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Research Article

# Can survival in cancer patients be accurately predicted with the Palliative Performance Scale?

## Kanser hastalarında sağkalım Palyatif Performans Skalası ile doğru olarak tahmin edilebilir mi?

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## Abstract

**Introduction:** Palliative Performance Scale (PPS), Karnofsky Performance Scale (KPS) and the Edmonton Symptom Assessment Scale (ESAS) are widely used prognostic scales in palliative care unit. Institutionalized palliative care services in our country are quite new compared to the practices in many countries. We do not have concrete data on the compatibility of these scales, which are developed with patient data from other countries, in our own palliative care practices with real cases. In this study, we aimed to evaluate the convenience of the Turkish versions of these scales on the first days of hospitalization of terminal cancer patients who were followed up in the palliative clinic of our hospital. We also questioned whether the initial estimated survival and actual survival were compatible.

**Methods**: PPS, KPS and ESAS on the first days of hospitalization of terminal cancer patients, hospitalized in the palliative clinic of our hospital between November 14, 2016 and November 14, 2017, were retrospectively evaluated one year later (n = 222). The survivors and those who lost their lives were determined. The survival estimates with PPS of the patients who died were compared with their actual survival.

**Results**: The average age of 222 patients (18% female, 82% male) participating in the study was 64.49 ± 11.62, and the range was 26-91. PPS, KPS, ESAS were determined as a mean value of 34.40±18.00 (min. 10-max. 90), 32.90±17.50 (min. 10-max. 90), 56.10±15.65 (min. 2-max. 90), respectively. The AUC of PPS is 0.83 ($p<0.001$) and the AUC of KPS is 0.78 ($p<0.001$) suggesting that KPS and PPS has at least one tie between alive and dead patients, which is 45%. Median survival time was found 14.00, 95% C.I. [10.87–17.13].

**Conclusion**: In our study, it was found that as the KPS and PPS scores decrease, the survival time of terminal cancer patients decrease. Patients with PPS <45% had a higher risk of death (sensitivity 71%, specificity 80%), patients with KPS <45% had a higher risk of death (sensitivity 60%, specificity 81%), and patients with ESAS> 60.50 had a higher risk of death (sensitivity 93%, specificity 45%). PPS is a useful assessment scale for predicting survival of terminal cancer patients in the palliative care unit. We think it is important in determining our patient-specific palliative approach and treatments.

**Keywords**: Palliative Performance Scale, Karnofsky Performance Status, Palliative Care

## Öz

**Giriş:** Palyatif Performans Ölçeği (PPS), Karnofsky Performans Ölçeği (KPS) ve Edmonton Semptom Değerlendirme Ölçeği (ESAS), palyatif bakım servislerinde yaygın olarak kullanılan prognostik ölçeklerdir. Ülkemizde kurumsallaşmış palyatif bakım hizmetleri birçok ülkedeki uygulamalara göre oldukça yenidir. Başka ülkelerdeki hasta verileriyle geliştirilen bu skalaların kendi palyatif bakım uygulamalarımızda oluşturduğu tahminlerin gerçek yaşamla uygunluğu konusunda somutlaşmış verilere sahip değiliz. Bu çalışmamızda, hastanemiz palyatif kliniğinde takip edilen terminal dönem kanser hastalarının ilk yatış günlerinde, bu ölçeklerin Türkçe versiyonlarının uygunluğunu değerlendirmeyi amaçladık. Ayrıca başlangıçtaki tahmini sağkalımla gerçek sağkalımın uygun olup olmadığını sorguladık.

**Yöntem**: 14 Kasım 2016 ile 14 Kasım 2017 tarihleri arasında hastanemiz palyatif kliniğinde yatan terminal kanser olgularının ilk yatış günlerindeki PPS, KPS ve ESAS, bir yıl sonra retrospektif olarak değerlendirildi (n=222). Hayatta kalanlar ve hayatını kaybedenler belirlendi. Ölen hastaların PPS ile yapılan sağkalım tahminleri gerçek sağkalımlarıyla karşılaştırıldı.

