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Investigation of parameters associated with mortality in a palliative care unit

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Abstract

Introduction: Effective palliative care reduces unnecessary hospital admissions and intensive care length of stay. The present study aimed to investigate the parameters associated with mortality in patients receiving palliative care support.

Material and methods: This prospective observational study was conducted among inpatients in a palliative care unit.

Results: A total of 177 patients hospitalized in the palliative care unit were included in the study. Of the patients, 84 (47.5%) were female and the mean age was 72.49 ±15.12 years. At the end of the follow-up period in the palliative care unit, 67 patients (37.9%) had died. A one-unit increase in albumin was associated with 66.6% lower odds of mortality [odds ratio (OR): 0.334, 95% confidence interval (CI): 0.141–0.791; $p = 0.013$] and a one-unit increase in Karnofsky performance scales (KPS) score was associated with 4.8% lower odds of mortality (OR: 0.952, 95% CI: 0.925–0.980; $p = 0.001$). In contrast, the odds of mortality were 4.851 times higher in patients with congestive heart failure (95% CI: 1.716–13.717; $p = 0.003$), 4.442 times higher in patients with solid organ malignancy (95% CI: 1.420–13.894; $p = 0.01$), 3.727 times in the presence of hypoxia at admission (95% CI: 1.504–9.239; $p = 0.005$), and 3.626 times higher in patients who developed an infection during follow-up (95% CI: 1.523–8.635; $p = 0.004$).

Conclusions: The results of this study suggest that congestive heart failure, solid organ malignancy, hypoxia at admission, infection during follow-up, and low albumin level and KPS score may be indicators of poor outcome.

Key words: mortality, palliative care, parameters.

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INTRODUCTION

Palliative care is specialized medical care focused on optimizing the quality of life of patients with serious and terminal diseases through the collaborative effort of a multidisciplinary team. Palliative care aims to meet patients' spiritual needs through comprehensive assessment and by addressing their pain and other physical and psychosocial problems [1]. Effective palliative care reduces unnecessary hospital admissions and length of stay in intensive care [2–4]. Diseases that require palliative care include motor neuron diseases such as Alzheimer's, advanced organ failure, refractory cancer, and progressive diseases such as AIDS. The World Health Organization stated that 56.8 million people need palliative care every year, and 25.7 million people annually experience the last year of their life in palliative care [5]. Palliative care involves making care and treatment plans for advanced diseases. Estimating prognosis is important to coordinate this plan among patients, families, and medical teams [6, 7].

Studies on palliative care support for cancer patients have shown that mortality is associated with anorexia, cachexia, delirium, poor palliative performance score, dyspnoea, leukocytosis, lymphopaenia, and high C-reactive protein (CRP) [8–11]. However, there are few studies in the literature demonstrating prognostic factors associated with mortality in patients who need palliative care for diagnoses other than malignancy [12]. The present study aimed to

investigate the parameters associated with mortality in patients receiving palliative care support.

MATERIAL AND METHODS

This prospective observational study was conducted between 1 October 2020 and 1 November 2021 among inpatients in the palliative care unit of Atatürk University Faculty of Medicine Hospital.

Inclusion criteria were as follows: being in the palliative care unit for at least 24 hours and signing an informed consent form to participate in the study. Patients who were hospitalized for 24 hours or less, who had been admitted to the palliative care centre previously, or did not sign the informed consent form were not included.

Patients' demographic characteristics, reasons for admission to palliative care, from where they were admitted to palliative care, their height, weight, and body mass index at admission to palliative care, and vital signs such as fever, blood pressure, heart rate, and oxygen saturation at admission were recorded. The palliative performance scale (PPS) and Karnofsky performance scale (KPS) were used to measure the patients' functional status upon admission to palliative care. The Karnofsky performance scale has been widely used since 1948. It correlates with other measures of patient functional status and well-being [13]. The palliative performance scale was first developed and used as a performance measure in palliative care patients by Anderson and Downing in 1996. It was shown to have adequate external validity in comparisons with other performance scales [14, 15]. Its sensitivity and specificity were reported to be 80% and 89%, respectively [10, 14, 16]. For both scales, patients received a score between 0–100.

