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Original Article

Factors Determining Mortality in Geriatric Palliative Care Patients

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SUMMARY

Background: As life expectancy at birth increases, the elderly population is growing, both in Turkey and globally. The aim of this study was to investigate the factors associated with 12-month mortality in patients receiving geriatric palliative care.
Methods: Geriatric inpatients who were treated for 48 hours or more in the palliative care unit of our hospital between January 2016 and January 2017 were included in the study.
Results: A total of 233 geriatric palliative care patients (50.6% women) with a mean age of 77.6 ± 11.0 were included in the study. Eighty of the patients in our study died while in palliative care. Chronic kidney disease (CKD) and chronic obstructive pulmonary disease (COPD) were significantly more common among the deceased patients. Of the 153 surviving patients, 94 (61.4%) died within 12 months of discharge and 59 (38.6%) survived beyond 12 months. Presence of CKD was associated with a 2.17-fold reduction in survival time and albumin level < 3.2 mg/L with 2.12-fold reduction in survival time. In addition, post-discharge 12-month survival time was 1.80-fold shorter in the presence of solid organ malignancy, 2.06-fold shorter with APACHE-II score > 20.5, 1.60-fold shorter with Charlson Comorbidity Index (CCI) > 6.5, and 1.98-fold shorter with albumin levels < 3.2 mg/L.
Conclusion: CKD and low albumin were identified as independent risk factors for reduced hospital survival time. Independent risk factors for shorter post-discharge survival time included the presence of solid organ malignancy, high APACHE-II score, high CCI, and low albumin level.

1. Introduction

Palliative care is an approach that increases quality of life for patients and families dealing with life-threatening illness by preventing or alleviating all associated physical, psychosocial, and mental problems, especially pain, through effective evaluation and early detection.[1]

Palliative care is not only provided in the terminal stage, but through all stages of illness. An estimated 40 million people worldwide are believed to be in need of palliative care due to recent increases in life expectancy, cancer incidence, cancer survival, neurodegenerative diseases such as dementia, and number of chronic diseases.[2]

The increase in life expectancy at birth results in a growing elderly population both globally and in Turkey. According to 2018 data from the Turkish Statistical Institute, 8.7% of the Turkish population is elderly.[3] The aging population is accompanied by higher incidence of chronic and life-threatening conditions. Members of the elderly population especially in need of palliative care include patients with dementia, heart failure, and kidney disease. In terms of quality of life, it is known that many aspects of geriatric care and palliative care overlap.[4]

As the elderly population grows and our understanding of the nature and necessity of palliative care increases, the number of palliative care centers is also rising. The aim of this study was to investigate the factors associated with 12-month mortality in patients who receive geriatric palliative care.

2. Methods

The study included patients aged 65 years or older who were treated in the palliative care unit of our hospital for 48 hours or longer between January 2016 and January 2017. Patients younger than 65 years of age, those who were hospitalized for less than 48 hours, and those who had previously been treated in the palliative care unit were not included in the study.

2.1. Definitions and data collection

At admission, all patients underwent clinical (temperature, blood pressure, pulse, and oxygen saturation) and laboratory (C-reactive protein [CRP], albumin, neutrophil percentage) evaluations, and demographic and clinical data were collected regarding comorbidities, number of comorbidities, presence of any risk factors (infection, central venous catheter, urinary catheterization, nasogastric intubation, transfusion, mechanical ventilation, admission to intensive care, surgery, history of steroid use) and feeding methods

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(enteral or parenteral nutrition). Moreover, the patients' APACHE II scores and Charlson Comorbidity Index (CCI) were calculated and recorded. Survival data were obtained from the Death Reporting System of the Republic of Turkey Ministry of Health, General Directorate of Public Health. The patients' in-hospital and 12-month post-discharge survival times were evaluated. Ethical approval for this study was obtained from the hospital ethics committee.

