A New Mortality Prediction Model in Advanced Stage Cancer Patients Requiring Hospitalisation while Receiving Active Systemic Therapy

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ABSTRACT

Objective: To predict short and long-term mortality in patients who were admitted to the emergency department and then hospitalised unplanned in medical oncology-ward.

Study Design: An observational study.

Place and Duration of the Study: Department of Medical Oncology, Tekirdag Namik Kemal University Hospital, Tekirdag, Turkiye, from May 2021 to May 2022.

Methodology: Consecutive patients admitted to the emergency department with unplanned hospitalisation in the oncology ward, were included. Patients receiving treatment with the curative intent, patients hospitalised for febrile neutropenia, and terminally ill patients requiring intensive care unit follow-up at admission were excluded from the study. Univariate and multivariate logistic regression analyses were used to identify predictive factors for short and long-term mortality-dependent variables.

Results: This study included 253 advanced cancer patients. The number of patients who died in the ward within 10 days (short-term mortality) was 28 (11.1%). Ninety patients (35.6%) died afterwards anytime in the ward during the study (long-term mortality). In the multivariate analysis established for short-term mortality, higher ALT (OR = 6.75, 95% CI: 2.09 - 21.85, p=0.001), rapid deterioration in performance status (OR = 5.49, 95% CI: 1.81-16.67, p=0.003), higher CRP (OR = 5.86, 95% CI: 1.20-28.53, p=0.029), higher procalcitonin (OR = 7.94, 95% CI: 0.99 - 63.82, p=0.051), and higher lactate (OR = 2.47, 95% CI: 0.94-6.51, p=0.067) showed significant predictive features.

Conclusion: The decision of whether to continue treatment or not is challenging in cancer patients who require unplanned hospitalisation while receiving palliative systemic therapy. New mortality estimation models can be used in making the transition from life-long to palliative treatments.

Key Word: *Mortality prediction, Hospitalisation, Estimation of survival, Chemotherapy.*

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INTRODUCTION

Accurate estimation of remaining life expectancy in patients with advanced cancer is important for the patient's future life plans and their caregivers and the effects on decision-making regarding medical procedures and end-of-life treatments for their cancer.[1] It is also critical for clinicians as it provides information on clinical practices such as aggressive cancer care, invasive end-of-life care procedures, or early specialist palliative care consultation as well.[2]

In developed countries, it has been shown that establishing a palliative care plan in the early period of cancer management of incurable patients provides a better quality of remaining life for the patient.[3]

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However, in clinical practice, the palliative care plan is hindered by reasons such as insufficient discussion of survival with patients or their caregivers, the clinician's optimism about the patient's survival, and the advantage of survival and symptom control provided by developing immunotherapy, targeted therapy, or chemotherapy options.[4] Unmet palliative care needs of patients or functional/secondary deterioration due to the nature of advanced disease lead to emergency admissions and unscheduled medical oncology service admissions.[5] In the case of unplanned hospitalisations, which can occur in a wide spectrum from simple drug side effects to life-threatening serious clinical conditions, the decision to switch from life-prolonging aggressive cancer treatments to more palliative approaches focusing on the quality of life and comfort is challenging for clinicians.[6,7] At this point, besides estimating how long the patient will live, the question of whether to continue palliative or curative treatment is a central issue for physicians, patients, and caregivers.

The rationale of this study was to assist clinicians in making the turning point decision, which means the transition from life-long treatments to palliative treatments, with the help of the mortality estimation model that consisted of advanced cancer patients who were admitted through the emergency department and

then hospitalised unplanned in the medical oncology ward. The objective of the study was to predict short and long-term mortality in patients who were admitted to the emergency department and then hospitalised unplanned in medical oncology-ward.

METHODOLOGY

Patients receiving chemotherapy or targeted therapy for advanced incurable cancer admitted to the Medical Oncology Inpatient Service, Tekirdag Namik Kemal University Hospital, Tekirdag, Turkiye, between May 2021 and May 2022 were consecutively included in this prospective, observational, and single-centred study. The patient population consisted of advanced cancer patients whose hospitalisations were unplanned into the medical oncology service after emergency department admission. Patients receiving treatment with the curative intent such as testicular cancer, patients with NYHA class 3-4 heart failure, patients hospitalised for febrile neutropenia, aged <18 years, patients hospitalised in the intensive care unit after emergency department admission, and non-metastatic were excluded from the study. Patients were followed up until discharge or the end of the study, and the last admission was taken into account in patients hospitalised more than once during the study.