**Bulgular**: Çalışmaya katılan 222 hastanın (%18 kadın, %82 erkek) yaşlarının ortalaması 64.49±11.62, aralığı ise 26-91'di. PPS ortalama değeri 34,40 ± 18,00 (min. 10-maks. 90), KPS 32,90 ± 17,50 (min. 10-maks. 90), ESAS 56,10±15,65 (min. 2-maks. 90) olarak saptandı. PPS için AUC değeri 0,83 ($p<0,001$), KPS için ise 0,78 ($p<0,001$) olarak hesaplandı ve %45 eşik değerine ulaşıldı. Medyan sağkalım süresi 14 gün (95% C.I. [10.87–17.13]) olarak bulundu.

**Sonuç**: Çalışmamızda KPS ve PPS skorları düştükçe terminal kanser hastalarının sağkalım sürelerinin azaldığı saptandı. PPS <%45 olan hastalarda ölüm riski daha yüksek bulundu (duyarlılık %71, özgüllük %80), KPS <%45 olan hastalarda ölüm riski daha yüksek bulundu (duyarlılık %60, özgüllük %81) ve ESAS >60.50 olan hastalarda ölüm riski daha yüksek bulundu (duyarlılık %93, özgüllük %45). PPS, palyatif bakım ünitesinde terminal kanser hastalarının sağkalım tahmininde kullanışlı bir değerlendirme ölçeğidir. Hastaya özgü palyatif yaklaşım ve tedavilerimizin belirlenmesinde önemli olduğunu düşünüyoruz.

**Anahtar Kelimeler**: Palyatif Performans Ölçeği, sağkalım, kanser

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## Introduction

Acceleration of aging of the population and the prevalence of life-limiting illnesses such as cancers lead to a requirement of palliative approach in clinical practice. The Palliative Care approach includes the early stage of oncologic diagnosis, the advanced disease period and even the end of life. Prognostic information provides the patients the transition from curative treatments to proper supportive care and the preparation on the end of life. Symptom burden and patients' frailty lead to expectation of survival knowledge by patient's relatives.

However, in such situations, it is not easy to assess the diagnosis, stages, degrees of symptom distress and treatment type. Measuring the symptom burden by ESAS may contribute to the clinician to estimate the survival. The Edmonton Symptom Assessment System (ESAS) is a validated, trusted and simplistic instrument proposed to evaluate various symptoms in patients of palliative care [1]. The ESAS scale shows the symptom burden in the palliative care unit (PCU).

There are many studies on prognostic models used in survival prediction. However, increasing the prognostic suitability, the accuracy of the predictions, and proving the reliability and validity of the prediction measurements with a large number of cases, determining the important parameters in the prognosis are the main subject of future prognosis studies in palliative care [2]. The Karnofsky Performance Scale is widely used for performance assessment of cancer patients [3]. In addition, the Palliative Performance Scale (PPS) as a prognostic performance model was adapted from the Karnofsky Performance Scale and divided into 11 classes from the death (0%) to the health (100%) [4].

Although our hospital is a reference center for lung cancer, the palliative care unit started to be established in 2016 quite recently. Institutionalized palliative care services in our country are quite new compared to the practices in many countries. Karnofsky Performance Scale, Palliative Performance Scale, the Edmonton Symptom Assessment Scale are widely used scales. We do not have enough information that has been evaluated with the data of our own patients about the compatibility of these scales, which are developed with patient data from other countries, with real life predictions in our own palliative care practices. Applying Turkish versions of these scales to our terminal cancer patients in palliative care unit would enable us to evaluate the suitability of the predictive survival with actual survival, to refrain from excessive treatment, to inform accurately patient's family and, to control symptoms.

In this study, we aimed to evaluate performance measurement such as KPS and PPS and symptom burden with ESAS at the beginning of the hospitalized days in palliative care settings of our terminal cancer patients. The secondary purpose of our study is to indicate whether the initial survival prediction is suitable with true survival.

## Methods

The patients were included consecutively admitted to our Palliative Care Unit (PCU) in a reference Chest Disease Center in İstanbul from November 14, 2016 to November 14, 2017.This unit commenced its service on November 14, 2016. The patients had been admitted to this unit from other chest disease wards, the emergency department and outpatient clinics for palliative and supportive care. However, the study was retrospectively achieved in November 2018.