2.2. Statistical analysis

The data were analyzed using SPSS 21.0 statistical software package. For descriptive statistics, categorical data were presented as frequency distribution and percentage, while continuous variables were presented as mean ± standard deviation. Receiver operating characteristic (ROC) curve analysis was performed to assess relationships between mortality and APACHE II score, CCI, admitting CRP level, neutrophil percentage, and albumin level. Area under the ROC curve (AUC) was calculated and cut-off points were determined using Youden's index (J = Sensitivity + Specificity – 1). Chi-square test was used in comparisons of categorical data between the surviving and deceased groups, while the nonparametric Kruskal–Wallis and Mann–Whitney U tests were used in comparisons of continuous data due to nonnormal distribution. Kaplan–Meier analysis was performed to identify risk factors associated with survival time. Risk factors that were significant in Kaplan–Meier analysis were used in a Cox regression model to identify independent risk factors. p value < 0.05 was accepted as statistically significant.

3. Results

A total of 233 patients who were followed in the palliative care unit were included in the study. The patients' mean age was 77.6 ± 11.0 years; 118 patients (50.6%) were women while 115 (49.4%) were men. There were no statistically significant differences in sex or age between the surviving and deceased groups (Table 1). Mean ages of the deceased and surviving patients were 78.5 ± 10.7 years and 77.1 ± 11.2 years, respectively (p = 0.182). Patients who died had significantly higher rates of chronic kidney disease (CKD) and chronic

Table 1
Associations between selected variables and mortality in patients receiving palliative care.

	Deceased (n = 80)	Survived (n = 153)	p
Sex			
Female	37 (68.6%)	81 (31.4%)	0.203
Male	72 (62.6%)	43 (37.4%)	
Comorbidities			
Diabetes mellitus	9 (22.5%)	31 (77.5%)	0.058
Chronic obstructive pulmonary disease	18 (47.4%)	20 (52.6%)	**0.049**
Chronic kidney disease	23 (59.0%)	16 (41.0%)	**< 0.001**
Coronary artery disease	16 (34.8%)	30 (65.2%)	0.536
Cerebrovascular event	20 (31.7%)	43 (68.3%)	0.365
Solid organ malignancy	18 (36.0%)	32 (64.0%)	0.452
Malnutrition	46 (35.9%)	82 (64.1%)	0.334
Dementia	34 (35.1%)	63 (64.9%)	0.447
Parkinson's disease	2 (25.0%)	6 (75.0%)	0.442
Risk factors			
Infection	73 (91.3%)	102 (66.7%)	**< 0.001**
Central venous catheterization	15 (65.7%)	9 (37.5%)	**0.003**
Urinary catheterization	48 (39.3%)	74 (60.7%)	0.060
Nasogastric intubation	5 (35.7%)	9 (64.3%)	0.560
Transfusion	24 (42.9%)	32 (57.1%)	0.085
Mechanical ventilation	6 (54.5%)	5 (45.5%)	0.132
ICU stay	22 (44.9%)	27 (55.1%)	0.058
Surgery history	18 (36.0%)	32 (64.0%)	0.462
History of steroid use	2 (20.0%)	8 (80.0%)	0.271
Number of comorbidities			
0	1 (16.7%)	5 (83.3%)	0.458
1	10 (29.4%)	24 (70.6%)	
2	25 (31.3%)	55 (68.8%)	
≥ 3	44 (38.9%)	69 (61.1%)	
Scoring systems			
APACHE II (> 20.5)	33 (55.0%)	27 (45.0%)	**< 0.001**
CCI (> 6.5)	43 (41.0%)	62 (59.0%)	**0.037**
Feeding			
Enteral	35 (29.1%)	85 (70.9%)	0.218
Parenteral	18 (50%)	18 (50%)	
Enteral + parenteral	27 (25.1%)	50 (64.9%)	
Laboratory results			
CRP (> 9.0 mg/dl)	50 (44.4%)	62 (55.4%)	**0.001**
Neutrophil ratio (> 82.5%)	42 (43.8%)	54 (56.3%)	**0.011**
Albumin (< 3.2 mg/L)	67 (41.1%)	58.9 (58.9%)	**0.001**
Vital signs at admission			
Fever (> 38.3 °C)	9 (34.6%)	17 (65.4%)	0.974
Tachycardia (> 100/min)	33 (60.0%)	22 (40.0%)	**< 0.001**
Hypoxia (< 90%)	38 (74.5%)	13 (22.5%)	**< 0.001**
Hypotension (< 90/60 mmHg)	21 (47.7%)	23 (52.3%)	**0.038**

