Comparison of the Laboratory Values at Admission to Palliative Care Unit:
Geriatric vs Non-Geriatric Patients

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Abstract

Aim: The aim of the present study is to compare the laboratory findings during the palliative care unit (PCU) admission of non-geriatric and geriatric patients and to evaluate the effects of these findings.

Methods: In the present study medical records of the patients hospitalized in PCU between 18.10.2018-18.10.2020 were reviewed. The patients were evaluated in 2 groups: Group I; 65 years and older and Group II; 18-64 years old. Demographic data and laboratory values of the patients (C-reactive protein, glucose, urea, creatinine, sodium, potassium, albumin, mean platelet volume and platelet, lymphocyte, neutrophil counts) were recorded. From these values, CRP/albumin, neutrophil/lymphocyte ratio, and platelet/lymphocyte ratio were calculated. Length of stay and mortality were also recorded.

Results: A total of 454 patients (Group I: 249 and Group II: 205) were included in the study. Blood glucose, urea, creatinine and sodium values were found to be statistically higher in Group I ($p=0.027$, $p<0.001$, $p<0.001$ and $p=0.032$, respectively). Albumin values were 2.70 g/dL (2.30–3.00 g/dL) in Group I and statistically lower than Group II ($p<0.001$). Albumin < 2.5 g/dL [odds ratio (OR) 2.75, 95% confidence interval (CI): 1.52–4.96, $p < 0.001$] was determined as an independent risk factor for mortality in Group I. While the sensitivity was determined as 79% for the albumin cut-off value of 2.5 g/dL, the specificity was determined as 66%.

Conclusions: Among the laboratory values at the time of admission of geriatric patients admitted to the PCU, only albumin has a prognostic value in poor sensitivity and specificity.

Keywords: Palliative Care Unit, Geriatric, Mortality

1. Introduction

In line with the recommendations of the World Health Organization (WHO), palliative care should be applied to anyone suffering from life-threatening diseases and should be started early according to the course of the disease. However, in clinical practice, palliative care is usually initiated much later and is often limited to cancer patients. Early integration of patients into palliative care is known to lead to better symptom control, prolonged survival, and better quality of life [1].

The elderly population is increasing all over the world, and the population over 65 in the United States is expected to double by 2050, from 9% in 1960 [2].

With the prolongation of average lifespan, the pressure of chronic diseases on health systems also increases [3]. This situation, which concerns the geriatric population, increases the need for palliative care units (PCU) proportionally. In addition, despite all this increase in the geriatric population, we cannot ignore the fact that the majority of the population still consists of non-geriatric people. The fact that non-geriatric people may need palliative care should not be ignored, although it is not as common as in the geriatric individuals. As a result of the combination of all these factors, the importance and requirement of PCUs are increasing day by day [4].

Geriatric care, palliative care, intensive care and home care services are intertwined in the Turkish health system and practice. The purpose of this integrated and intertwined structure is to provide patients with the necessary care in every environment. Determining the patient profiles and factors affecting the length of stay in PCUs will enable more efficient use of the limited number of PCU beds. In addition, the determination of the differences of these factors between age groups, especially between geriatric and non-geriatric patients, may be important for the goal and quality of care. For all these reasons, it is important to examine the clinical characteristics of the patients and the factors affecting the prognosis

in PCU. Among these factors, it appears as laboratory findings that appear to be modifiable and/or correctable. In particular, the effect of laboratory findings during admission to PCU profoundly affects the initiation of treatment and palliative care.

The aim of the present study is to compare the laboratory findings during the PCU admission of non-geriatric and geriatric patients and to evaluate the effects of these findings.

2. Materials and methods

The present retrospective study was approved by the ethics committee of Selcuk University Medical Faculty (Approval date and number: 13.11.2021 and 2021/08) and the medical records of the hospitalized patients in Selcuk University Medical Faculty Hospital palliative care unit between 18.10.2018-18.10.2020 were reviewed. The present study was conducted in accordance with the principles of the Declaration of Helsinki. Patients younger than 18 years of age and patients with a diagnosis of malignancy were excluded from the study. In addition, patients with more than one admission were also excluded from the study. The patients were evaluated in 2 groups: Group I; 65 years and older and Group II; 18-64 years old. The following variables evaluated at admission to PCU were obtained from medical records: Age, gender, platelet, mean platelet volume (MPV), lymphocyte, neutrophil counts, glucose, sodium, potassium, urea, creatinine, albumin and the C-reactive protein (CRP). CRP/albumin ratio, platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) were calculated from the data obtained from medical records. Apart from these data, length of stay in PCU and survival were also obtained from medical records. The starting point for survival was evaluated for the date of first admission to the PCU and continuing for three months.