For each hospitalised patient, during the first 24 hours of admission, the attending physician evaluated the patient's mental status (confused or not), shortness of breath at rest (yes/no), pretibial oedema (yes/no), and reduced oral intake (<5 spoons per meal, yes). In addition, demographic data and clinical variables at the admission time were assessed. Hemogram and serum biochemical parameters were recorded from blood samples obtained from the patients at hospitalisation. Palliative prognostic index (PPI), palliative prognostic score (PaP), and objective prognostic score (OPS) have been calculated separately for each patient.[8-10]

Statistical analyses were performed using SPSS Statistic software 24 (SPSS Inc., Chicago, III). Continuous variables were summarised as mean or median (interquartile range). The categorical measurements were summarised as numbers (percentage of the diagnostic group). Survival time was determined as the time from hospitalisation to death in the medical oncology ward. The short-term survival time was accepted as 10 days, which is the 25th percentile interquartile range of survival time. All continuous variables were categorized according to optimal cut-offs. Optimal cut-off values were determined by the receiver operating characteristic (ROC) curve and the area under the curve (AUC). The median value was used for the factors whose cut-off could not be determined by ROC-AUC. Univariate and multivariate logistic regression analyses were used to identify predictive factors for short-term and long-term mortality-dependent variables. The calibration of the models was evaluated using the Hosmer-Lemeshow goodness-of-fit test. The receiver operating characteristic curve (ROC curve) and ROC-AUC were calculated to compare the independent prognostic factors. Statistical significance was accepted as $p < 0.05$.

RESULTS

A total of 253 consecutive patients were prospectively included in the study. The median age of the patients was 64 (19-88) years and 65.6% of the patients were males. The number of patients who died in the ward within 10 days, which refers to short-term mortality, was 28 (11.1%). Ninety (35.6%) of the entire patient population died anytime (long-term) in the ward during the study. Fifty-five (21.7%) patients were discharged to the intermediate care facility or hospice care. One hundred and eight (42.7%) patients were discharged home. Sixty-nine of 108 patients who were discharged home continued their systemic treatment (chemotherapy or targeted therapy or immunotherapy). The general characteristics of the patients are shown in Table I.

Table I: Patients' clinicopathological features (n = 253).

Clinical parameters	n	%
Survival time (Days)	23*	20.19**
Time from diagnosis to admission (months)	14.6*	17.31**
Age	62.7*	10.87**
Gender (Female)	87	34.4
BMI (≥25)	104	41.1
ECOG PS (≥2)	160	63.2
Karnovski PS (≥%70)	86	34.0
Rapid worsening of performance status (<7 days)	45	17.8
Cancer types		
Lung / Breast / Gastrointestinal / Gynecologic / Genitourinary / Others	73/21/82/18/29/29	29/8/32/7/12/12
Metastasis site		
Liver/ Brain/ Bone / Lung	128/36/77/100	51/14/30/40
Number of metastasis sites (≥3	68	26.9
AKI at admission (yes)	59	23.3
Reduced oral ıntake (yes)	157	62.0
Confusion (yes)	31	12.3
Oedema (yes)	79	31.2
Dispnea at rest (yes)	101	40.0
Laboratory Parameters	**Mean**	**SD**
Albumin (g/dL)	2.89	0.61
Protein (g/dL)	5.83	0.79
CRP (mg/dL)	127.21	104.75
Procalcitonin (mg/dL)	9.07	39.49
Sodium (mmol/L)	133.72	5.57
Lactate dehydrogenase (mg/dL)	491.07	617.61
AST (mg/dL)	63.14	113.03
ALT (mg/dL)	34.36	47.68
Bilirubin (mg/dL)	1.60	3.14
Bicarbonate (mmol/L)	24.71	6.07
Lactate (mmol/L)	2.39	2.17
pH (log (H +) -	7.43	0.08
pCO_2	37.56	8.42
White blood cell (103 /uL)	11747	9467
Rdw (%)	17.18	3.07
Neutrophil (103 /u)	9379	8467
Lymphocyte (103 /u)	1222	695
Haemoglobin (g/dL)	10.15	2.26
Platelet count (103 /u)	291820	182098
NLR	8.87	7.82
PLR	283.82	197.55
PNI	34.99	7.06
ABR	6.36	6.47

