	0.006	0.406	0.214	0.214
4	0.073	0.490	0.225	0.225
SII score	<0.001	1.001	1.001	1.001
SII group (Ref: 1)	<0.001			
2	0.079	2.671	0.892	0.892
3	<0.001	6.441	2.260	2.260
4	<0.001	7.781	2.695	2.695
5	<0.001	14.017	4.802	4.802
6	<0.001	8.327	2.831	2.831
7	<0.001	9.715	2.717	2.717
8	<0.001	17.141	4.544	4.544
HALP score	<0.001	0.434	0.325	0.325
HALP score (Ref: 2)	<0.001			
3	0.191	0.769	0.519	0.519
4	0.002	0.407	0.231	0.231
5	<0.001	0.115	0.036	0.036
6	0.012	0.080	0.011	0.011
7	0.109	0.198	0.027	0.027
8	0.209	0.281	0.039	0.039

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Table.7 Mortality risk factors univariate and multivariate Cox Regression Analysis

		p	HR	95% CI (Min-Max)
Charlson Comorbidity Index	<0.001	1.389	1.302	1.302
Solid State Comorbidity Index (Ref: local/locally) metastatic	<0.001	5.028	3.392	3.392
Doctor's performance evaluation (Ref: active)	<0.001			
ECOG-PS 1	0.013	3.585	1.306	1.306
ECOG-PS 2	<0.001	10.187	3.672	3.672
ECOG-PS 3	<0.001	23.541	5.794	5.794
Patient performance evaluation (Ref: active)	<0.001			
ECOG-PS 1	0.408	1.837	0.436	0.436
ECOG-PS 2	0.046	4.175	1.026	1.026
ECOG-PS 3	0.032	5.079	1.154	1.154
PROMIS depression comment (Ref: none, mild)	0.001			
Moderate	0.003	0.525	0.343	0.343
Mid	<0.001	0.413	0.256	0.256
Severe	0.952	0.000		
PROMIS anxiety comment (Ref: none, mild)	0.126			
Moderate	0.297	0.803	0.532	0.532
Mid	0.056	0.641	0.406	0.406
Severe	0.111	0.317	0.077	0.077
SII study	0.763	1.000	0.999	0.999
SII study group (Ref: 1)	0.090			
2	0.003	0.504	0.320	0.320
3	0.712	0.910	0.553	0.553
4	0.947	1.023	0.519	0.519
5	0.922	0.958	0.411	0.411
6	0.850	0.873	0.212	0.212
7	0.444	1.577	0.491	0.491
HALP study	0.687	1.038	0.867	0.867
HALP study group (Ref: 1)	0.096			
2	0.669	1.131	0.642	0.642
3	0.165	1.480	0.851	0.851
4	0.016	2.148	1.156	1.156
5	0.506	0.692	0.234	0.234
6	0.715	0.687	0.092	0.092
7	0.663	0.639	0.085	0.085
Multivariate Cox Regression Analysis of mortality risk factors				
Age	0.058	0.962	0.925	0.925
Diagnosis				
Lung	<0.001	7.598	2.670	2.670
Breast	0.028	0.247	0.071	0.071
GI (Gastrointestinal System)	0.377	1.559	0.582	0.582
GU (Genitourinary System)	0.554	1.352	0.498	0.498

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Table.7 Mortality risk factors univariate and multivariate Cox Regression Analysis

		p	HR	95% CI (Min-Max)
Others	.			
SII score	0.541	1.000	0.999	0.999
HALP score	0.090	0.635	0.376	0.376
Charlson Comorbidity Index	<0.001	1.419	1.276	1.276
Doctor's performance evaluation (Ref: ECOG-PS 0)	0.001			
ECOG-PS 1	0.960	0.968	0.269	0.269
ECOG-PS 2	0.685	1.330	0.335	0.335
ECOG-PS 3	0.006	12.740	2.102	2.102
Patient's performance evaluation (Ref: ECOG-PS 0)	0.123			
ECOG-PS 1	0.615	1.565	0.273	0.273
ECOG-PS 2	0.348	2.396	0.386	0.386
ECOG-PS 3	0.857	1.197	0.169	0.169
PROMIS depression comment (Ref: none, mild)	0.758			
Moderate	0.329	0.771	0.457	0.457
Mid	0.388	0.763	0.413	0.413
Severe	0.964			