2.1. Statistical Analysis

Statistical analysis was performed using the SPSS Version 22.0 (IBM, Chicago, IL, USA). Evaluation of data in terms of normality was performed with Shapiro–Wilk and Kolmogorov–Smirnov tests. Categorical data were expressed as number (percentages). The numerical data resulting from the descriptive statistics were expressed as the median [interquartile range (IQR)]. Patients were divided into 2 groups according to their mortality results; the survivor and the non-survivor groups. Demographic and clinical data were compared using Chi-Square or Fisher's Exact test for categorical variables and Mann-Whitney U test for numerical variables. A p value <0.05 is statistically significant. The significant parameters of univariate analysis were subjected to multivariate linear regression analysis to identify any independent risk factor associated with mortality. Receiver operating characteristic (ROC) curve analysis was performed.

3. Results

Of the 820 patients admitted to PCU between 18.10.2018-18.10.2020, 454 were eligible for inclusion criteria and analysis of data. While there were 249 patients in Group I, there were 205 patients in Group II. Comparison of laboratory values and general characteristics of two groups are presented in Table 1. A statistically significant difference was found between the groups in terms of gender distribution (p<0.001). While 51.4% of the patients in Group I were female, only 38% of the patients in Group II were female. When the groups were compared in terms of accompanying illnesses, it was seen that there was no difference only in the presence of neurological disease (p=0.153), however, diabetes, hypertension, organ failure and nutritional disorders were found to be significantly higher in Group I (<0.001, <0.001, <0.001 and 0.004, respectively).

Table 1

Comparison of General Characteristics and Laboratory Values of Two Groups

Variable	Group I (n= 249) Median (IQR), n (%)	Group II (n= 205) Median (IQR), n (%)	p
Age, year	77.00 (71.00-82.00)	44.00 (30.00-56.00)	<0.001
Gender, (M/F) n (%)	121 (48.6) / 128 (51.4)	127 (62.0) / 78 (38.0)	0.004
Length of Stay, day	12.00 (7.00-18.00)	10.00 (6.00-21.00)	0.543
Accompanying Illnesses, n(%)			
Diabetes	71 (28.5)	16 (7.8)	<0.001
Hypertension	121 (48.6)	26 (12.7)	<0.001
Neurological Diseases	115 (46.2)	81 (39.5)	0.153
Organ Failure	56 (22.5)	16 (7.8)	<0.001
Nutritional Disorder	144 (57.8)	91 (44.4)	0.004
Blood Glucose, mg/dL	114.00 (95.00-139.00)	108.00 (93.00-124.00)	0.027
Blood Urea, mg/dL	46.00 (32.00-68.00)	34.00 (27.00-46.00)	<0.001
Blood Creatinine, mg/dL	0.74 (0.53-1.03)	0.55 (0.40-0.75)	<0.001
Blood Sodium, mEq/L	138.00 (135.00-141.00)	137.00 (135.00-140.00)	0.032
Blood Potassium, mmol/L	3.93 (3.49-4.30)	3.98 (3.68-4.33)	0.257
Neutrophil count, (10^9/L)	6.40 (4.23-9.40)	6.80 (5.02-10.26)	0.099
Lymphocyte count, (10^9/L)	1.20 (0.80-1.70)	1.50 (1.00-2.10)	<0.001
Platelet count, (10^9/L)	239000 (178000-323000)	269000 (194000-385000)	0.007
Mean Platelet Volume, fl	8.70 (7.80-9.50)	8.30 (7.70-9.15)	0.034
Neutrophil to lymphocyte ratio	5.62 (3.08-10.55)	4.58 (2.96-8.13)	0.017
Platelet to lymphocyte ratio	216.11 (140.00-310.66)	196.15 (135.76-274.54)	0.050
C-reactive protein, mg/L	4.32 (1.50-9.14)	4.98 (1.55-10.30)	0.590
Albumin, g/dL	2.70 (2.30-3.00)	2.90 (2.50-3.30)	<0.001
C-reactive protein/Albumin Ratio	1.72 (0.54-3.81)	1.68 (0.50-3.74)	0.926
Mortality, n (%)	63 (25.3)	30 (14.6)	0.005