Non-cancer patients (advanced stage COPD, elderly pneumonia, interstitial lung disease etc., n=50/272) and the patients under the age of 18 were excluded from the study. All non-curative cancer patients were followed up at palliative care unit in our hospital (n=222/272), where some of them died**.** We looked back on all patient data at the specified dates above one year later. Mortality data of the discharged patients was obtained from national death notification system after one year (2018), also. The patients who died and survived as well as those living less than 30 days and more than 30 days were identified when the study was conducted.

Patients' data had been recorded on the first 1-3 days of their hospitalization. Yedikule Chest Diseases Hospital ethics committee reviewed and approved the database for using this study (August 6, 2020- No: 10). PPS score was modified from Karnofsky Performance Scale's functional status of ambulation, activity level, evidence of disease, and amounts of self-care oral intake, level of consciousness [5-7].

The Edmonton Symptom Assessment System (ESAS) is a validated self-reported tool to measure the nine prevalent symptoms of cancer [1].All patients' baseline prognostic evaluations were performed on the first two days of hospitalization by using Palliative Performance Scale (PPS), Karnofsky Performance Scale (KPS) and Edmonton Symptom Assessment System (ESAS) for standardized symptom screening.

### Ethical approval, informed consent and permissions

Yedikule Chest Diseases Hospital ethics committee granted approval for this study (August 6, 2020- No: 10). At the beginning of their hospitalization, all patients had been informed that their data could be tracked, and their written consents had been received.

### Statistical analysis

IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA) is used for statistical analysis. Descriptive statistics are revealed as number and percentage for categorical variables and mean, standard deviation, minimum, and maximum for scale variables. Shapiro-Wilk test is used to test normality assumption. Comparisons of the two independent patient groups are made by Student's t test when scale variables are normally distributed and when the normality condition is not provided, by Mann Whitney U test. Comparisons of ratios in independent groups are performed with Chi-square test. To examine the relationships, Pearson and Spearman correlations are used for parametric and non-parametric variables, respectively. The survival analyzes are performed with Life Tables and Kaplan-Meier Analysis. Cutoff points are determined by receiver operating characteristic curves and tested by Log-Rank test of equality. The significance level is 0.05.

## Results

Total number of non-curative cancer cases was 222. Mean age was 64.49±11.62 (min 26-max 91). Female/ Male Ratio was 40/182. The most frequent symptom was dyspnea (77.90%) followed by pain, lack of appetite, cough, tiredness, respectively. Hence, 84.70% of patients had lung cancer and 15.30% of cases had other types of cancer. In 188 lung cancer patients, 5.85% (n=11) had small cell lung cancer (SCLC) and 94% (n=177) had non-small cell lung cancer (NSCLC). Distant metastasis was determined in 22.07% of patients (n=49). Bone and liver metastasis were equally frequent (11.26%, n=25). Malign pleural effusion was in 10.81% of patients (n=24). Endobronchial obstruction causing the patients worsen was detected in 4.95% of patients (n=11)). Patients' Edmonton Symptom Assessment Scale (ESAS) was calculated as a mean value of 56.10±15.65 (min. 2-max. 90). When patients' functional status was measured by KPS and PPS, PPS was determined as a mean value of 34.40±18.00 (min. 10-max. 90), KPS was calculated as 32.90±17.50 (min. 10-max. 90) (Table1).

After one year of follow-up, 11.26% of cases were alive and 88.74% of cases were dead. Maximum survival time was 348 days. Median survival time was found 14.00, 95% *C.I. [10.87–17.13]*. While surviving patients have higher Karnofsky and Palliative Performance Scale, they have lower Edmonton Symptom Assessment System than dead patients (respectively, p=0.002, p=0.001, p=0.045). Additionally, the patients who died have more frequent dyspnea symptom (p=0.022). However, there is no other difference in both clinical features and laboratory parameters.