Discussion

In our study, we demonstrated the impact of ECOG-PS, a short, easily understandable part of the global oncology language used worldwide from decision-making in oncology treatment or monitoring to predicting prognosis, on progression and survival. Additionally, we identified that ECOG-PS, while demonstrating its prognostic effect on cancer, is also a useful parameter reflecting the depression and anxiety status of patients. While showing the impact of ECOG-PS determined by doctors on oncological outcomes, we simultaneously tried to reveal the effects and reasons for differences between the self-ECOG-PS determined by the patients themselves and the two evaluations.

1- In our study, while demonstrating the prognostic effect of ECOG-PS on cancer, it was also determined to be a useful parameter reflecting patients' depression and anxiety status. The difference between the self-ECOG-PS levels evaluated by patients and the ECOG-PS levels evaluated by doctors and their effects on prognosis and survival were also shown. Additionally, uniquely compared to studies in the literature review, we believe we will contribute significantly to the literature by demonstrating the influence of patient and doctor-sourced factors that could provide insight into the reasons for the differences in the performance score evaluations in our study.

2- In our study, we examined the effects of ECOG-PS, evaluated by doctors and patients on their own performance score, on progression and survival, and the results of the evaluation difference we revealed between the doctor and patient. While revealing the impact of ECOG-PS, widely used worldwide for everything from decision-making in oncology treatment or monitoring to predicting prognosis, we also demonstrated the factors affecting such an important parameter and the influence of doctor and patient-sourced factors that could cause a difference between doctor and patient performance evaluations.

The performance score evaluated by oncologists Conill and colleagues, is an important parameter that has been shown to be an independent factor on the prognosis of patients in studies conducted in the early 1990s [19-21]**.** After these studies, in numerous works of Oken and colleagues, the use of the performance score has become one of the indispensable parameters and an application that can be used by oncologists in practical and daily clinical settings [2,22,23]. Alongside these studies that emphasize the strong aspects of ECOG-PS, the weak aspect of ECOG-PS is that it's a one-dimensional functional score. It's mostly evaluated by the doctor, is subjective, and therefore prone to bias. It does not take into account multimorbidity, frailty, psychological state, or cognitive level. Usually, the PS is recorded only once, deliberately ignoring the patient's changing physical condition. From this perspective, studies have been conducted that aim to determine their own performance scores alongside ECOG-PS, traditionally used by oncologists, and that take into account the differences in performance evaluation levels between the doctor and the patient. In a study by Dajczman and colleagues on this subject, it was determined that performance scores determined by the patients were not consistent with the scores determined by the doctors in 54% of the cases and when they were not consistent, 41/59 (69%) of the patients evaluated themselves as having a worse PS than the doctor's assessment [22]. In our study, while there was a doctor-patient ECOG-PS inconsistency in 51.6% of our patients, when it was not consistent,

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the performance evaluation of the patients was 1 point higher in 90.1% of the cases and 2 points higher in 8.6%. Also, among the non-compliant patients, we found that only 0.9% (n=5) of the patients had a better ECOG-PS according to the doctors.