IQR: Inter Quantile Range, M: Male, F: Female

Blood glucose, urea, creatinine and sodium values were found to be statistically higher in Group I (p=0.027, p<0.001, p<0.001 and p=0.032, respectively). The median lymphocytic and platelet counts and the MPV were higher in Group I; 1.20 (0.80–1.70), 239000 (178000–323000) and 8.70 (7.80–9.50), respectively. Albumin values were 2.70 g/dL (2.30–3.00 g/dL) in Group I and statistically lower than Group II (p<0.001). The NLR, PLR and CRP/albumin ratio, calculated from the above laboratory values, were as follows in Group I and statistically higher than Group II: 5.62 (3.08–10.55), 216.11 (140.00–310.66) and 1.72 (0.54–3.81), respectively. The mortality rate of the patients were higher in Group I 25.3% (n =63). The patient characteristics of Group I with regard to mortality are shown in Table 2. Survivor patients of Group I, albumin values were higher (2.70 g/dL vs 2.40 g/dL; p < 0.001), than the non-survivor patients. In the non-survivor patients of Group I, blood urea values were higher (53.00 g/mdL vs 44.00 mg/dL; p=0.013), than the survivor patients.

Table 2

The Patient Characteristics of Group I in Terms of Mortality

	Univariate analysis			Multivariate analysis	
	Mortality		P	OR	P
	Survivor (n= 186)	Non-Survivor (n= 63)			
	Median (IQR), n (%)	Median (IQR), n (%)			
Age, year	76.00 (71.00-82.00)	78.00 (71.00-84.00)	0.334		
Gender, (M/F) n (%)	86 (46.2) / 100 (53.8)	35 (55.6) / 28 (44.4)	0.201		
Length of Stay, day	11.00 (7.00-17.00)	13.00 (7.00-22.00)	0.171		
Accompanying Illnesses, n(%)					
Diabetes	53 (28.5)	18 (28.6)	0.991		
Hypertension	94 (50.5)	27 (42.9)	0.292		
Neurological Diseases	91 (48.9)	24 (38.1)	0.136		
Organ Failure	46 (24.7)	10 (15.9)	0.146		
Nutritional Disorder	101 (54.3)	43 (68.3)	0.053		
Blood Glucose, mg/dL	112.00 (94.00-137.00)	122.00 (99.00-144.00)	0.118		
Blood Urea, mg/dL	44.00 (30.75-65.25)	53.00 (36.00-77.00)	0.013		NS
Blood Creatinine, mg/dL	0.76 (0.57-1.03)	0.70 (0.45-1.06)	0.089		
Blood Sodium, mEq/L	138.00 (136.00-141.00)	137.00 (134.00-141.00)	0.368		
Blood Potassium, mmol/L	3.98 (3.55-4.30)	3.85 (3.36-4.41)	0.210		
Neutrophil count, mm3 [a]	6.40 (4.24-9.09)	7.00 (4.20-10.90)	0.243		
Lymphocyte count, mm3	1.20 (0.80-1.70)	1.10 (0.60-1.55)	0.318		
Platelet count, mm³	240000 (180000-324000)	222000 (154000-324000)	0.220		
Mean Platelet Volume, fl [a]	8.70 (7.90-9.60)	8.50 (7.60-9.30)	0.237		
Neutrophil to lymphocyte ratio	5.48 (3.03-9.94)	5.94 (3.18-12.48)	0.151		
Platelet to lymphocyte ratio	214.26 (138.84-311.30)	224.41 (140.00-307.50)	0.765		
C-reactive protein, mg/L [a]	4.65 (1.72-9.12)	2.80 (1.34-9.37)	0.284		
Albumin, g/dL	2.70 (2.40-3.10)	2.40 (2.00-2.90)	<0.001	2.75 (1.52-4.96)	<0.001
C-reactive protein/Albumin Ratio [a]	1.85 (0.55-3.79)	1.12 (0.46-4.41)	0.601		

The parameters in bold indicates the significant ones in univariate and multivariate analysis. a Marked parameters which were significant in univariate analysis and not associated with each other were included in the multivariate analysis. IQR: Inter Quantile Range, OR: Odds Ratio, M: Male, F: Female.