Mean SD, Standard deviation. BMI, Body-Mass Index; ECOG PS, Eastern Cooperative Oncology Group Performance Score; AKI, Acute Kidney Injury; CRP, C-Reactive Protein; AST, Aspartate Aminotransaminase; ALT, Alanine Aminotransaminase; RDW, Red Cell Distribution Width; PPI, Palliative Prognostic Index; NLR, Neutrophil to Lymphocyte Ratio; PLR, Platelet-Lymphocyte Ratio; PNI, Prognostic Nutritional Index; ABR, Albumin-Bilirubin Ratio.*

The ideal cut-off values of the laboratory variables to predict short-term and long-term mortality were determined by ROC-AUC curves. For predicting short-term mortality, The ideal cut-off value was found to be 2.43 mg/dl for albumin (AUC: 0.631), 64.5 mg/L for C-reactive protein (CRP) (AUC: 0.667), 0.24 ng/mL for procalcitonin (AUC:0.664), 282 IU/L for LDH (AUC:0.677), 55 IU/L for aspartate aminotransaminase (AST) (AUC: 0.670), 20.5 IU/L for alanine aminotransaminase (ALT) (AUC:0.688), 0.78 mg/dl for serum bilirubin (AUC: 0.653), 21 mmol/L for bicarbonate (AUC: 0.650), 2.74 mmol/L for lactate (AUC: 0.677), 151 for PLR (AUC: 0.666), 2.98 for ABR (AUC:0.699).

As regard to long-term mortality prediction, the ideal cut-off values in the ROC analysis were found to be as 3.05 mg/dl for albumin (AUC: 0.605), as 162.5 mg/L for CRP (AUC: 0.604), as 0.26 ng/mL for procalcitonin (AUC:0.611), as 303.5 IU/L for Lactate Dehydrogenase (AUC:0.606), as 66 IU/L for AST (AUC: 0.633), as 20.5 IU/L for ALT (AUC:0.688), as 48.5 IU/L for ALT (AUC:0.576), as 1.02 mg/dl for bilirubin (AUC:0.616), as 24.55 mmol/L for bicarbonate (AUC: 0.617), as 1.62 mmol/L for lactate (AUC: 0.597), as 35.6 mmHg for pCO_2 (AUC:604), as 13970 103/uL for white blood cell (AUC: 0.591), as 10850 103/uL for neutrophil (AUC: 0.675), as 10 g/dL for haemoglobine (AUC: 0.577), as 4.83 for neutrophil-lymphocyte ratio (NLR) (AUC: 0.577), as 34.9 for Prognostic nutritional index (PNI) (AUC: 0.599), as 2.39 for albumin-bilirubin ratio (ABR) (AUC: 0.631).

In the univariate analysis performed, male gender (OR [odds ratio] = 0.20, 95% CI: 0.06-0.69, p=0.011), rapid deterioration in performance status (OR = 3.02, 95% CI: 1.29-7.08, p=0.011), acute kidney injury (AKI) at admission to the hospital (OR = 2.39, 95% CI: 1.05-5.43, p=0.038), serum albumin (OR = 0.31, 95% CI: 0.14-0.68, p=0.004), serum CRP (OR = 8.83, 95% CI: 2.05-38.12, p=0.004), serum procalcitonin (OR = 5.45, 95% CI: 1.60-18.60, p=0.007), serum LDH (OR = 3.44, 95% CI: 1.35-8.82, p=0.01), Serum AST (OR = 4.44, 95% CI:1.97-9.97, p <0.001), serum ALT (OR = 5.30, 95% CI:2.07-13.58, p=0.001), serum bilirubin (OR = 3.54, 95% CI:1.53-8.19, p = 0.003), serum bicarbonate (OR = 0.27, 95% CI:0.12-0.60, p=0.001), serum lactate (OR = 5.34, 95% CI:2.36-12.09, p <0.001), thrombocyte (OR = 0.28, 95% CI: 0.12-0.63, p=0.002), PLR (OR = 0.17, 95% CI: 0.07-0.39, p<0.001) and ABR (OR =0.20, 95% CI:0.90-0.49, p<0.001) were determined to be predictive for short-term mortality (Table II). In the multivariate analysis established with factors that were significant in the univariate analysis, serum ALT (OR = 6.75, 95% CI: 2.09-21.85, p=0.001), rapid deterioration in performance score (OR = 5.49, 95% CI: 1.81-16.67, p=0.003) and serum CRP (OR = 5.86, 95% CI: 1.20-28.53, p=0.029) remained its strong predictive feature, while procalcitonin (OR =7.94, 95% CI: 0.99-63.82, p=0.051) and lactate (OR = 2.47, 95% CI: 0.94-6.51, p=0.067) showed significance as mild predictive for short-term mortality (Table II). The Hosmer-Lemeshow test showed that the model was well-calibrated (p=0.872).