After the doctor and patient performance evaluations, in studies conducted for the discrepancy or conformity situation arising between the two; Blagden and colleagues [24] identified a moderate level of agreement (weighted κ 0.45) between patients and oncologists, while Ando and colleagues [24] identified a higher agreement (κ score 0.53). In another study conducted by Dajczman and colleagues [22], even though this agreement was found to be moderate (Kappa coefficient=0.42), in the study group selected only from patients receiving active chemotherapy, actually, more than half of the patients did not show agreement with the performance decision given by the doctors and even a considerable portion of the patients were grouped as ECOG-PS 2, which should be excluded from the study for patients receiving active chemotherapy. In the study conducted by Blanden and colleagues mentioned above, a moderate performance evaluation relationship between the patient and doctors was identified, but at the same time, they mentioned that performance scores were evenly distributed and they saw this as a discrepancy. In another study by Dajczman and colleagues, this moderate relationship is under debate due to both the large difference in terms of patient-doctor agreement and the unexpected surplus of patients with self-ECOG-PS 2 who are receiving active chemotherapy. They thought this might be due to the patient or doctors not making a correct performance evaluation. However, in our study, this agreement situation regarding the doctor and patient ECOG-PS evaluation was identified at a much weaker level (Kappa Agreement Coefficient 0.22) and it was observed in our study that ECOG-PS evaluated by both doctors and patients did not show an even distribution. This was an important parameter showing the consistency of our study. The ECOG-PS evaluation results of our patients were significantly higher according to the doctors. Nearly half of the patients stated that they had a higher performance score in their own performance evaluation, compared to the performance level determined by the doctors.

In the study conducted by Blagden and colleagues [23], despite there being no statistical difference in subjective PS scoring between female and male patients, they showed that oncologists tend to score female patients more pessimistically than males. In our study, when female and male patients evaluated their own ECOG-PS, while females evaluated their own ECOG-PS worse, it was found that oncologists evaluated males as having worse ECOG-PS. In addition, the difference in performance levels evaluated by both doctors and patients in female patients was statistically significantly higher than in male patients. While this gender difference was attributed to women being pessimistic in the study above, based on the author's subjective interpretation, in our study, this difference could be explained more objectively using anxiety and depression scales. The average Promis depression and anxiety score at diagnosis was statistically significantly higher in females compared to males.

Although there are studies showing a lack of agreement between doctor and patient performance evaluations, the patient's own performance evaluation has not been used for the purpose of making treatment decisions. The disparity in performance evaluation between patients and doctors observed in these studies could be linked to numerous physiological and psychological factors. However, these studies did not incorporate a plan for psychological evaluation. In our study, we focused on the cause of this difference and used a scale that indicated patients' levels of anxiety and depression. The significance of this approach is demonstrated by Hopwood and colleagues who found that 33% of patients with lung cancer reported having depressive illness which could potentially negatively affect their response to treatment [25]. Even though ECOG-PS is a universally accepted standard score, it is undeniable that there are numerous factors that could lead to subjective assessment. Therefore, one of the most important parameters we incorporated into our study design was the PROMIS depression and anxiety scale that we used to indicate patients' depression and anxiety states.

The PROMIS is a recently employed and effective method of measurement and has been reported to be applicable to all patients and diseases. [26]. Patient-reported outcomes, scored and defined with specific scales, can identify patients' ultimate psychosocial statuses, enabling more accurate treatment planning. One of the previous studies in this field, carried out by Ando and colleagues, highlighted the significant difference between performance scores rated by patients and oncologists and indicated that depression could act as a confounder when functional status is in question [24]. While the study conducted by Ando and colleagues incorporated nurses' assessments in a distinctively designed study, they demonstrated that oncologists could better predict performance scores. However, their study, which only included one type of cancer, might not represent the psychological distress in patients with other types of cancer. In our study, we conducted analyses of patients' depression and anxiety and examined the factors that could influence them. Factors such as being female, being unemployed, having a higher level of education, being a healthcare worker, and living in more central locations were found to correlate with higher depression and anxiety scores. However, we found that having breast cancer, a history of surgery, and being born in the Marmara or Central Anatolia regions only increased depression scores, while being married increased anxiety scores. In the correlation analyses; a weak and inverse significant relationship was found between the PROMIS depression score and age (r=-0.462), educational level (r=-0.220), and CCI (r=-0.253), while a positive significant relationship was detected with the HI (r=0.238) and the number of patients seen on the day of the study (0.287). A weak and inverse significant relationship was also found between the PROMIS anxiety score and age (r=-0.441), educational level (r=-0.172), and CCI (r=-0.199), while a positive significant relationship was detected with the HI (r=0.313) and stage at diagnosis (r=0.132).