Table 3

Receiver operating characteristic analysis for the prediction of mortality in Group I. Cut-off for Survivor group versus Non-Survivor group mean Albumin based on ROC analysis

		AUC	p value	Asymptotic 95 % confidence intervals lower bound -upper bound	Cut off value
Mean Albumin		0.358	<0.001	0.227-0.443	< 2.5
				Outcome: Death	
		Yes	No		Total
	Yes	50	63		113
Mean Albumin < 2.5	No	13	123		136
	Total	63	186		249
					95 % confidence intervals
Sensitivity			0.79		0.67-0.88
Specificity			0.66		0.58-0.72
Predictive value of positive test			0.44		0.38-0.50
Predictive value of negative test			0.90		0.85-0.93
Positive likelihood ratio			2.34		1.85-2.97
Negative likelihood ratio			0.31		0.19-0.51

ROC: Receiver operating characteristic; AUC: Area Under The Curve.

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Table 4

The Patient Characteristics of Group II in Terms of Mortality

	Univariate analysis		Multivariate analysis		
	Mortality		P	OR	P
	Survivor (n= 175)	Non-Survivor (n= 30)			
	Median (IQR), n (%)	Median (IQR), n (%)			
Age, year	42.00 (29.00-55.00)	55.00 (41.00-59.00)	0.006		NS
Gender, (M/F) n (%)	111 (63.4) / 64 (34.6)	16 (53.3) / 14 (46.7)	0.293		
Length of Stay, day	10.00 (6.00-20.00)	10.00 (6.00-36.00)	0.577		
Accompanying Illnesses, n(%)					
Diabetes	16 (9.1)	0	0.085		
Hypertension	21 (12.0)	5 (16.7)	0.478		
Neurological Diseases	74 (42.3)	7 (23.3)	0.060		
Organ Failure	11 (6.3)	51 (16.7)	0.059		
Nutritional Disorder	72 (41.1)	19 (63.3)	0.054		
Blood Glucose, mg/dL	107.00 (93.00-124.00)	116.00 (95.00-127.00)	0.539		
Blood Urea, mg/dL	33.00 (27.00-44.00)	35.00 (27.00-55.00)	0.320		
Blood Creatinine, mg/dL	0.55 (0.41-0.74)	0.52 (0.36-0.84)	0.955		
Blood Sodium, mEq/L	137.00 (135.00-140.00)	136.00 (132.00-139.00)	0.087		
Blood Potassium, mmol/L	4.00 (3.70-4.30)	3.78 (3.51-4.27)	0.077		
Neutrophil count, mm^3 [a]	6.80 (5.00-10.30)	6.75 (5.33-9.87)	0.926		
Lymphocyte count, mm^3	1.56 (1.10-2.20)	0.97 (0.49-1.38)	<0.001		NS
Platelet count, mm^3	273000 (198000-389000)	245000 (182000-346000)	0.204		
Mean Platelet Volume, fl [a]	8.40 (7.70-9.20)	8.20 (7.70-9.05)	0.508		
Neutrophil to lymphocyte ratio	4.25 (2.93-7.06)	7.65 (3.76-13.41)	0.004		NS
Platelet to lymphocyte ratio	187.77 (133.10-264.58)	219.97 (165.47-533.93)	0.021		NS
C-reactive protein, mg/L [a]	4.70 (1.50-10.01)	7.56 (2.40-13.67)	0.115		
Albumin, g/dL	3.00 (2.60-3.35)	2.47 (1.99-3.02)	0.002		NS
C-reactive protein/Albumin Ratio [a]	1.65 (0.50-3.42)	2.83 (0.93-5.64)	0.041		NS

The parameters in bold indicates the significant ones in univariate and multivariate analysis. a Marked parameters which were significant in univariate analysis and not associated with each other were included in the multivariate analysis. IQR: Inter Quantile Range, OR: Odds Ratio, M: Male, F: Female.

Multivariate analysis was applied for the parameters with significant results according to univariate analysis. Among the evaluated parameters, only albumin <2.5 g/dL was determined as an independent risk factor [odds ratio (OR) 2.75, 95% confidence interval (CI): 1.52–4.96, p < 0.001].

The ROC curve analysis for the prediction of cut-off value and mortality of Group I (survivor's vs non-survivor's) was performed. Albumin values obtained as a result of the ROC curve analysis are shown in Table 3. The cut-off value of mean albumin value according to the ROC curve analysis was found as 2.5 g/dL (Figure 1). Sensitivity (79%) and specificity (66%) for albumin cut-off value (2.5 g/dL) determined as a result of ROC analysis. Positive and negative predictive values were detected as 0.44 and 0.90, respectively. Positive likelihood ratio and negative likelihood ratio were detected as 2.34 and 0.31, respectively. The area under the curve (AUC) was 0.358 and 95% CI: 0.227–0.443 (p < 0.001) (Table 3).