Infectious diseases that occurred while the patients were in the palliative care unit and the microorganisms isolated were evaluated. At admission to palliative care, the following laboratory parameters were recorded: white blood cell, neutrophil, lymphocyte, and platelet counts, mean platelet volume, haemoglobin, haematocrit, erythrocyte sedimentation rate (ESR), procalcitonin, CRP, sodium (Na), chlorine (Cl), potassium (K), magnesium (Mg), calcium (Ca), phosphorus (P), albumin, creatinine, blood urea nitrogen, aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transferase, alkaline phosphatase, thyroid-stimulating hormone, and basal cortisol. Erythrocyte transfusion during hospitalization and discharge results were noted.

Statistical analysis

The data were analysed using a statistical software package. Categorical data were presented as frequency and percentage values; continuous variables were presented as mean, standard deviation, median, and range. Between-group comparisons of categorical data were performed with χ^2 test or Fisher's exact test if the value in any cell was less than 5. Because continuous data showed a non-normal distribution, the non-parametric Kruskal-Wallis and Mann-Whitney *U* tests were used for analysis. Receiver operating characteristic analysis was performed to assess the power of biomarkers to predict an unfavourable outcome. Optimal cut-off points were determined using the Youden index (J = sensitivity + specificity – 1). Categorical and continuous variables found to be significantly associated with unfavourable outcome were used to create a multivariate logistic regression model (backward: LR; entry: 0.05; removal: 0.10). *P*-values less than 0.05 were considered statistically significant.

Permission to conduct the study was obtained from the Atatürk University Faculty of Medicine Clinical Research Ethics Committee (date: 01.10.2020, meeting number: 08; decision number: 50).

RESULTS

Demographic characteristics of the patients

A total of 177 patients hospitalized in the palliative care unit were included in the study. Of the patients, 84 (47.5%) were female and the mean age was 72.49 ±15.12 years. At the end of the follow-up period in the palliative care unit, 67 patients (37.9%) had died. Of our patients, 69 (39.0%) were retired, 20 (11.3%) were employed, 10 (5.6%) were unemployed, and 78 (44.1%) were homemakers. In addition, 170 (96.0%) were living at home, while 7 (4.0%) were living in nursing homes.

The relationship between patient characteristics and mortality

A comparison of the patients' demographic and clinical characteristics according to mortality is presented in Table 1. Congestive heart failure and solid organ malignancy were significantly more common among patients who died during palliative care ($p = 0.001$ and $p = 0.039$, respectively). In addition, patients with mortality had significantly lower PPS and KPS scores ($p < 0.001$) and more frequently received erythrocyte suspension replacement ($p = 0.005$).

Patients who died had significantly higher rates of infection at admission to the palliative care unit ($p = 0.004$) and infection acquired during inpatient palliative care ($p < 0.001$). Urinary tract infections were the most common infection detected both at admission and during follow-up in the palliative care unit. The distributions and causative pathogens of in-

