ORIGINAL ARTICLE

# VARIABLES AFFECTING MORTALITY IN PATIENTS IN PALLIATIVE CARE UNITS: OR IS IT STILL JUST ALBUMIN?

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Abdullah YEŞİLKAYA[1]
Müge ARIKAN[1]
Büşra Nur TAŞDELEN[1]
Emre MERİÇ[1]
Ayşe AKHAN[1]
Murat DİNDAR[1]
Arda ULUTAŞ[1]
Didem ADAHAN[2]
Ufuk KARADAVUT[3]
Mehmet Murat ŞAHİN[4]

CORRESPONDANCE
[1]Abdullah YEŞİLKAYA
Phone : +905327160016
e-mail : dr.abdullahyesilkaya@gmail.com

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[1] Karabuk University Faculty of Medicine, Department of Anesthesiology, Karabük, Turkey

[2] LÖSANTE Children\'s and Adult Hospital, Department of Family Medicine, Ankara, Turkey

[3] Karabuk University Faculty of Medicine, Department of Biostatistics, Karabük, Turkey

[4] Karabuk University Faculty of Medicine, Department of Family Medicine, Karabük, Turkey

## Abstract

**Introduction:** This study aimed to evaluate the relationship between biomarkers, clinical prognostic indexes, and mortality in patients without malignancy.

**Materials and Method:** This retrospective study included patients who were followed up in palliative care units between January 2020 and January 2024. Data were collected from patients' digital database records. Demographic characteristics, clinical features, comorbidities, main reasons, and length of hospital stay were recorded. Laboratory parameters were measured at admission. Patient outcomes were also documented.

**Result:** The study included 416 patients. The mortality rate was 28.36% (n=118). When survivors and nonsurvivors were compared, variables including albumin, protein, white blood cells, neutrophils, C-reactive protein, procalcitonin, CRP/albumin, CRP/protein, neutrophil/lymphocyte, and platelet/lymphocyte ratios significantly affected mortality. Logistic regression analysis revealed that only the albumin level was statistically significant (0.010). It was found significant that the albumin value was below 2.76 g/dL (odds ratio 3.688; the area under the curve (AUC)=0.670, and P<.000). The sensitivity and specificity of an albumin cutoff value of 2.05 g/dL were 85% and 97%, respectively.

**Conclusion:** Our study highlights the pivotal role of hypoalbuminaemia as the most significant predictor of mortality in patients on the palliative care unit (PCU) without malignancy. To optimise patient care in palliative settings and better tailor therapeutic interventions, we must recognise the vital role of hypoalbuminaemia as a critical risk factor.

***Keywords:*** Palliative Care; Mortality; Albumin.

## INTRODUCTION

Palliative care (PC) is a multidisciplinary approach that improves the quality of life of patients with life-threatening diseases and their families. The need for palliative care units (PCU) is rapidly increasing worldwide owing to the ageing population and rising prevalence of cancer and comorbidities (1,2). Despite this need, PC applications have still not been developed at the desired level in many parts of the world, such as our country.

The standard protocol is unclear in our country, although PC protocols have been established in many countries worldwide, such as the United States, Canada and Germany (3). One of the most important reasons is that PC is not a specific medical speciality in Turkey. Physicians from various medical specialities, such as Anaesthesiology and Reanimation, Family Medicine, Neurology, and Internal Medicine, provide services. Palliative care and its features are not well-known to society or general health professionals (1,4).

This study aimed to conduct a descriptive analysis by evaluating patients admitted to the PCU. This study also aimed to determine factors affecting mortality. Our research effectively uses a limited number of PCU beds. We assume this will help us create a PCU management protocol for our hospital.

## MATERIALS AND METHOD

After obtaining approval from the local ethics committee (2024/1684), this single-centre retrospective study was conducted at Karabuk University Hospital in Karabuk, Turkey. This study was conducted in accordance with the principles of the Declaration of Helsinki.

All patients admitted to the PCU between 1 January 2020 and 1 January 2024 were evaluated. Data were obtained by scanning patients' hospital digital database records. Patients who were hospitalised with a diagnosis of COVID-19, stayed ≤ 24 hours, were under the age of 17, and had insufficient file information were excluded. Only the first admission was considered for patients with recurrent PCU. Patients diagnosed with malignancy were excluded based on the study design.