The patient characteristics of Group II in terms of mortality are shown in Table 4. Survivor patients of group II, lymphocyte counts were higher (1.56 mm3 vs 0.97 mm3; p < 0.001), than the non-survivor patients. In the non-survivor patients of group II, NLR, PLR and CRP/albumin ratio were higher (7.65 vs 4.25; p=0.004, 219.97 vs 187.77; p=0.021 and 2.83 vs 1.65; p=0.041, respectively), than the survivor patients.

Figure 1

Receiver Operating Characteristic (ROC) curve for mean Albumin Value
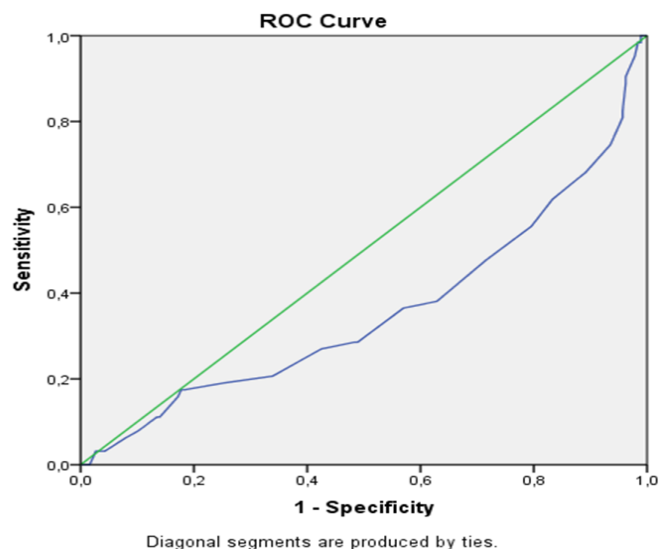
Diagonal segments are produced by ties.

Multivariate analysis was applied for the parameters with significant results according to univariate analysis. Among the evaluated parameters none of them could be determined as an independent risk factor.

4. Discussions

In this retrospective study, laboratory values at admission to PCU of geriatric (65 years and older) and non-geriatric (18-64 years old) patients admitted were compared. Among the evaluated parameters, only albumin values were found to have an effect on predicting mortality in the geriatric patient group, but this effect was also weak. Although there are many studies to predict mortality in PCUs, most of these studies have been performed in patient populations including cancer patients. In addition, studies in which patients under the age of 65 are evaluated as a separate group are limited, since the elderly patient groups are naturally the first to come to mind when PCU is mentioned.

In a survey conducted with palliative care doctors in Canada, it was seen that there was no consensus on the tools used to predict the prognosis of patients [5]. Participants also stated that there is a need for the development of training materials and programs to optimize the understanding of prognostic information.
It was stated that the WPCBAL score developed by Niki et al. objectively predicts the prognosis of two or three weeks for terminal cancer patients in the palliative care unit [6]. The following laboratory parameters were used in the WPCBAL score: White blood cell, platelet, CRP, blood urea nitrogen, aspartate aminotransferase, and lactate dehydrogenase. It was also stated that the WPCBAL score was superior in comparison with the previously described Glasgow prognostic score (GPS) and Palliative Prognostic Index (PPI) [7,8].

Although the half-life of albumin, an acute phase protein synthesized by the liver, is 15-19 days, this period is much shorter in critically ill patients [9]. Binding, which is one of the primary tasks of albumin, gains more importance especially in the geriatric population. In hypoalbuminemia, the concentration of free drugs in the circulation increases, and as a result, increased bioavailability may cause side effects [10]. In previous studies, hypoalbuminemia was associated with increased mortality, prolonged hospital stay, and other complications [9,11]. Albumin has an increased prognostic role in patients with severe comorbidities. However, it is unclear whether it can be a marker for mortality in patients admitted to PCU. In a retrospective study evaluating the effect of albumin levels on survival at admission to PCU, it was reported that albumin levels below 3.1 g/dL were associated with poor survival [12]. In the present study, albumin values below 2.5 g/dL were found to be an independent risk factor for mortality in geriatric patients.