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Finally, when examining the relationship between patients' identified PROMIS depression and anxiety statuses and their ECOG-PS levels; surprisingly, a weak and inverse relationship was found between the PS determined by doctors and patients' depression status. When patients evaluated their own performance, we found that the higher their depression and anxiety scores, the higher they rated their self-ECOG-PS levels. Although this was not one of the main findings of our study, Hsien and colleagues [27] have examined the relationship between patients' depression and anxiety statuses and the performance evaluation between patients and doctors. In this differently angled evaluation, they have highlighted the practical significance of quickly screening psychological distress in the cancer clinic using ECOG PS scoring and have indicated a relationship between psychosomatic complaints and psychological distress. They noted that this indirect relationship obtained with ECOG-PS could provide insight into patients' anxiety or depression status when evaluating their own performance. The above results in our study are confirmatory of this previous work and we have emphasized that self-ECOG-PS evaluation is a useful parameter that also reflects patients' anxiety and depression statuses.

In our study, the anxiety and depression statuses of the patients were determined based on the survey results they provided while determining their self-ECOG-PS. We established a relationship between the ECOG-PS evaluated by the patients and doctors and the patients' depression status. Between the depression level determined by patients' own ECOG-PS; as the performance score increased, the depression level worsened as expected, but interestingly and in complete contrast, the worse the patients' depression status, the better the doctors showed the patients' performance level. As a reflection of this situation, we showed that as the difference in the level of patient-doctor performance evaluation increased, the patients' depression status also increased. The majority of patients with mild depression had either no difference or -1, while in those with moderate depression, the difference was 1 in more patients, and in severe depression, this difference significantly increased to reach 2. From this perspective, patients who could affect the clear difference that emerged were evaluated regarding demographic data, comorbidities, and oncological diagnosis, stage, and treatment statuses, primarily depression-anxiety statuses. The number of patients seen by the oncologist conducting the study on the day of our study was also included in the analyses, considering it could be a significant parameter that could affect this difference.

When examining the factors associated with the patient performance evaluated by the doctors, we detected a weak inverse relationship with the HI score we used to determine patients' SES (r=-0.127). This is an expected situation, and we believe that as the SES level increases, a better performance evaluation could be expected. There are studies showing that SES affects cancer patients at different levels. In a study conducted by Stavraki and colleagues, a weak relationship was identified between the HI score, indicating SES in cancer patients, and survival in breast and prostate cancers [28]. In another study by Herndon and colleagues, the negative impact of low SES on breast cancer survival was shown [29]. A weak negative relationship was found between the performance score evaluated by the doctors and the patients' PROMIS depression score (r=-0.198). This could be considered as an indication that the psychosocial status of patients is not taken into account when the traditional ECOG-PS is clinically evaluated. In our study, we found a positive relationship as a result of clinical evaluation between doctors' ECOG-PS evaluation and patients' CCI (r=0.344). A similar relationship between the comorbidity status and ECOG-PS has been demonstrated in a study conducted by Ozgun and colleagues [30].

When analyzing the factors related to patients' self-assessment of their performance results; a reverse relationship with the HI (r=-0.122) and a direct relationship with the CCI (r=0.317) were present as expected. We showed that the higher the patients' PROMIS depression (r=0.255) and anxiety scores (r=0.140), the more they evaluated their performance as poor.