The patients were separated into three groups according to their KPS, PPS, ESAS and Kaplan Meier Survival Analysis was conducted (Table 2, Figure 1). Log-Rank test of equality of survival distributions suggested a significant difference for the different KPS, PPS, ESAS groups (respectively, p<0.001, p<0.001, p=0.016). *As the PPS and KPS decreased and ESAS increased, survival time shortened.*

Receiver Operating Characteristics (ROC) curves of KPS, ESAS and PPS indicators are observed to determine the cutoff points and Area Under Curve (AUC) values. The AUC of KPS is 0.78 (p<0.001) and PPS is 0.83 (p<0.001) suggesting that KPS and PPS has at least one tie between alive and dead patients, which is 45%. The patients, who have KPS and PPS lower than 45%, have more risk than the other patients do (Table 3, Figure 2). The AUC of ESAS is 0.72 (p=0.012) suggesting that ESAS has at least one tie between alive and dead patients which is 60.50. The patients, who have ESAS greater than 60.50, have more risk than the other patients do (Table 3, Figure 2).

Survival time was positively correlated with KPS and PPS showing functional status, negatively correlated with ESAS showing symptom burden.

**Table 1.** Patient features of palliative care unit

| | | **Mean±SD** | **Min-Max** |
|---|---|---|---|
| **Age** | | 64.49±11.62 | 26-91 |
| **Karnofsky Performance Status** | | 32.90±17.50 | 10-90 |
| **Edmonton Symptom Assessment System** | | 56.10±15.65 | 2-90 |
| **Palliative Performance Scale** | | 34.40±18.00 | 10-90 |
| | | **n** | **%** |
| **Gender** | Female | 40 | 18 |
| | Male | 182 | 82 |
| **Symptom** | Pain | 69 | 31 |
| | Dyspnea | 173 | 78 |
| | Cough | 65 | 29 |
| | Hemoptysis | 11 | 5 |
| | Tiredness | 63 | 28 |
| | Lack of appetite | 78 | 35 |
| | Constipation | 11 | 5 |
| | Insomnia | 15 | 7 |
| | Nausea | 13 | 6 |
| | Lack of well-being | 17 | 8 |
| **Diagnosis** | Lung Cancer | 188 | 85 |
| | Brain Tumor | 1 | 1 |
| | Liver Cancer | 1 | 1 |
| | Colon Cancer | 3 | 1 |
| | Laryngeal Cancer | 2 | 1 |
| | Malignant Melanoma | 1 | 1 |
| | Breast Cancer | 9 | 4 |
| | Bladder Cancer | 2 | 1 |
| | Malign Pleural Mesothelioma | 6 | 3 |
| | Gastric Cancer | 1 | 1 |
| | Ovarian Cancer | 1 | 1 |
| | Esophageal Cancer | 3 | 1 |
| | Pancreatic Cancer | 2 | 1 |
| | Prostate Cancer | 1 | 1 |
| | Renal Cancer | 1 | 1 |

**Table 2.** Patient groups for KPS, ESAS and PPS

| | | Mean Survival Time | | Median Survival Time | | |
|---|---|---|---|---|---|---|
| **KPS** | | **Estimate** | **St. Error** | **Estimate** | **St. Error** | **N** |
| | Group 1: [10% – 20%] | 16.19 | 2.25 | 9 | 1.72 | 93 |
| | Group 2: [30% – 60%] | 38.15 | 5.54 | 20 | 3.46 | 75 |
| | Group 3: [70% – 100%] | 118.11 | 23.87 | 83 | 40.31 | 18 |
| **ESAS** | | | | | | |
| | Group 1: [0 – 40] | 48.90 | 9.45 | 34 | 12.24 | 31 |
| | Group 2: [41 – 70] | 37.28 | 5.48 | 14 | 1.81 | 118 |
| | Group 3: [71 – 100] | 18.94 | 5.22 | 8 | 2.39 | 33 |
| **PPS** | | | | | | |
| | Group 1: [10% – 20%] | 14.90 | 2.51 | 9 | 1.56 | 74 |
| | Group 2: [30% – 50%] | 34.83 | 4.63 | 19 | 3.07 | 93 |
| | Group 3: [60% – 100%] | 116.21 | 22.54 | 83 | 34.10 | 19 |

**KPS:** Karnofsky Performance Status, **ESAS:** Edmonton Symptom Assessment System, **PPS:** Palliative Performance Scale. Kaplan Meier Survival Analysis is conducted, and Log-Rank test of equality suggested a significant difference for different groups of KPS, ESAS and PPS.