Univariate analysis revealed that male gender (OR = 0.49, 95% CI: 0.28-0.87, p=0.014), serum albumin (OR = 0.39, 95% CI: 0.21-0.69, p=0.001), serum crp (OR = 2.51, 95% CI: 1.45-4.35, p=0.001), serum procalcitonin (OR = 2.88, 95% CI: 1.56-5.29, p=0.001), serum LDH (OR= 2.29, 95% CI: 1.35-3.31, p=0.002), serum AST (OR = 4.27, 95% CI: 2.31-7.91, p <0.001), serum ALT (OR = 2.95, 95% CI: 1.48-5.89, p=0.002), serum bilirubin (OR = 3.11, 95% CI: 1.76-5.52, p <0.001), serum bicarbonate (OR = 0.39, 95% CI: 0.23-0.66, p <0.001), serum lactate (OR = 2.38, 95% CI: 1.35-4.19, p=0.003), pCO2 (OR = 0.43, 95% CI: 0.25-0.73, p=0.002), WBC (OR = 2.57, 95% CI: 1.43-4.60, p=0.002), neutrophil (OR = 2.49, 95% CI: 1.40-4.42, p=0.002), haemoglobine (OR = 0.54, 95% CI: 0.32-0.90, p=0.019), neutrophil-lymphocyte Ratio (NLR) (OR = 3.67, 95% CI: 1.94-6.93, p <0.001), PNI (OR = 0.44, 95% CI: 0.26-0.76, p=0.003) and ABR (OR = 0.25, 95% CI: 0.14-0.46, p <0.001) were predictive for long-term mortality. The multivariate analysis indicated that serum AST (OR = 3.20, 95% CI: 1.60-6.41, p=0.001), serum procalcitonin (OR = 2.22, 95% CI: 1.12-4.40, p=0.022), serum bicarbonate (OR = 0.46, 95% CI: 0.25-0.83, p=0.011), and NLR (OR = 3.52, 95% CI: 1.74-7.13, p <0.001) were independent predictive markers for long term mortality (Table III). The Hosmer-Lemeshow test confirmed the model (p=0.673).

DISCUSSION

In the 1970s, the 5-year relative survival rate for all cancers was 49%, whereas, this rate has increased to 68% nowadays.[11] For the most frequently diagnosed cancers today; when considering all stages of prostate cancer, the 5-year relative survival is 98% and for breast cancer 90%.[12] The 3-year survival rate for non-small cell lung cancer, one of the most common cancers, which was 19% in the 2000s, has increased to 31% today.[13] In the developing era of modern oncological treatments, these increased survival advantages compared to the past years will make patients and physicians undecided between the continuation of palliative cancer treatment and focusing on the quality of remaining life. Predicting mortality in any hospitalisation due to complications related to modern therapies or disease-related causes will be increasingly significant in dealing with this dilemma.

This study revealed that the model created with clinical and biochemical data obtained at admission in unplanned hospitalised cancer patients receiving active treatment for advanced cancer could provide short and long-term mortality predictions. While approximately 11% of the patients admitted to the medical oncology ward died in the first 10 days (short-term), about 35% of patients died in the ward (long-term) during the study. Female gender, rapid deterioration in performance status, presence of AKI on admission, albumin, CRP, procalcitonin, LDH, AST, ALT, bilirubin, blood gas lactate, platelet level, PLR, and ABR were separately prognostic markers for short--term mortality. In the established multivariate model; ALT, CRP, procalcitonin, blood gas lactate levels, and rapid deterioration in performance status were able to predict short-term mortality. For long-term mortality prediction; AST, serum procalcitonin, serum bicarbonate, and NLR were found to be independent predictors in the multivariate model.

Table II: Univariate analysis of factors for patients died within 10 days and any time at hospital after admission.