The PCU is a 14-bed unit staffed by a family medicine anaesthesiologist on a 24-hour-per-day, 7-days-a-week basis. The following data were recorded: age, sex, place of admission, including from home, intensive care unit (ICU), emergency department (ED), and other services; feeding style; respiratory pattern, including spontaneous breathing, tracheostomy, home invasive mechanical ventilation; decubitus status, and comorbidities. Patient comorbidities were retrospectively analysed by scanning their ICD-10 (International Statistical Classification of Diseases) codes. They were categorised as cardiovascular disease, including hypertension, heart failure, and arrhythmia; neurological disease, including cerebrovascular disease, epilepsy, Alzheimer disease, and Parkinson disease; respiratory disease, including asthma and chronic obstructive pulmonary disease; metabolic disease, including diabetes mellitus, hypo/hyperthyroidism, renal failure, and cirrhosis; psychiatric disease, including depression, bipolar disorder, schizophrenia, and other diseases such as peptic ulcer, gastroesophageal reflux disease, Schögren scleroderma, Behçet disease, benign prostatic hyperplasia, and osteoporosis.

Charlson Comorbidity Index (CCI) was used as a clinical prognostic index. Charlson Comorbidity Index (CCI) is used as an index of survival and prognosis, like other prognostic scoring such as the APACHE II, Palliative Prognostic Index or the Karnofsky Performance Scale (5,6). We preferred to use CCI. This index was calculated using the MDcalc website (https://www.mdcalc.com/calc/3917/charlson-comorbidity-index-cci) with comorbidities.

The feeding style was classified as parenteral, nasogastric tube (NG), percutaneous endoscopic gastrostomy (PEG), or oral and percutaneous

endoscopic jejunostomy (PEJ). The main reasons for PCU admission (palliation, nutritional difficulty, decubitus, and pain) and the length of hospital stay were recorded. The laboratory values of each patient were recorded, including haemogram — haemoglobin, platelet count, neutrophils, and lymphocytes; biochemistry — liver and kidney function tests, electrolytes, albumin, and protein values; infection markers — C-reactive protein (CRP) and procalcitonin). CRP/albumin ratio (CAR), CRP/protein ratio (CPR), neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) were calculated. Additionally, the discharge status of the patients was evaluated, and the mortality rate was calculated.

### Data analysis

In this study, variables that were the primary reasons for hospital admission and comorbidities were proportionally assigned according to the number of admissions. Descriptive statistics of the variables used in the data set, number of observations (N), and mean ± SD are given. To determine mortality rates, data obtained for those who lived and died were compared. Before comparison, normality tests were performed using the Kruskal–Wallis and Shapiro-Wilk methods. For comparison, the t-test was used for parametric data, whereas the Mann–Whitney U test was used for non-parametric data. The significance level was set at $P<.05$. Logistic regression analysis was performed to determine the variables affecting mortality. Therefore, we attempted to explain the variables that caused these deaths. The Wald test was applied for model selection in logistic regression. In addition, the Receiver Operating Characteristic (ROC) curve method was applied to distinguish between deceased and living individuals based on the determining factors. The SPSS 22 V statistical programme was used for all analyses.

## RESULTS

During the study period, 934 patients were admitted to a PCU. Data from 269 patients were excluded due to recurrent PCU admissions other than the first admission. A total of 249 patients were excluded for the following reasons: 128 patients were diagnosed with COVİD, 90 patients were diagnosed with malignancy, 17 patients had missing data, and 8 patients stayed ≤24 hours. Six patients still hospitalised were excluded from the study.

A total of 416 patients were included in this study. The mean age of the patients was 74.65± 13.58 years, and 228 were men (54.81%). Most patients were admitted to the ICU and ED. The clinical and demographic characteristics of patients are presented in Table 1. The mean length of stay was 15.84 ± 13.37 days. The mortality rate was 28.36% (n = 118).

The most common comorbidities were cardiovascular and neurological disease; 293 patients had three or more comorbidities (Table 1).

Education of patients' relatives (for patients admitted from the ICU for nutrition or home mechanical ventilator training), malnutrition, decubitus, and pain were the main reasons for admission to the PCU.The most common reason for admission was palliation with 43.27%. Other reasons were malnutrition in 25.24%, decubitus in 19.23%, pain in 6.25% and other in 6.01%.

Among them, 118 died, with a mortality rate of 28.36%. There were significant differences in albumin, protein, WBC, neutrophil, CRP, procalcitonin, CAR, CPR, NLR, and PLR between survivors and nonsurvivors. The data obtained from the *t* test of mortality analysis conducted according to the characteristics examined in this study are shown in Table 2.