In addition to the PS and related factors evaluated by doctors and patients, factors associated with the evaluated difference in performance level between doctors and patients were also examined. Among the factors affecting this difference was the "number of patients seen in the outpatient clinic on the day of the assessments," a factor we thought could affect the doctor's performance decision, for which there are no reviews in the literature. In conclusion, we showed that the higher the performance evaluation difference between the doctor and patient, the significantly greater the number of patients seen in the outpatient clinic where the evaluation was made (r=0.474). Although there is no study directly similar to ours, in a study conducted by Atasoy and colleagues, it has been noted that busy outpatient conditions could hinder the recording and grading of side effects, and cause difficulties in patients' correct evaluation [31]. As a result, while various patient-related factors related to ECOG-PS evaluation have been researched in the literature, we found that we are the first to look at one of the factors related to the doctor. The fact that the difference between patient and doctor performance evaluation in a busy outpatient clinic is increasing even more is important in indicating not only concerns about whether ECOG-PS is evaluated correctly, but also that patients are not evaluated with sufficient accuracy in terms of psychosocial aspects. As seen in the results mentioned above, it has been shown that patients' self-ECOG-PS evaluation is associated with their depression and anxiety scores. We determined that the most significant cause of the performance difference between patient and doctor stems from patients assessing themselves one or two levels worse than doctors. With these results, it can be said that patients' psychological states are taken into account less in clinics where many patients are treated. Actually, in relation to this result, the greater the difference in performance assessment between doctor and patient - which was actually due to patients assessing their performance as worse than doctors - the higher the patients'

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PROMIS depression (r=0.503) and anxiety scores (r=0.254). While patients might be evaluated worse as a result of being affected by their psychological status in their own performance assessments, doctors could not make a correct evaluation associated with these states of patients, the busier they were with treating patients. Another factor related to this evaluation difference was the HI score we used for socioeconomic level. Above, we had mentioned that we found a reverse relationship as an expected result between the HI and each individual doctor and patient performance assessments. Here, only those in the Nurse/Health Officer profession among the occupational groups had a higher difference in performance levels evaluated by doctors and patients than those in the Farmer/Fishing profession (p=0.005). In our study, a significant increase in both depression (r=0.238) and anxiety (r=0.313) scores as the HI increased can explain that this performance evaluation difference with the HI is through depression and anxiety states. In a study conducted by Fond and colleagues, the relationship between profession and depression status and the situation in health workers, in particular, have been demonstrated [32]. From this perspective, the higher doctor-patient evaluation difference we found in our study especially in the Nurse/Health Officer working group compared to those in the Farmer/Fishing profession can be explained by higher depression and anxiety scores as the HI increases.

In a study conducted by Bonomi and colleagues on hospitalized patients, univariate and multivariate analyses have shown that PS 0, 1, and 2 evaluations by Oncologists successfully determined survival, whereas patients themselves could not distinguish the survival of PS 1 and 2 patients [33]. On the contrary, Loprinzi and colleagues, in their study, suggested that patient-assessed PS could provide independent prognostic information, however, this prognostic value disappeared in their advanced statistical modeling [9]. In our study, while no significant difference was found in terms of progression among other ECOG-PS evaluation levels compared to those with ECOG-PS 0 in the assessment of their own ECOG-PS by patients, it was found that the doctor's evaluation of patient performance increased the risk of progression 3.1 times (HR: 3.080, 95% CI: 1.671-5.675) for those with ECOG-PS 2 compared to those with ECOG-PS 0, and 5 times (HR: 4.980, 95% CI: 1.405-17.646) for those with ECOG-PS 3 compared to those with ECOG-PS 0. When these results were adjusted according to PROMIS depression-anxiety statuses, those with ECOG-PS 2 were found to be 3.1 times and those evaluated as ECOG-PS 3 were found to be 5.7 times the risk factor for progression compared to those with ECOG-PS 0. No difference was observed in terms of progression when the results of patient self-ECOG-PS assessment and doctor-patient performance assessment were adjusted according to the PROMIS depression-anxiety status.