obstructive pulmonary disease (COPD). No statistically significant correlation was detected between mortality and number of comorbidities. However, as the number of comorbidities increased, there was a tendency toward higher mortality rate. History of infection and central venous catheterization was significantly more common among patients who died. Cut-off values determined in ROC curve analysis using Youden's index were 20.5 for APACHE II score (AUC: 0.642, 95% CI: 0.565–0.719; p < 0.001), 6.5 for CCI (AUC: 0.578, 95% CI: 0.501–0.655; p < 0.039), 9.0 mg/dl for CRP (AUC: 0.631, 95% CI: 0.559–0.703; p = 0.001), 82.50% for neutrophil percentage (AUC: 0.608, 95% CI: 0.532–0.683; p = 0.007), and 3.2 mg/L for albumin (AUC: 0.642, 95% CI: 0.565–0.719; p < 0.001). There were significant differences between the surviving and deceased groups in proportion of patients with high APACHE II and CCI scores, CRP levels, and neutrophil percentage and low albumin level based on the specified thresholds (Table 1).

Of 153 patients who were discharged, 94 (61.4%) died within the first 12 months after discharge and 59 (38.6%) survived beyond 12 months. Several significant risk factors for mortality and their correlation with survival time are presented in Table 2.

A Cox regression model using risk factors found to significantly shorten mean survival times (CKD, COPD, tachycardia, hypoxia, albumin < 3.2 mg/L) and APACHE II score > 20.5 showed that CKD reduced in-hospital survival time by 2.170 fold (95% CI: 1.307–3.603; p = 0.003) and low albumin level reduced in-hospital survival time by 2.120 fold (95% CI: 1.170–3.863; p = 0.013).

Another Cox regression model was made using risk factors associated with 12-month post-discharge survival time: solid organ malignancy, APACHE II score, CCI, history of central venous catheter, and albumin level less than 3.2 mg/L). According to this model, presence of solid organ malignancy reduced 12-month post-discharge survival time by 1.799 fold (95% CI: 1.098–2.947; p = 0.020), APACHE II score > 20.5 by 2.062 fold (95% CI: 1.247–3.411; p = 0.005), CCI > 6.5 by 1.598 fold (95% CI: 1.042–2.451; p = 0.032), and albumin level < 3.2 mg/L by 1.976 fold (95% CI: 1.256–3.107; p = 0.003).

Table 2
Association between selected risk factors and in-hospital and 12-month post-discharge survival time.

	In hospital (n = 223)			12 months post-discharge (n = 153)		
	Median survival (days)	95% confidence interval	p	Median survival (days)	95% confidence interval	p
Solid organ malignancy			0.891			**0.003**
(–)	34.69	28.25–41.13		207.72	180.29–235.15	
(+)	35.87	21.72–50.02		121.375	72.21–170.53	
CKD			**< 0.001**			0.479
(–)	38.94	31.75–46.14		192.05	165.66–218.45	
(+)	17.20	10.96–23.44		169.18	103.27–235.09	
COPD			**0.042**			0.884
(–)	37.47	30.37–44.58		191.80	165.53–218.07	
(+)	23.22	16.20–30.24		175.45	105.00–245.89	
APACHE II score			**0.006**			**0.027**
< 20.5	42.78	30.83–54.73		200.31	173.21–227.40	
> 20.5	20.37	9.68–31.06		140.00	84.46–195.53	
CCI			0.089			**0.004**
< 6.5	34.14	27.71–40.58		214.57	183.18–245.96	
> 6.5	33.66	24.78–42.54		153.22	115.21–191.00	
Infection			0.086			0.887
(–)	30.25	18.83–41.67		186.12	143.32–228.91	
(+)	34.16	27.78–40.54		191.38	161.25–221.52	
CVC history			0.338			**0.043**
(–)	35.98	29.39–42.57		195.00	169.50–220.49	
(+)	29.71	16.42–43.09		104.33	28.55–180.10	
CRP (mg/dl)			0.285			0.838
< 9	28.06	22.48–33.64		188.61	157.04–220.18	
> 9	34.53	27.08–41.97		191.21	151.83–230.58	
Neutrophil fraction (%)			0.205			0.616
< 82.5	39.27	30.18–48.37		192.15	161.91–222.38	
> 82.5	31.81	23.80–39.82		185.11	142.68–227.53	
Albumin (mg/L)			**0.006**			**0.008**
> 3.2	46.12	33.36–58.87		236.42	197.59–275.25	
< 3.2	31.79	24.81–38.77		161.90	131.44–192.36	
Fever			0.682			0.747
(–)	35.19	28.45–41.93		191.11	164.92–217.31	
(+)	32.96	23.33–42.59		178.05	105.67–250.44	
Tachycardia			**< 0.001**			0.389
(–)	42.70	34.54–49.86		194.56	168.05–221.07	
(+)	18.50	12.77–24.23		160.50	95.07–225.92	
Hypoxia			**< 0.001**			0.473
(–)	43.53	35.53–51.53		192.57	166.77–218.38	
(+)	13.72	8.61–18.82		158.30	77.32–239.29	
Hypotension			0.150			0.447
(–)	39.08	31.57–46.58		165.54	121.11–209.97	
(+)	25.09	18.07–32.11		214.88	122.94–306.83	