Logistic regression analysis was applied to all the significant parameters, and the results are presented in Table 3. The table shows that only the albumin level was statistically significant among the

**Table 1.** The demographic and clinical features of the patients

| | | | |
|---|---|---|---|
| **Age** | | **n** | **Mean ± SD** |
| | Total | 416 | 74.65 ± 13.58 |
| | Women | 188 | 77.16 ± 12.95 |
| | Men | 228 | 72.57 ± 13.75 |
| **Sex** | | **n** | **%** |
| | Women | 188 | 54.81% |
| | Men | 228 | 45.19% |
| **Place of acceptance** | ICU | 159 | 38.22% |
| | ED | 109 | 26.20% |
| | Service | 75 | 18.03% |
| | Home | 73 | 17.55% |
| **Tracheostomy** | Yes | 88 | 21.15% |
| | No | 328 | 78.85% |
| **Home mechanical ventilator** | Yes | 79 | 18.99% |
| | No | 337 | 81.01% |
| **Feeding style** | Parenteral | 81 | 19.47% |
| | NG | 132 | 31.73% |
| | PEG | 124 | 29.81% |
| | Oral | 78 | 18.75% |
| | PEJ | 1 | 0.24% |
| **Decubitus** | Yes | 285 | 68.51% |
| | No | 131 | 31.49% |
| | | | **Mean ± SD** |
| **LOS** | | | 15.84 ± 13.37 |
| **CCI** | | | 7.45 ± 2.60 |
| **Comorbidity** | | | **n** |
| | Neurological disease | | 366 |
| | Cardiovascular disease | | 438 |
| | Pulmonary disease | | 68 |
| | Metabolic disease | | 217 |
| | Psychiatric disease | | 36 |
| | Postoperative | | 9 |
| | Others | | 107 |
| **Number of Comorbidity** | 1 and less | | 43 |
| | 2 | | 80 |
| | 3 | | 110 |
| | 4 | | 102 |
| | 5 and more | | 81 |

ICU: Intensive Care Unit, ED: Emergency Department, NG: Nasogastric Tube, PEG: Percutaneous Endoscopic Gastrostomy, PEJ: Percutaneous Endoscopic Jejunostomy, LOS: Length of Stay, CCI: Charlson Comorbidity Index.

**Table 2.** A comparison of survivors and nonsurvivors

| | Mortality analysis | | *P* values |
|---|---|---|---|
| | Survivors (n=298) | Nonsurvivors (n=118) | |
| Age, years | 74.45 ± 14.25 | 75.12 ± 11.74 | .624 |
| LOS, day | 15.04 ± 11.39 | 17.92 ± 17.30 | .097 |
| Sodium, mEq/L | 138.34 ± 5.17 | 138.21 ± 6.52 | .838 |
| Albumin, mg/dL | 3.12 ± 0.62 | 2.76 ± 0.52 | .000* |
| Protein, mg/dL | 5.85 ± 0.97 | 5.44 ± 1.05 | .000* |
| WBC, 10'9/L | 8.96 ± 4.27 | 10.57 ± 6.12 | .010* |
| Haemoglobin, g/dL | 10.34 ± 2.11 | 9.91 ± 1.95 | .051 |
| Platelet, 10'9/L | 283.69 ± 127.77 | 258.99 ± 144.76 | .107 |
| Neutrophil count, 10'9/L | 8.69 ± 12.32 | 13.53 ± 18.56 | .010* |
| Lymphocyte count, 10'9/L | 1.77 ± 2.53 | 2.08 ± 4.59 | .502 |
| CRP, mg/L | 75.74 ± 73.61 | 114.26 ± 72.09 | .000* |
| Procalcitonin, ng/mL | 0.69 ± 1.55 | 1.57 ± 4.23 | .030* |
| CAR | 26.84 ± 27.99 | 42.32 ± 25.80 | .000* |
| CPR | 13.79 ± 14.06 | 21.42 ± 13.27 | .000* |
| NLR | 6.42 ± 5.87 | 10.94 ± 10.70 | .000* |
| PLR | 245.04 ± 176.17 | 301.66 ± 281.02 | .043* |

* Statistically significant; WBC: white blood cell; CRP: C-reactive protein; CAR: C-reactive protein/albumin ratio; CPR: C-reactive protein/protein ratio; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio.