Variable	Category		Univariate analysis of patients died within 10 days		Univariate analysis of patients died anytime at hospital	
			HR (95% CI)	p	HR (95% CI)	p
Age	<65 *vs* ≥65		0.69(0.29-1.49)	0.315	0.65(0.38-1.09)	0.103
Gender	Female *vs* Male		0.20(0.06-0.69)	0.011	0.49(0.28-0.87)	0.014
BMI	<25 *vs* ≥25		1.50(0.68-3.30)	0.313	1.15(0.68-0.94)	0.593
ECOG PS	<2 *vs* ≥2		0.89(0.40-1.98)	0.769	1.08(0.63-1.85)	0.768
Karnovski PS	<70% *vs* ≥70%		0.616(0.25-1.51)	0.290	0.82(0.47-1.41	0.473
Rapid worsening of performance status	<7 days *vs* ≥7 days		3.02(1.29-7.08)	0.011	1.58(0.82-3.04)	0.172
Cancer types	A/B/C/D/E*		0.82(0.58-1.16)	0.265	1.05(0.85-1.30)	0.673
Metastasis site						
Liver	No *vs* Yes		1.14(0.52-2.51)	0.738	1.27(0.76-2.13)	0.363
Brain	No *vs* Yes		1.77(0.66-4.72)	0.253	1.35(0.66-2.78)	0.411
Bone	No *vs* Yes		1.56(0.69-3.51)	0.283	1.05(0.60-1.84)	0.862
Lung	No *vs* Yes		0.83(0.37-1.89)	0.662	0.89(0.53-1.51)	0.673
Number of metastasis sites	<3 *vs* ≥3		1.60(0.70-3.66)	0.267	1.18(0.57-2.44)	0.654
Comorbidity	No *vs* Yes		1.50(0.66-3.38)	0.336	0.86(0.51-1.44)	0.568
AKI at admission	No *vs* Yes		2.39(1.05-5.43)	0.038	1.33(0.73-2.42)	0.350
Reduced oral intake	No *vs* Yes		1.11(0.49-2.53)	0.797	1.09(0.64-1.85)	0.756
Delirium	No *vs* Yes		1.66(0.58-4.75)	0.342	1.58(0.74-3.38)	0.237
Oedema	No *vs* Yes		0.71(0.29-1.74)	0.453	1.16(0.67-2.02)	0.591
Dyspnea at rest	No *vs* Yes		1.59(0.72-3.49)	0.251	1.08(0.64-1.83)	0.774
Laboratory parameters	**Died within 10 days at hospital**	**Died anytime at hospital**				
Albumin	<2.43 *vs* ≥2.43	<3.05 *vs* ≥3.05	0.31(0.14-0.68)	0.004	0.39(0.21-0.69)	0.001
Protein	<5.79 *vs* ≥5.79	<5.79 *vs* ≥5.79	0.87(0.40-1.92)	0.738	0.69(0.41-1.15)	0.152
CRP	<64.5 *vs* ≥64.5	<162.5 *vs* ≥162.5	8.83(2.05-38.12)	0.004	2.51(1.45-4.35)	0.001
Procalcitonin	≤ 0.24 *vs* >0.24	< 0.26 *vs* ≥0.26	5.45(1.60-18.60)	0.007	2.88(1.56-5.29)	0.001
Sodium	<134 *vs* ≥134	<134 *vs* ≥134	0.76(0.34-1.67)	0.491	0.99(0.59-1.676)	0.977
Lactate dehydrogenase	<282 *vs* ≥282	<303.5 *vs* ≥303.5	3.44(1.35-8.82)	0.010	2.29(1.35-3.31)	0.002
AST	<55 *vs* ≥55	<66 *vs* ≥66	4.44(1.97-9.97)	<0.001	4.27(2.31-7.91)	<0.001
ALT	<20.5 *vs* ≥20.5	<48.5 *vs* ≥48.5	5.30(2.07-13.58)	0.001	2.95(1.48-5.89)	0.002
Bilirubin	<0.78 *vs* ≥0.78	<1.02 *vs* ≥1.02	3.54(1.53-8.19)	0.003	3.11(1.76-5.52)	<0.001
Bicarbonate	≤ 21 *vs* >21	≤ 24.55 *vs* >24.55	0.27(0.12-0.60)	0.001	0.39(0.23-0.66)	<0.001
Lactate	<2.74 *vs* ≥2.74	<1.62 *vs* ≥1.62	5.34(2.36-12.09)	<0.001	2.38(1.35-4.19)	0.003
pH	<7.43 *vs* ≥7.43	<7.43 *vs* ≥7.43	1.16(0.53-2.55)	0.706	1.09(0.65-1.83)	0.751
pCO2	<35.6 *vs* ≥35.6	<35.6 *vs* ≥35.6	0.97(0.92-1.02)	0.224	0.43(0.25-0.73)	0.002
White blood cell	<10500 *vs* ≥10500	<10430 *vs* ≥10430	1.12(0.51-2.47)	0.773	2.57(1.43-4.60)	0.002
Rdw	<16.7 *vs* ≥16.7	<16.7 *vs* ≥16.7	0.86(0.39-1.89)	0.705	1.01(0.66-1.69)	0.963
Neutrophil	<7550 *vs* ≥7550	<10850 *vs* ≥10850	1.01(0.46-2.21)	0.982	2.49(1.40-4.42)	0.002
Lymphocyte	<1200 *vs* ≥1200	<1200 *vs* ≥1200	1.01(0.46-2.23)	0.985	1.58(0.93-2.69)	0.089
Haemoglobin	<10 *vs* ≥10	<10 *vs* ≥10	0.91(0.41-1.99)	0.807	0.54(0.32-0.90)	0.019
Platelet count	<218500 *vs* ≥218500	<267500 *vs* ≥267500	0.28(0.12-0.63)	0.002	1.04(0.62-1.74)	0.894
NLR	<7 *vs* ≥7	<4.83 *vs* ≥4.83	0.74(0.34-1.64)	0.463	3.67(1.94-6.93)	<0.001
PLR	<151 *vs* ≥151	<238 *vs* ≥238	0.17(0.07-0.39)	<0.001	0.97(0.57-1.63)	0.894
PNI	<34.9 *vs* ≥34.9	<34.9 *vs* ≥34.9	0.67(0.30-1.52)	0.336	0.44(0.26-0.76)	0.003
ABR	<2.98 *vs* ≥2.98	<2.39 *vs* ≥2.39	0.20(0.90-0.49)	<0.001	0.25(0.14-0.46)	<0.001
Palliative prognostic index	≤ 4/4 - ≤6/>6		1.25(0.79-1.99)	0.346	1.06(0.78-1.44)	0.709
Palliative prognostic score	≤5.5/5.5 - ≤11/>11		0.36(0.54-5.42)	0.363	1.87(1.21-2.88)	0.005
Objective prognostic score	<3 *vs* ≥3		2.23(1.00-4.99)	0.050	1.78(1.06-3.00)	0.030