We demonstrated that, as expected, ECOG-PS results evaluated by doctors could predict PFS and OS durations. The worse the ECOG-PS, the shorter the mPFS (55 months in ECOG-PS 0, 36 months in ECOG-PS 1, 20 months in ECOG-PS 2, and 18 months in ECOG-PS 3) and mOS durations (mOS of the group with ECOG-PS 0 and 1 was 84 months, while the group with PS 2 and 3.

According to the patient's self-ECOG-PS evaluations, the only significant difference in terms of m PFS was between ECOG-PS 1 and 2 (m PFS 47 months in self-ECOG-PS 1 vs. m PFS 28 months in ECOG-PS 2). From this perspective, just like we did not observe the effect of patient self-ECOG-PS in predicting progression, it was determined that patient self-ECOG-PS did not have as significant an effect on PFS as the ECOG-PS evaluated by doctors. As a result, the fact that mPFS durations are longer according to similar ECOG-PS levels determined by doctors (38 months in Doctor ECOG-PS 0-1 vs 44 months in patient self-ECOG-PS 0-1 and 20 months in Doctor ECOG-PS 2-3 vs 28 months in patient self-ECOG-PS 2-3) suggested that patients evaluated themselves with worse and less accurate performance in terms of progression status and duration. However, it was observed that the mOS durations determined by the patients' self-ECOG-PS were more accurately predicted than the mPFS durations for OS (mOS of the group with ECOG-PS 0 and 1 was 84 months, while the group with PS 2 and 3 had mOS of 34 months). In fact, the mOS duration according to self-ECOG-PS 0-1 was the same as the mOS duration according to the ECOG-PS 0-1 determined by doctors (mOS 84 months; Doctor SE 14.6, 95% CI: 55.4-112.6 vs Patient SE: 15.3, 95% CI: 54-114). However, when mOS was evaluated according to self-ECOG-PS 2-3 level (34 months vs 26 months), there was a longer mOS duration compared to the doctors. This situation was thought to arise from patients seeing their own performance levels worse due to increased depression and anxiety scores as the self-ECOG-PS assessment level increases. Because we demonstrated that the patient-doctor performance evaluation difference did not have a statistically significant effect on survival compared to those without evaluation difference when adjusted for PROMIS depression-anxiety score statuses.

There are many factors that can influence mortality. Especially when the heterogeneity of the randomly determined patient population in such a cross-sectional study is concerned, this situation is undeniable. From this perspective, as a result of our univariate and subsequent multivariate analyses; it was found that factors such as age, gender, stage, lung or breast cancer, smoking, inflammatory scores, HI, CCI, doctor and patient ECOG-PS evaluation level, and PROMIS depression status affected survival. However, in the subsequent multivariate analysis, it was found that only factors such as having lung or breast cancer, CCI, and ECOG-PS level evaluated by doctors were associated with survival.

Our study has limitations. Our study is a clinical trial consisting of random patient groups without cross-sectional, prospective randomization. Patients were selected randomly not according to their diseases, but according to their clinic applications, and they are patients who have been under long-term follow-up. From this point of view, its lack of randomization has resulted in

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heterogeneous patient groups. Although this situation increases the confounder effect, we would like to emphasize that it reflects real-life data and reduces the bias handicap, and also allowed us to analyze our study in different types of cancer.

Our study differs from other studies in the literature on self-ECOG-PS, not only by its application in different patient groups, but also by the use of indices and scales for clinical, psychological, and socioeconomic conditions that may affect patients' performance evaluation. From this perspective, while inflammatory indices (SII and HALP) were used for the clinical characteristics of the patients, a special comorbidity index was also used. From a socioeconomic perspective, a special index was used to group according to indicators such as education, profession, marital status, and whether they were actively working or not, and the characteristics of the place they were born and lived in were also examined. As a factor that enhances the importance of the study, the ECOG-PS assessment was evaluated by applying the PROMIS depression and anxiety survey, a special evaluation scale for all patients evaluated by doctors and themselves. When these points are taken into account, it is seen as a study that includes comprehensive and cause-oriented examinations that are not encountered in the literature.