**Table 3.** Logistic regression mortality analysis of all parameters

| Parameters | B | SE | Wald | Sig. | Odds Ratio |
|---|---|---|---|---|---|
| Albumin | 1.305 | 0.667 | 3.828 | 0.010 | 3.688 |
| Protein | -0.388 | 0.412 | 0.888 | 0.346 | 0.678 |
| WBC | -0.043 | 0.050 | 0.732 | 0.392 | 0.958 |
| Neutrophil | 0.002 | 0.025 | 0.005 | 0.945 | 1.002 |
| CRP | -0.018 | 0.017 | 1.188 | 0.276 | 0.982 |
| Procalcitonin | -0.041 | 0.103 | 0.155 | 0.694 | 0.960 |
| CAR | 0.102 | 0.412 | 2.662 | 0.105 | 0.981 |
| CPR | 0.089 | 0.090 | 0.982 | 0.322 | 1.093 |
| NLR | -0.012 | 0.029 | 0.163 | 0.686 | 0.988 |
| PLR | 0.156 | 0.389 | 1.093 | 0.518 | 0.771 |

WBC: white blood cell; CRP: C-reactive protein; CAR: C-reactive protein/albumin ratio; CPR: C-reactive protein/protein ratio; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio.

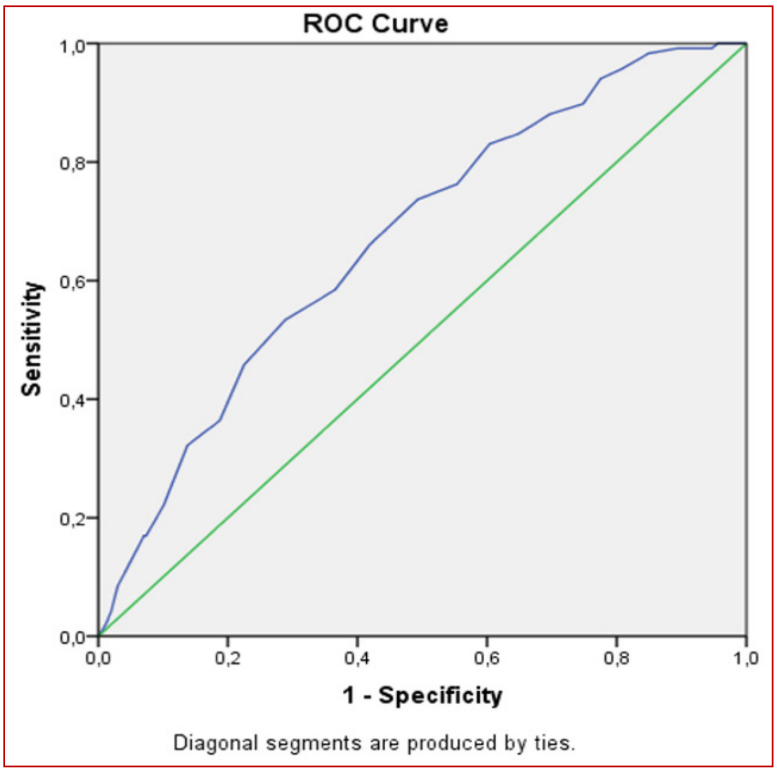


**Figure 1.** Receiver Operating Characteristic (ROC) curve for mean albumin value

**Table 4.** Cut off between survivor and nonsurvivor groups and albumin values based on ROC analysis.

| Area Under the curve | | | | | | |
|---|---|---|---|---|---|---|
| Test Result Variable(s): Albumin | | | | | | |
| | Area | Std. Error | Asymptotic Sig. | Asymptotic 95% Confidence Interval | | Cuttoff Value |
| | | | | Lower Bound | Upper Bound | |
| Albumin | .670 | .028 | .000 | .614 | .726 | 2.05 |
| Positive Likelihood Ratio | | | 2.81 | | | 1.56-4.12 |
| Negative Likelihood Ratio | | | 0.01 | | | 0.00-0.015 |
| Sensitivity | | | 0.85 | | | 0.77-0.93 |
| Specificity | | | 0.97 | | | 0.91-0.99 |

mortality variables (*P*=.010). The other variables were not significant. Accordingly, albumin levels were the main variable that explained mortality.

The receiver operating characteristic (ROC) curve method was applied to distinguish between survivors and nonsurvivors based on albumin level, which was significant after logistic regression analysis. The results are shown in Figure 1, and the other test results for albumin are shown in Table 4. According to the ROC analysis, the cutoff value for mean albumin was 2.05 mg/dL. The sensitivity and specificity of the albumin cutoff value of 2.05 mg/dL were 85% and 77%, respectively.

## DISCUSSION

In this study, we concurrently evaluated laboratory values and clinical prognostic indexes that affect mortality rates in PCU patients without malignancy. The mortality rate in this study was 28.36%. We found that only hypoalbuminaemia was strongly associated with mortality.

The majority of patients were men, and their mean age was 74.65 ± 13.58 years. Most patients were admitted to the ICU and ED; the majority were administered NG and PEG, and 88 patients underwent a tracheostomy. Our patients' demographic and clinical features were consistent with those reported in the literature (2, 7-10).