*s Significant values are indicated in bold. BMI, Body-Mass Index; ECOG PS; Eastern Cooperative Oncology Group Performance Score; AKI, Acute Kidney Injury; CRP, C-Reactive Protein; AST, Aspartate Aminotransaminase; ALT, Alanine Aminotransaminase; RDW, Red Cell Distribution Width; PPI, Palliative Prognostic Index; NLR, Neutrophil to Lymphocyte Ratio; PLR, Platelet-Lymphocyte Ratio; PNI, Prognostic Nutritional Index; ABR, Albumin-Bilirubin Ratio *A, Lung; B, Breast; C, Gastro-intestinal; D, Gynecologic; E, Genitourinary.*

Table III: Multivariate analyses of factors for patients who died within 10 days and any time at the hospital after admission.

Variable	Category	Multivariate analysis of patients died within 10 days		Multivariate analysis of patients died anytime at hospital	
		HR (95% CI)	P [f]	HR (95% CI)	P [f]
Rapid worsening of ECOG/Karnovsky PS	<7 days *vs* ≥7 days	5.49(1.81-16.67)	0.003		
CRP	<162.5 *vs* ≥162.5	5.86(1.20-28.53)	0.029		
Procalcitonin	< 0.26 *vs* ≥0.26	7.94(0.99-63.82)	0.051	2.22(1.12-4.40)	0.022
AST	<66 *vs* ≥66			3.20(1.60-6.41)	0.001
ALT	<48.5 *vs* ≥48.5	6.75(2.09-21.85)	0.001		
Bicarbonate	≤ 24.55 *vs* >24.55			0.46(0.25-0.83)	0.011
Lactate	<1.62 *vs* ≥1.62	2.47(0.94-6.51)	0.067		
NLR	<4.83 *vs* ≥4.83			3.52(1.74-7.13)	<0.001

[s]Significant values are indicated in bold. [f].: Forward:LR method. Hosmer-Lemeshow test for short-term p=0.872, for long-term mortality p=0.673 ECOG PS; Eastern Cooperative Oncology Group Performance Score; CRP; C-Reactive Protein, AST; Aspartate Aminotransaminase, ALT; Alanine Aminotransaminase, NLR, Neutrophil to Lymphocyte Ratio.