Conclusion

In conclusion, our study found that the consistency between the Doctor ECOG-PS and patient self-ECOG-PS evaluations was low. Factors that could cause this difference were identified in relation to both the levels of depression and anxiety in patients and the patient density in the clinic on the day doctors made their assessments. While identifying this, thanks to the close relationship we determined between self-ECOG-PS and the anxiety and depression levels of patients, it was also demonstrated that the practical application ECOG-PS could be used as a preliminary assessment of anxiety and depression, with the aim of referring the individuals identified for further examination and treatment to the relevant doctors. Ultimately, while emphasizing the known effect of ECOG-PS on survival outcomes, it was particularly demonstrated that the ECOG-PS determined by doctors was more determinant than the self-ECOG-PS determined by patients for progression and PFS. While there were similar survival times for ECOG-PS 0-1 with good performance levels in terms of OS outcomes, survival times evaluated by doctors for ECOG-PS 2-3 were shorter. When this performance evaluation difference between the patient and doctor was corrected according to the results of the PROMIS anxiety and depression scale, we demonstrated that there was no difference in survival compared to those without a doctor and patient ECOG-PS evaluation difference. This finding was considered important in demonstrating how influential the current anxiety and depression states are as a factor in patients' self-ECOG-PS assessment. In the final analysis, while it was shown in the uni- and multivariate analyses of the survival-impacting factors emphasized above that the self-ECOG-PS levels determined by the patients had no effect on survival, only the influence of the doctor ECOG-PS, having breast and lung cancer, and the CCI were demonstrated.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical Approval
The study was approved by the İnönü University Non-Invasive Clinical Research and Publication Ethics Committee (Decision No: 2022/4054).

References

1. Karnofsky DA, Abelmann WH, Craver LF, et al. The use of the nitrogen mustards in the palliative treatment of carcinoma: With particular reference to bronchogenic carcinoma. Cancer. 1948;1:634-56.

2. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5: 649-56.

3. Taylor AE, Olver IN, Sivanthan T, et al. Observer error in grading performance status in cancer patients. Support Care Cancer. 1999;7:332-5.

4. Sargent DJ, Köhne CH, Sanoff HK, et al. Pooled safety and efficacy analysis examining the effect of performance status on outcomes in nine first-line treatment trials using individual data from patients with metastatic colorectal cancer. J Clin Oncol. 2009;27:1948-55.

5. Chow E, Harth T, Hruby G, et al. How accurate are physicians' clinical predictions of survival and the available prognostic tools in estimating survival times in terminally ill cancer patients? A systematic review. Clin Oncol (R Coll Radiol). 2001;13:209-18.

6. Kelly CM, Shahrokni A. Moving beyond Karnofsky and ECOG performance status assessments with new technologies. J Oncol. 2016;2016:6186543.

7. Ahles TA, Blanchard EB, Ruckdeschel JC. The multidimensional nature of cancer-related pain. Pain. 1983;17:277-88.

8. Atkinson TM, Andreotti CF, Roberts KE, et al. The level of association between functional performance status measures and patient-reported outcomes in cancer patients: a systematic review. Support Care Cancer. 2015;23:3645-52.

9. Loprinzi CL, Laurie JA, Wieand HS, et al. Prospective evaluation of prognostic variables from patient-completed questionnaires. North Central Cancer Treatment Group. J Clin Oncol. 1994;12:601-7.

10. Schnadig ID, Fromme EK, Loprinzi CL, et al. Patient–physician disagreement regarding performance status is associated with worse survivorship in patients with advanced cancer. Cancer. 2008;113:2205-14.

11. Hollingshead AA. Four-factor index of social status. Unpublished manuscript, Yale University, New Haven, CT. 1975.

12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373-83.