Table 1. Distribution of basic patient characteristics according to mortality

Parameters	Mortality		*p*-value*
	No, *n* = 110	Yes, *n* = 67	
Demographic characteristics, *n* (%)			
Age, median (IQR)	74.5 (65–82.2)	78 (65–84)	0.254
Female sex, *n* (%)	54 (49.1)	39 (58.2)	0.239
Body mass index, median (IQR)	24.2 (21.2–29.1)	23.3 (20.2–30.3)	0.432
Smoking (former and current smokers), *n* (%)	41 (37.3)	35 (52.2)	0.051
Alcohol use, *n* (%)	2 (1.8)	–	0.267
Underlying diseases, *n* (%)			
HT	53 (48.2)	36 (53.7)	0.474
DM	37 (33.6)	20 (29.9)	0.601
CAD	27 (24.5)	18 (26.9)	0.731
CHF	13 (11.8)	22 (32.8)	0.001
Cerebrovascular accident	24 (21.8)	19 (28.4)	0.325
Dementia	13 (11.8)	12 (17.9)	0.259
Parkinson's disease	4 (3.6)	2 (3.0)	0.589
COPD	16 (14.5)	5 (7.5)	0.158
Chronic liver disease	3 (2.7)	1 (1.5)	0.512
PVD	1 (0.9)	2 (3.0)	0.320
Malignancy	17 (15.5)	17 (25.4)	0.104
Solid organ malignancy**	12 (10.9)	15 (22.4)	0.039
Haematological malignancy**	5 (4.5)	2 (3.0)	0.605
Palliative performance scale, median (IQR)	40 (30–60)	30 (10–40)	< 0.001
Karnofsky performance scale, median (IQR)	50 (37.5–60)	30 (20–40)	< 0.001
Erythrocyte suspension replacement, *n* (%)	45 (40.9)	42 (62.7)	0.005
Infectious disease at presentation	56 (50.9)	49 (73.1)	0.004
Infectious disease during follow-up, *n* (%)	20 (18.2)	37 (55.2)	< 0.001
Vital signs, n (%)			
Fever (≥ 38°C)	5 (4.5)	1 (1.5)	0.276
Hypotension (≤ 90/60 mm Hg)	4 (3.6)	5 (7.5)	0.261
Tachycardia (≥ 100/min)	14 (12.7)	22 (32.8)	0.001
Hypoxia (SO_2 < 90)	16 (14.5)	29 (43.3)	< 0.001
Laboratory findings, median (IQR)			
WBC count [/µl]	8365 (5957.5–11150)	8340 (6020–11500)	0.841
Neutrophil count [/µl]	6015 (4062.5–8402.5)	6250 (4220–8960)	0.538
Lymphocyte count [/µl]	1380 (917.5–1990)	1130 (720–1870)	0.045
Haemoglobin [g/dl]	11.6 (10.075–13.425)	10.2 (9.3–11.5)	0.001
Haematocrit (%)	36.2 (31.075–40.8)	31.7 (28.9–35.6)	0.002
Platelet count [/µl]	272000 (173750 –325250)	240000 (172000–299000)	0.221
MPV [fl]	10 (9.5–10.725)	10.2 (9.7–11)	0.200
CRP [mg/l]	33.525 (9.43–79.8475)	60.96 (35.5–91.65)	0.001
Procalcitonin [µg/l]	0.11 (0.06–0.22)	0.24 (0.12–0.61)	< 0.001
ESR [mm/h]	30 (14.75–55)	58 (26–77)	< 0.001
Na [mEq/l]	137 (134–140)	138 (136–142)	0.054
K [mEq/l]	4.01 (3.6–4.405)	3.9 (3.5–4.21)	0.217
Cl [mEq/l]	102 (98–105)	102 (96–105)	0.575
BUN [mg/dl]	20.795 (15–33.18)	23 (14.35–37.38)	0.675

Table 1. Cont.

Parameters	Mortality		*p*-value*
	No, *n* = 110	Yes, *n* = 67	
Creatinine [mg/dl]	0.735 (0.53–1.045)	0.76 (0.44–1.13)	0.990
Ca [mg/dl]	8.65 (7.9–9.1)	8.2 (7.8–8.8)	0.015
Mg [mg/dl]	1.89 (1.6975–2.085)	1.8 (1.67–2.19)	0.965
P [mg/dl]	3.1 (2.6–3.725)	3 (2.5–3.9)	0.488
ALT [IU/l]	25 (16.75–33.25)	25 (18–38)	0.508
AST [IU/l]	18 (12–33)	15 (10–24)	0.064
ALP [IU/l]	92 (72.75–128.25)	105 (82–147)	0.042
GGT [IU/l]	31.5 (21–65)	38 (20–86)	0.479
Albumin [g/dl]	3.045 (2.6575–3.6025)	2.7 (2.34–2.91)	< 0.001
Cortisol [mg/dl]	13.25 (9.4525–18.5375)	15.36 (11.33–22)	0.109
TSH [mU/ml]	1.17 (0.53–1.83)	1.35 (0.6–3)	0.058

ALP – alkaline phosphatase, ALT – alanine aminotransferase, AST – aspartate aminotransferase, BUN – blood urea nitrogen, CAD – coronary artery disease, CHF – congestive heart failure, COPD – chronic obstructive pulmonary disease, CVD – cerebrovascular disease, DM – diabetes mellitus, GGT – γ-glutamyl transferase, HT – hypertension, IQR – interquartile range, MPV – mean platelet volume, PVD – peripheral vascular disease, TSH – thyroid-stimulating hormone, WBC – white blood cell
**Fisher's exact test, chi-square test, and Mann-Whitney U test were used*
***Lung: 4 (2.3%), brain: 1 (0.6%), colon: 1 (0.6%), larynx: 3 (1.7%), breast: 2 (1.1%), stomach: 6 (3.4%), oesophagus: 3 (1.7%), pancreas: 1 (0.6%), prostate: 2 (1.1%), cervix: 3 (1.7%), and thyroid: 1 (0.6%)*
****Acute myeloid leukaemia: 1 (0.6%), chronic lymphocytic leukaemia: 3 (1.7%), multiple myeloma: 1 (0.6%), myelodysplastic syndrome: 2 (1.1%)*