Factors affecting mortality rates in PCUs have been reported in various studies. Several laboratory values and ratios, such as protein, sodium, WBC, CRP, procalcitonin, CAR, CPR, and NLR, have been widely studied as prognostic markers in patients on the PCU (1, 7, 9-11).

C reactive protein (CRP) is a classical acute phase protein that increases rapidly. There are many factors (infection, rheumatological disease, cancer, etc.) that affect the CRP value. It is a laboratory parameter whose relationship with mortality and prognosis has been studied in the literature (1,12, 13). It has been shown in studies that high serum CRP concentrations are associated with organ failure and mortality. (14, 15) Karaşahin et al. stated in their study that evaluating CRP in the first 24 hours of hospitalization would be important in determining prognosis (16).

The CRP/albumin ratio, a combination of systemic inflammation and nutritional status markers, has been studied as an independent prognostic marker in critically ill patients (17-18). Oh et al. reported that a one-unit increase in CAR resulted in an 11% increase in the risk of 30-day mortality in critically ill ICU patients (19). Ranzani et al. conducted a study in an intensive care unit and found that CRP level and CAR were independent risk factors for mortality (12). In their study, Sargın et al. analysed laboratory values (such as neutrophils, PLT, CRP, CAR, and NLR) that affect patient mortality (1). None of these factors was significant.

Neutrophil-lymphocyte ratio (NLR) is a marker that shows systemic inflammation in clinical practice and can be easily measured and repeated with a blood count device. Increased NLR has been shown to be an independent prognostic risk factor in many types of cancer and its association with mortality rate (17, 20). However, studies conducted on patients followed in the palliative service are limited.

However, the results of these studies remain controversial. There are significant differences between survivors and nonsurvivors regarding protein, WBC, neutrophil, CRP, procalcitonin, CAR, CPR, and NLR. However, when logistic regression analysis was applied, we found that only the effect of hypoalbuminaemia on mortality rates was significant.

Hypoalbuminaemia is associated with short-term mortality, hospital stay, and other complications (21, 22). In a study conducted by Akirov et al., mortality was 12% in patients with mild hypoalbuminaemia and 34% in those with significant hypoalbuminemia (23). Sargın et al. reported in their study that hypoalbuminaemia is a risk factor for mortality (1). However, they did not use a clinical index in their study and presented this as a limitation. Taşar et al. stated that hypoalbuminaemia is an independent risk factor for mortality (24). Aung et al. found that albumin values < 3.1 mg/dL were the most important determinant of mortality (25). We studied mortality markers in a specific group of patients without malignancy. In our study, albumin values < 2.76 mg/dL were significant in mortality, and the sensitivity and specificity values were 85% and 97%, respectively.

Current studies have focused on determining the factors affecting mortality, especially in critically ill patients who are followed up in the ICU and PCU (1, 2, 11, 13, 22, 26-28). Apart from the

laboratory values of the patients, comorbidities also affect mortality. The scoring systems used in the ICU and PCU were based on organ failure and comorbidities such as APACHE II, SOFA, PPI and CCI. The Charlson Comorbidity Index (CCI) is a widely used comorbidity index for critically ill patients (29, 30). Vural et al. They determined high CCI, high APACHE II score and low albumin values as indicators of mortality. However, they studied a heterogeneous patient group (31). We used this to evaluate effects on mortality but it did not affect on mortality.

Palliative care requires a multidisciplinary approach. It is still essential as a health policy to develop PCU services both in our country and globally.

Our study was conducted in a specific patient group and included a relatively large number of patients. Additionally, the effects of laboratory parameters and clinical features on the mortality rate of the patients were investigated. We believe these are the strengths of the present study.

This study had several limitations. The most important limitations of our study are its retrospective and single-centre nature, and the fact that the study was conducted in a patient group with a high average age and high comorbidities. We did not use other widely used and accepted prognostic scales for PCU patients, such as the Palliative Prognostic Index or the Karnofsky Performance Scale.

We believe more prospective studies should be conducted by grouping patients according to age and main disease. In particular, we plan to evaluate patients diagnosed with malignancy.

## CONCLUSION

Our study highlights the pivotal role of hypoalbuminaemia as the most significant predictor of mortality in PCU patients without malignancy. By recognising and addressing this critical risk factor, healthcare providers can better tailor therapeutic interventions and optimise patient care in palliative settings. Further research is warranted to elucidate the underlying mechanisms linking hypoalbuminemia to adverse outcomes, and to explore targeted therapeutic strategies aimed at mitigating its detrimental effects on patient survival.

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