Except for the study conducted by Barbot *et al.* with 176 patients who were admitted to the ward while receiving treatment in 2006, this study is the first study in the literature that investigated the prediction of mortality in unplanned medical oncology ward hospitalisation in metastatic patients with ongoing active cancer treatment.[14] Barbot *et al.* reported a lower Karnofsky performance score, lower albumin value, higher LDH, and the presence of more than two metastases as independent predictors of mortality.[14] While albumin and LDH levels were found to be predictive for short and long-term mortality in this study, they did not provide independent predictive features in multivariate analysis. A notable finding in this study was that rapid deterioration in performance (<7 days) rather than patients with worse performance scores (ECOG or Karnofsky) was found to be a strong predictor of mortality. It may be related to disease progression or may be a reflection of the fact that cancer, which is a systemic disease, causes acute organ failure.

It is known that elevated serum liver enzymes may be associated with mortality in non-cancer diseases.[15] However, there are conflicting data regarding the relationship between elevated or low-serum liver enzymes and mortality in cancer patients. Mazza, *et al*. reported that as serum ALT increases, the risk of cancer-related mortality increases, while Kim HC *et al*. reported that even if the aminotransferase level is in the normal range, it may be associated with cancer-related mortality.[16] In this study, the authors addressed these controversial results by showing that elevated serum liver enzymes predict short or long-term mortality.

In the present study, inflammatory markers like serum CRP, procalcitonin, and NLR were shown to be predictive of mortality. It is known that inflammation and derived signalling pathways ultimately provide the appropriate microenvironment for cancer to spread and grow.[17] In a study including hospitalised patients, Christ *et al.* showed that low albumin values were poor prognostic for mortality, whereas Forrest *et al*. reported high CRP as a poor prognostic for mortality in their study.[18,19] However, there are few studies investigating the inflammatory markers with a methodology similar to this study including patients who were admitted to the emergency department and were hospitalised in the ward unscheduled while receiving active chemotherapy.

To date, many prognostic scoring systems and validation research have been established related to palliative care patients.[20] PPI, PaP, and OPS could not reach statistical significance in this study for short-term mortality prediction. The patient population in this study consisted of individuals with relatively better performance status, which allowed them to receive active therapy. Considering that the patients in these scoring systems were mostly terminal patients, it could be assumed as the reason for this difference.

This study has some limitations. One of the main limitations of the study is the heterogeneous patient population consisting of different cancers. Another limitation is that patients were hospitalised with different aetiologies. On the other hand, the strengths of this study were that prospective design and only advanced-stage cancer patients were included. Terminally ill patients which would affect death were excluded from the study.

CONCLUSION

ALT, CRP, procalcitonin, blood gas lactate levels, and rapid deterioration in performance status at admission predict short-term mortality in unplanned hospitalisations for patients receiving active anti-cancer therapy in this comprehensive study. Using there mortality prediction models, clinicians can determine high-risk patients and will be able to avoid procedures that will not benefit survival.

AVAILABILITY OF DATA AND MATERIAL:
Data are held securely by the research team and may be available upon reasonable request and with relevant approvals in place.

ETHICAL APPROVAL:
The present study was performed in line with the principles of the Declaration of Helsinki. The Tekirdag Namik Kemal University Ethics Committee granted formal approval to this study (Approval No. 2021.86.04.04 on April 13th, 2021).

PATIENTS' CONSENT:
Informed consent was obtained from all individual participants included in the study.

COMPETING INTEREST:
The authors declare that they have no competing interest.

AUTHORS' CONTRIBUTION:
KK: Conception and design, administrative support, and manuscript writing.
KK, YI, EC, OA, ESS: Collection and assembly of data, data analysis and interpretation, and final approval of the manuscript.
All authors are accountable for all aspects of the work.

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