Table 2. Evaluation of the power of initial laboratory findings and performance scales in predicting unfavourable outcome

Parameters	Cut-off point	AUC (95% CI)	Sensitivity (%)	Specificity (%)	*p*-value
CRP [mg/l]	> 30.3	0.646 (0.565–0.727)	82.0	49.1	0.001
Procalcitonin [µg/ml]	> 0.225	0.692 (0.615–0.770)	55.2	77.2	< 0.001
Sedimentation [mm/h]	> 58.5	0.666 (0.583–0.749)	49.2	80.9	< 0.001
Lymphocyte count [mcl]	< 1175	0.590 (0.502–0.678)	55.2	61.8	0.045
Haemoglobin [g/dl]	< 11.75	0.650 (0.569–0.731)	49.1	83.5	0.001
Haematocrit (%)	< 34.75	0.638 (0.556–0.720)	55.4	73.1	0.002
Calcium [mg/dl]	< 8.85	0.609 (0.526–0.692)	40.0	80.5	0.015
Albumin [g/dl]	< 3.00	0.735 (0.662–0.808)	55.5	85.0	< 0.001
PPS	< 35	0.738 (0.665–0.811)	62.7	74.6	< 0.001
KPS	< 45	0.759 (0.688–0.831)	54.5	85.0	< 0.001

AUC – area under the curve, CI – confidence interval, CRP – C-reactive protein, KPS – Karnofsky performance scale, PPS – palliative care performance scale

fectious diseases present at admission and during follow-up in the palliative care unit are presented in Supplementary Tables 1 and 2. In terms of vital signs, tachycardia and hypoxia at admission were significantly more common among patients who died ($p = 0.001$ and $p < 0.001$, respectively). Of the initial laboratory findings, patients with mortality had significantly lower lymphocyte, haemoglobin, haematocrit, calcium, and albumin values and significantly higher CRP, ESR, and procalcitonin levels (Table 1).

Predictive power of laboratory parameters and performance scales for unfavourable outcomes in palliative care

Evaluation of the predictive power of initial laboratory values and performance scales for mortality are presented in Table 2, Figure 1 and 2. Among the biomarkers, albumin had the greatest predictive power for negative outcome. At levels lower than 3.00 (unit), albumin had 55.5% sensitivity and 85.5% specificity in predicting mortality. C-reactive protein was the biomarker with the highest sensitivity for mortality. The Karnofsky performance scale score had greater predictive power for mortality than PPS, with an optimal cut-off value of 45.

Evaluation of independent risk factors for mortality

To determine independent risk factors for mortality in patients hospitalized in the palliative care unit, a logistic regression model was created including the variables of congestive heart failure, solid organ mali-

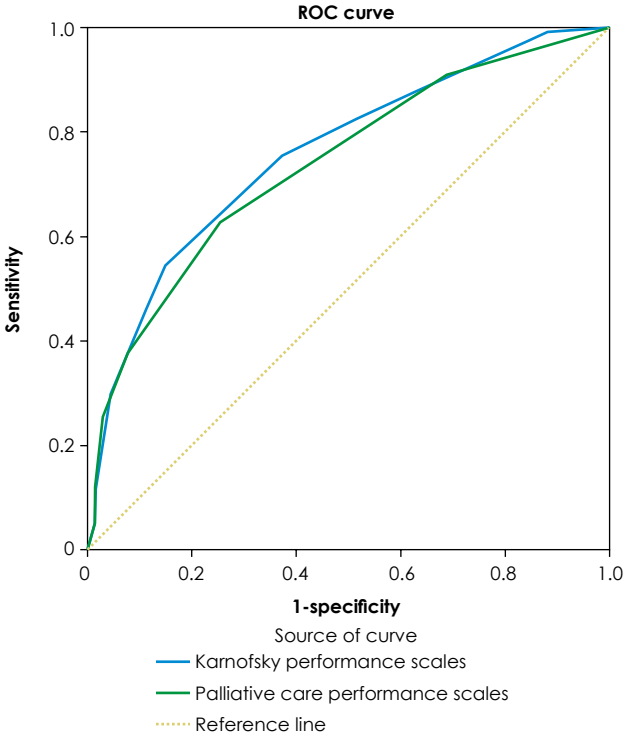

Fig. 1. Receiver operating characteristic curve analysis of the predictive power of initial laboratory parameters for negative outcome in palliative care