**Table 3.** ROC Curve Analysis for Prognostic Estimates of Dead and Alive Patients

| | **Sensitivity** | **Specificity** | **AUC** |
|---|---|---|---|
| **KPS (Cutoff Value: 45%)** | 60% | 81% | 0.78 (p<0.001) |
| **ESAS (Cutoff Value: 60.5%)** | 93% | 45% | 0.72 (p=0.012) |
| **PPS (Cutoff Value: 45%)** | 71% | 80% | 0.83 (p<0.001) |

**KPS:** Karnofsky Performance Status, **ESAS:** Edmonton Symptom Assessment System, **PPS:** Palliative Performance Scale. ROC curves are observed to determine the cutoff points.

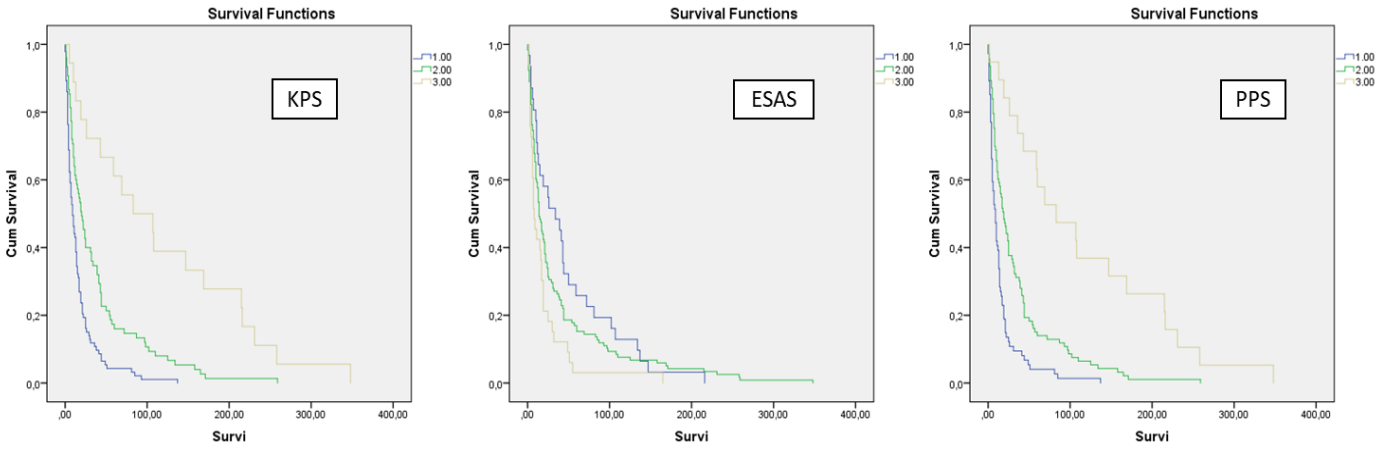


**Figure 1.** Survival functions of different KPS, ESAS and PPS groups (KPS: Karnofsky Performance Status, ESAS: Edmonton Symptom Assessment System, PPS: Palliative Performance Scale, Cum Survival: Cumulative Survival, Survi: Survival)