In a study conducted with cancer patients, young age, sodium and BUN values were found to be prognostic factors in PCU [13]. Unlike this study, it was shown inthe present study that sodium and BUN values are not a prognostic factor in both geriatric and non-geriatric patients. In addition, as another difference, mortality was lower in young patients in the present study compared to geriatric patients. We think that the reason for this fundamental difference is that cancer patients weren't included in the present study.
In a study conducted in patients with malignant hematological disorders treated in the palliative care unit, it was reported that low platelet count, high LDH, and low albumin levels were associated with poor prognosis [14].

Apart from laboratory parameters, clinical features of PCU patients were also evaluated. It has been reported that advanced pressure ulcer is the most important clinical factor prolonging the hospital stay in PCU patients [15].

The limitations of the present study are that it is retrospective, single-centered, and no scoring was applied to the patients at the time of admission to the PCU.

5. Conclusion

In non-geriatric PCU patients, routinely evaluated laboratory values during hospitalization do not have a prognostic significance, whereas in geriatric patients, only Albumin has a prognostic value in poor sensitivity and specificity. It is obvious that prospective studies with wider participation are needed on this subject.

References

1. Dalgaard KM, Bergenholtz H, Nielsen ME, et al. Early integration of palliative care in hospitals: A systematic review on methods, barriers, and outcome. Palliat Support Care. 2014;12(6):495-513.
https://doi.org/10.1017/S1478951513001338
2. Bureau of the Census. Projections of the population by age and sex for the United States: 2010 to 2050. 2008.
3. Centers for Disease Control and Prevention (CDC). The state of aging and health in America-2013. 2013.
4. Higginson IJ, Davies E. Better Palliative Care for Older People. World Health Organization, Copenhagen, Denmark, 2004.
5. Corkum M, Viola R, Veenema C, et al. Prognosticating in palliative care: a survey of Canadian palliative care physicians. J Palliat Care. 2011; 27(2): 89-97.
https://doi.org/10.1177/082585971102700204
6. Niki K, Okamoto Y, Matano Y, et al. Validation of a Short-Term, Objective, Prognostic Predictive Method for Terminal Cancer Patients in a Palliative Care Unit Using a Combination of Six Laboratory Test Items. J Palliat Med. 2019; 22(6): 685-90.
https://doi.org/10.1089/jpm.2018.0422
7. Forrest LM, McMillan DC, McArdle CS, et al. Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. Br J Cancer. 2003; 89(6): 1028-30.
https://doi.org/10.1038/sj.bjc.6601242
8. Morita T, Tsunoda J, Inoue S, et al. The Palliative Prognostic Index: a scoring system for survival prediction of terminally ill cancer patients. Support Care Cancer. 1999; 7(3): 128-33.
https://doi.org/10.1007/s005200050242
9. Lyons O, Whelan B, Bennett K, et al. Serum albumin as an outcome predictor in hospital emergency medical admissions. Eur J Intern Med. 2010; 21(1): 17-20.
https://doi.org/10.1016/j.ejim.2009.10.010
10. Tal S, Guller V, Shavit Y, et al. Mortality predictors in hospitalized elderly patients. QJM. 2011; 104(11): 933-8.
https://doi.org/10.1093/qjmed/hcr093
11. Haller C. Hypoalbuminemia in renal failure: pathogenesis and therapeutic considerations. Kidney Blood Press Res. 2005; 28(5-6): 307-10.
https://doi.org/10.1159/000090185

12. Aung A, Alqudihy S, Rybicki L, et al. Does serum albumin and creatinine predict survival of inpatient palliative care patients?. Am J Hosp Palliat Care. 2014; 31(8): 862-6.

https://doi.org/10.1177/1049909113501851

13. Elsayem A, Mori M, Parsons HA, et al. Predictors of inpatient mortality in an acute palliative care unit at a comprehensive cancer center. Support Care Cancer. 2010; 18(1): 67-76.
https://doi.org/10.1007/s00520-009-0631-5

14. Kripp M, Willer A, Schmidt C, et al. Patients with malignant hematological disorders treated on a palliative care unit: prognostic impact of clinical factors. Ann Hematol. 2014; 93(2): 317-25.
https://doi.org/10.1007/s00277-013-1861-7

15. Yürüyen M, Özbaş Tevetoğlu I, Tekmen Y, et al. Prognostic Factors and Clinical Features in Palliative Care Patients. Konuralp Tıp Dergisi. 2018; 10(1): 74-80.
https://doi.org/10.18521/ktd.368570