ROC – receiver operating characteristic

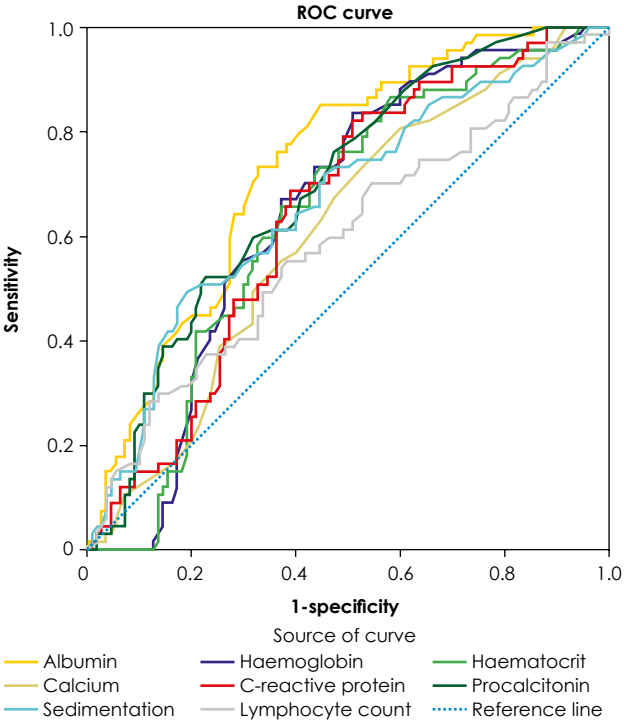

Fig. 2. Receiver operating characteristic curve analysis of the predictive power of performance scales for negative outcome in palliative care

ROC – receiver operating characteristic

gnancy, erythrocyte suspension transfusion, infection at admission and during follow-up, lymphocyte count, haemoglobin, haematocrit, CRP, procalcitonin, ESR, calcium, albumin, KPS, and PPS. The last line of the generated model is presented in Table 3. Low albumin value, low KPS score, congestive heart failure, solid organ malignancy, hypoxia at admission, and development of infection disease during follow-up were identified as independent risk factors for negative outcome. A one-unit increase in albumin was associated with 66.6% lower odds of mortality (odds ratio [OR]: 0.334, 95% confidence interval [CI]: 0.141–0.791; $p = 0.013$), and a one-unit increase in KPS score was associated with 4.8% lower odds of mortality (OR: 0.952, 95% CI: 0.925–0.980; $p = 0.001$). In contrast, the odds of mortality were 4.851 times higher in patients with congestive heart failure (95% CI: 1.716–13.717; $p = 0.003$), 4.442 times higher in patients with solid organ malignancy (95% CI: 1.420–13.894; $p = 0.01$), 3.727 times in the presence of hypoxia at admission (95% CI: 1.504–9.239; $p = 0.005$), and 3.626 times higher in patients who developed infection during follow-up (95% CI: 1.523–8.635; $p = 0.004$).

Table 3. Independent risk factors for unfavourable outcomes in patients hospitalized in the palliative care unit

Parameters	Multivariable OR (95% CI)	*p*-value
Albumin	0.334 (0.141–0.791)	0.013
KPS	0.952 (0.925–0.980)	0.001
Presence of chronic heart failure	4.851 (1.716–13.717)	0.003
Hypoxia	3.727 (1.504–9.239)	0.005
Solid organ malignancy	4.442 (1.420–13.894)	0.010
Infectious disease during follow-up	3.626 (1.523–8.635)	0.004

CI – confidence interval, KPS – Karnofsky performance scale, OR – odds ratio

DISCUSSION

In the palliative care unit, accurate prediction of prognosis is important to conduct treatment and care planning and family interviews more efficiently. This study aimed to determine the indicators of poor prognosis in palliative care inpatients.