13. Chen XL, Xue L, Wang W, et al. Prognostic significance of the combination of preoperative hemoglobin, albumin, lymphocyte and platelet in patients with gastric carcinoma: a retrospective cohort study. Oncotarget. 2015;6:41370-82.

14. Hu B, Yang XR, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Res. 2014;20: 6212-22.

15. Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. J Clin Epidemiol. 2010;63:1179-94.

16. Pilkonis PA, Choi SW, Reise SP, et al. Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS): depression, anxiety, and anger. Assessment. 2011;18:263-283.

17. Aşık E, Çökmüş F, Aydemir O, et al. Reliability and validity of Turkish Form of Level 2 Anxiety Scale. Anatolian Journal of Psychiatry. 2017;18:45-50.

18. Dikici DS, Aşçıbaşı K, Aydemir Ö, et al. Reliability and validity of Turkish Versionof DSM-5 Depression Scale. Anatolian Journal of Psychiatry. 2017;18:51-6.

19. Conill C, Verger E, Salamero M. Performance status assessment in cancer patients. Cancer. 1990;65:1864-6.

20. Roila F, Lupattelli M, Sassi M, et al. Intra and interobserver variability in cancer patients' performance status assessed according to Karnofsky and ECOG scales. Ann Oncol. 1991;2:437-9.

21. Sørensen JB, Klee M, Palshof T, Hansen HH. Performance status assessment in cancer patients. An inter-observer variability study. Br J Cancer. 1993;67:773-5.

22. Dajczman E, Kasymjanova G, Kreisman H, et al. Should patient-rated performance status affect treatment decisions in advanced lung cancer?. J Thorac Oncol. 2008;3:1133-6.

23. Blagden SP, Charman SC, Sharples LD, et al. Performance status score: do patients and their oncologists agree?. Br J Cancer. 2003;89:1022-7.

24. Ando M, Ando Y, Hasegawa Y, et al. Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. Br J Cancer. 2001;85:1634-9.

25. Hopwood P, Stephens RJ. Depression in patients with lung cancer: prevalence and risk factors derived from quality-of-life data. J Clin Oncol. 2000;18:893-903.

26. Voloshin I. Editorial commentary: Patient-Reported Outcomes Measurement Information System (PROMIS) is important part of future clinical research. Arthroscopy. 2020;36:1429-30.

27. Mei Hsien CC, Wan Azman WA, Yusof M, et al. Discrepancy in patient-rated and oncologist-rated performance status on depression and anxiety in cancer: a prospective study protocol. BMJ Open. 2012;2:e001799.

28. Stavraky KM, Skillings JR, Stitt LW, Gwadry-Sridhar F. The effect of socioeconomic status on the long-term outcome of cancer, Journal of Clinical Epidemiology. 1996;49:1155-60.

29. Herndon JE, Kornblith AB, Holland JC, Paskett ED. Effect of socioeconomic status as measured by education level on survival in breast cancer clinical trials. Psycho-oncology. 2013;22:315-23.

30. Özgün MA, Karagöz B, Bilgi O, et al. The prognostic significance of comorbidity and relation of comorbidity with the other prognostic factors in patients with non small cell lung cancer. International Journal of Hematology and Oncology. 2009;19:63-8.

31. Atasoy BM, Ünsal DK, Dinçbaş, FÖ, et al. The results of questionnaire on assessing and reporting of side effects in Turkey: "Turkish Oncology Group (TOG) Early-Late Side Effects Working Party" study. Türk Onkoloji Dergisi. 2007;22:13-9.

32. Fond G, Fernandes S, Lucas G, et al. Depression in healthcare workers: results from the nationwide AMADEUS survey. Int J Nurs Stud. 2022;135:104328.

33. Bonomi P, Gale M, Rowland K, et al. Pre-treatment prognostic factors in stage III non-small cell lung cancer patients receiving combined modality treatment. Int J Radiat Oncol Biol Phys. 1991;20:247-52.