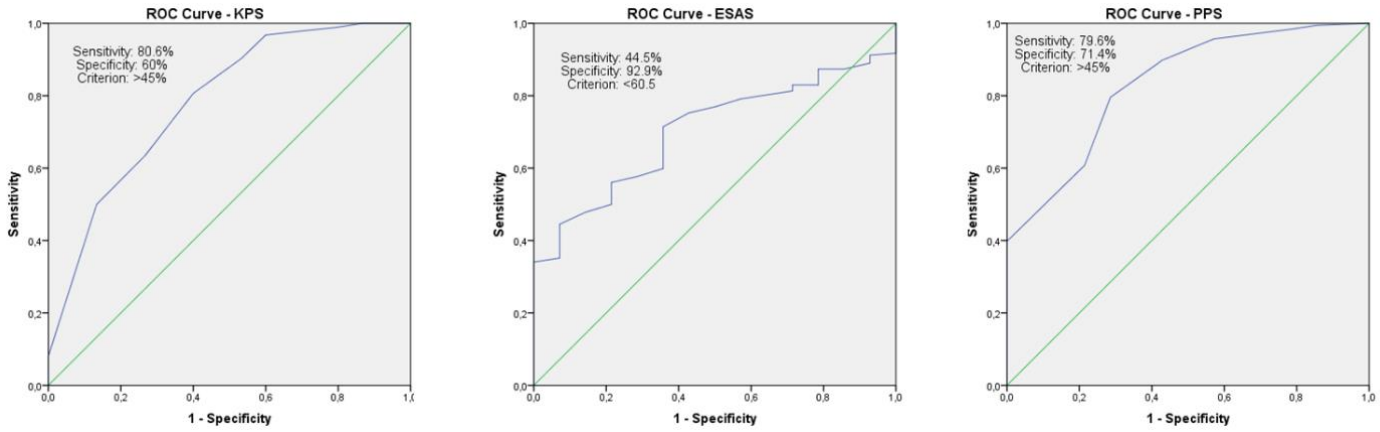


**Figure 2.** ROC Curves – KPS, ESAS and PPS (KPS: Karnofsky Performance Status, ESAS: Edmonton Symptom Assessment System, PPS: Palliative Performance Scale)

## Discussion

In this study, baseline symptoms of cancer patients were determined by palliative care clinicians when referred to Palliative Care Unit (PCU). Additionally, ESAS was calculated as total symptom burden according to self–expressions of patients. Clinicians estimated that the most common symptom was dyspnea (78 %), followed by pain, lack of appetite, cough, tiredness, respectively. Patients' Edmonton Symptom assessment Scale (ESAS) was calculated as 56.10±15.65 (min 2-max 90) in mean within our palliative care unit. As it can be observed, our patients had heavy symptom burden. Since our hospital is a reference center for chest diseases, COPD exacerbations and advanced lung cancers are accepted for general chest inpatients clinical units. Patients who are admitted to the palliative care unit are not likely to receive oncologic treatment, their treatment is terminated, and the terminal stage is established. Some of our cases are end-of-life patients while some of our cases receive supportive treatment in our PCU leading to a large number of clinical case diversity, but in general, the ESAS scale average is high. ESAS is not a diagnostic instrument; it is only a screening tool. The most important role is to call the clinician's attention to the presence and severity of symptoms [8]**.**

The measurement may enable the medical, radiation oncologist and other specialist to decide for referring to PCU. ESAS is moderately associated with performance status in several studies with KPS in review of validity and reliability of the ESAS by Richardson and colleagues [9-11].

In this study, ESAS was negatively correlated with PPS and KPS and similarly, there was a negative association with patient performance status. The ESAS scale was quite high in some patients but very low in some of them. However, the patients were investigated deeply, the causative symptom for hospitalization was hemoptysis and they had no other symptoms. In a study by Yennurajalingam et al, low ESAS scale as 0-2 meant either no symptom or not a clinically significant symptom [12]. We thought that this diversity of clinical conditions was a limiting factor for our study, as well as the presence of a small number of other malignancies besides lung cancer. However, these malignancies were generally sent to our hospital because of lung metastasis.

ESAS scale may change daily, also. Some patients had low ESAS scale at first hospitalization period, while it was elevated in following days in some patients. Inversely, baseline high ESAS scale might decrease in progress. However, one of this study's aims was the relationship between ESAS scale and survival. Mc Gee et al showed that the patients with a higher symptom burden had significantly reduced overall survival. Higher ESAS total symptom burden score showed a tendency to significance as an independent predictor of survival in multivariate analysis in their study [13]. Similarly, we found that the symptom burden measured with ESAS scale was negatively correlated with survival time. Additionally, we determined that the patients who had ESAS greater than 60.50 had more risk than other patients did in our palliative unit. Although our findings support the contribution of ESAS scale to a survival estimate, it cannot be a prognostic indicator alone because of its low specificity.

However, predicting the prognosis of patients is important in the physician's management of treatment in the palliative care unit; furthermore, it is crucial for informing and directing patients, relatives and caregivers. Especially in recent years, due to the violence against physicians and health workers in our country, it has become more important in the management of the mourning period and in the preparation of the patients' relatives. Therefore, functional prognostic measurements and prediction of survival are very important. Already, the main purpose of our study was the evaluation of the concordance between prediction and actual survival**.**

In this study, it was determined that as the measurement of KPS and PPS decreased, the actual survival time also decreased. Mei et al similarly showed a significant difference in survival length for patients across PPS percentile ranges [14]. There was a significant difference between in three percentile range groups (Group 1: 10%-20%, Group 2: 30%-50%, Group 3: 60%-100%) in our study, as well. Additionally, median survival time was 14 days in the whole group.