Albumin is a protein synthesized in the liver that enables the transport of various substances such as hormones, is responsible for maintaining oncotic pressure, and also acts as a negative acute phase reactant [17]. Serum albumin level is an easily accessible, simple, and useful biomarker that provides a clue about prognosis in high-risk patients [18]. Low albumin values were found to be an important indicator of in-hospital mortality in studies evaluating older patients, people with congestive heart failure, and cancer patients, as well as in the general population [18–22]. In a previous study conducted

in a palliative care unit, an albumin level below 3.2 mg/l was found to be an independent risk factor for mortality in addition to Acute Physiology and Chronic Health Evaluation II (APACHE-II) score and Charlson Comorbidity Index [12]. Although there are many scoring systems for estimating prognosis, measuring albumin levels saves time and is a useful marker for many diagnoses and conditions. In this study, albumin level had the highest predictive strength and specificity for mortality, with a cut-off value of 3 mg/l. In addition, an increase in albumin level is noteworthy as an independent variable in reducing the risk of mortality.

There are many assessment tools used to evaluate patients in palliative care. The purpose of these tools is to learn the needs of patients and their relatives, their severity, and the challenges they face. The Karnofsky performance scale (KPS) has been described as an indicator of functionality in terminal patients [23]. In our study, the KPS had higher diagnostic power for mortality than all biomarkers measured at admission; it was an independent indicator in which a one-unit increase reduced the risk of mortality by 4.8%. It may be a strong prognostic indicator in this end-of-life patient population, as found in previous studies [24, 25].

The presence of solid organ malignancy was another independent risk factor associated with 4.5-fold higher odds of mortality in our study. Contrary to expectation, haematological malignancy was found to have no effect on mortality. However, higher mortality among patients with haematological malignancies has been reported previously in the literature. This has been attributed to the more aggressive antineoplastic therapy these patients receive throughout their lifetime [26, 27] and their more frequent need for intensive care [28]. In addition, these patients require more blood transfusions until the end of their lives, which leads to more frequent admission to palliative care [29]. The differences between our findings and those in the literature may be related to the presence of only 7 patients with haematological malignancies in our centre during the study period.

In our study, the mortality rate was higher for patients with tachycardia and hypoxia at admission. The presence of hypoxia at the time of admission was determined to be an independent risk factor for mortality. Previous studies have shown that heart rate, respiratory rate, and hypoxia requiring oxygen affect mortality in patients with advanced malignancy [30]. Tachypnoea and oxygen use are believed to be indicators of respiratory failure [31]. In the literature, studies of intensive care patients have also yielded similar results [32]. These vital signs are thought to result from physiological changes caused by acute illness in a dying patient.

Patients receiving palliative care support have a high rate of infection due to factors such as advanced age, steroid use, immunosuppression induced by disease or its treatment, delirium, immobilization, catheterization, tracheostomy, and prolonged hospital stays. The symptoms of infection also reduce quality of life [33]. Studies on cancer patients receiving palliative care have shown that between 29.3 and 83.3% of patients have at least one episode of infection [33–36]. Vitetta *et al*. [35], Homsi *et al*. [37], and Pereira *et al*. [33] reported that the most common infection was urinary tract infection, whereas Lam *et al*. reported that pneumonia was most common [38]. Similarly to the literature, 59.3% of the patients in our study had an infection at the time of their admission to palliative care. The most common infection was urinary tract infection, at a rate of 24.9%. Urinary tract infection was also the most common infection (67.9%) in a retrospective study conducted in our country by Akdoğan *et al*. among older patients receiving palliative care [39]. Discrepancies in these findings are probably explained by the different study populations. It is known that the presence of infection increases mortality, especially in intensive care patients [40]. Similarly, in our study, it was shown that the development of an infectious disease during follow-up was an independent risk factor associated with increased mortality.

Despite advances in cardiovascular therapies, heart failure remains a highly symptomatic and fatal disease. Palliative care has applications throughout the stages of heart failure, including the early stages, and is often used in conjunction with life-extending therapies [41]. Previous studies have identified heart failure in care units as an independent risk factor for in-hospital mortality [42]. Comorbidities play a key role in predicting mortality in palliative care, especially in older patients [43]. In our study, heart failure was identified as another independent risk factor for mortality, along with solid organ malignancy.

Although this research has value as a prospective study investigating mortality risk factors in palliative care patients in our country, it has some limitations. The main limitations are that the study was conducted in a single centre and included a limited number of patients. However, we believe our findings are important in terms of guiding future studies on this subject.

CONCLUSIONS

In the palliative care unit, prognosis estimation is essential in communication, joint decision-making, and care planning. The results of this study suggest that congestive heart failure, solid organ malignancy, hypoxia at admission, infection during follow-up, and low albumin level and KPS score may be indicators of poor outcome.

The authors declare no conflict of interest.

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