In the study by Mei et al, the patients who were measured 10%-20% PPS score at baseline assessment had a shorter median survival time of 9 days, compared to other functional status measurement (30%-50%). The median survival time was 19 days for 30%-50% PPS score and 83 days for 60%-100% PPS score. Most of patients in their unit had PPS score in B (40%-60%), whereas most of patients in our unit were in group 1 (10%-20%). Our patients' median survival time was shorter than their patients' survival (14). However, the study by Harrold et al also determined higher mortality rates as 7 days for 10%-20% PPS score [15]. Hence, when focusing on the worsening score relation to shorter survival time, we obtained

same result. Furthermore, the AUC of PPS 0.83 suggested that PPS at least one tie between alive and dead patients, which are 45% (the AUC of KPS is 0.78) in this study. Our patient who had PPS lower than 45% had more risk for death (sensitivity 71%, specificity 80%). The mean PPS baseline score lower than 45% suggests that patients with terminal cancer are likely to be functionally dependent and they have more risk for short survival time. Kim et al reported that the PPS scores are <30%, the predictive accuracy of the PPS for three- and four-week survival was agreeable (AUC=0.73 and 0.77) [16].

The AUC under the ROC curve for PPS at 90 days in the study included hospice patients by Harrold and colleagues was between 0.65 and 0.70 with predictive accuracy being greater for early deaths [15].

Eighteen studies taking place after 2005 concerning the PPS have been examined by Simmons and colleagues. They included the patients diagnosed with several cancer types. They found that the patients with PPS categories greater than 50% had lower hazard ratios than the patients with lower PPS [17]. Lau et al determined that performance status as measured by PPS score is quite predictive for survival time in their largest survival prediction study comprising both cancer and other disease in palliative care setting [18]. In their earlier study, they had already reached same results also in end-of-life cancer patients [5]. Just as other studies, our study stated that the PPS score was a good predictor of survival length [19].Seedhom et al have recently determined that even the non-cancer patients at the emergency department who had a cutoff value >40 had a better survival time [20]. In this study, the cut-off value was >45. When Baik et al reviewed the studies focused on examining the association between the PPS and survival, they found a few studies searched the predictive accuracy of the PPS by using sensitivity, specificity, or AUC [21]. In this regard, our study is important in terms of contributing to optimal survival estimation with PPS by determining the PPS cutoff value.

KPS validity and reliability of Turkish palliative cancer patients was shown [22]. Our patients who had KPS lower than 45% had more risk for death (60% sensitivity, 81% specificity, AUC 0.78). PPS score has been created from Karnofsky Performance Scale's. The PPS and the KPS can be used interchangeably as functional tools and within prognostic tools [23].

## Limitations

Our study should be assessed by noticing the limitations: the study is conducted retrospectively after one year of follow-up and the data was collected in a single palliative care setting of our hospital.

## Conclusion

Median actual survival time of our palliative patients was 14 days. The measurement of KPS and PPS decreased, the actual survival time also decreased. Patients with PPS and KPS <45% had a higher risk of death (AUC =0.83 (PPS), AUC=0.78 (KPS)). PPS is an important indicator of survival prediction with 71% sensitivity and 80% specificity. There is a contribution of ESAS scale to a survival estimate; it cannot be a prognostic indicator alone because of its low specificity (45% specificity). Measuring PPS can provide quite accurate prediction of survival of cancer patients in palliative care unit. This study is important for translating knowledge into practice and identifying appropriate prognostic.

## Conflict of interest

| Author Contributions | | Author Initials |
|---|---|---|
| SCD | Study Conception and Design | GA, FSA, ED |
| AD | Acquisition of Data | FSA |
| AID | Analysis and Interpretation of Data | ED |
| DM | Drafting of Manuscript | GA, FSA, ED |
| CR | Critical Revision | GA, FSA, ED |

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