CVC: central venous catheter; CCI: Charlson Comorbidity Index; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein.

4. Discussion

Albumin is the major component of plasma proteins, and is involved in maintaining oncotic pressure and preserving microvascular permeability, acid-base equilibrium, and platelet aggregation.[5] Moreover, it is used as an indicator of nutritional status in patients with acute and chronic diseases.[6] Albumin levels decrease in nephrotic syndrome and chronic inflammatory diseases such as infectious diseases and malignancy, and conditions in which interleukin-1 and TNF-alpha secreted during inflammation repress albumin production in the liver.[7,8]

Previous studies have shown that hypoalbuminemia increases mortality in patients with acute myocardial infarction,[9] heart failure,[10] stroke,[11] kidney disease,[12] hip fracture,[13] and malignancy.[14,15] Studies in the literature have also associated hypoalbuminemia in the elderly with higher mortality.[16–18] A study by Akirow et al. showed that hypoalbuminemia not only increases short- and long-term mortality among the elderly, but also among young adults.[19] Similar to the literature, the results of our study demonstrated that hypoalbuminemia in elderly patients in geriatric palliative care was as an independent risk factor that reduced in-hospital survival time by 2.120 fold and 12-month post-discharge survival time by 1.976 fold.

Patients with CKD have many potential risk factors for mortality, including old age, comorbidities, poor response to vaccination, immunosuppressive treatment, uremia, dialysis access route, and dialysis method. Studies conducted in Turkey on hemodialysis patients have associated the presence of CKD with increased mortality.[20] Consistent with the literature, we found in the present study that CKD was associated with a 2.170-fold reduction in survival time. However, not evaluating CKD stage or etiology and not recording whether patients received renal replacement therapy are among the limitations of our study.

Advanced chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide.[20,21] Previous studies of COPD patients receiving palliative care have reported poor prognosis in patients with poor pulmonary functions (FEV_1 < 30%), hypoxia in arterial blood gas analysis, and cor pulmonale secondary to pulmonary hypertension.[22] Although not assessing FEV_1, hypoxia on arterial blood gas analysis, or pulmonary hypertension are limitations of our study, we found that the incidence of COPD was higher among patients who died.

Furthermore, in our study, solid organ malignancy and high CCI were identified as independent risk factors for shorter post-discharge survival time in elderly patients, which was consistent with the literature.[23]

Studies investigating the effect of gender on mortality have yielded conflicting results. There are some studies associating male gender with mortality,[24,25] while others report that gender has no effect on mortality.[26,27] Although the underlying mechanism is not fully understood, it has been shown that the incidence of acute and chronic cardiovascular and septic events is higher among men[25,28] and the immunoprotective effect of estrogen has been demonstrated in both human and animal studies.[29,30] Although women were predominant in our patient population, we found that gender was not associated with mortality.

To our knowledge, there are few studies on mortality in palliative care in the literature. Similarly, there have been no studies in Turkey investigating mortality in palliative care centers, which are newly emerging in our county. Therefore, our study is important as the first research to be conducted on this subject. However, this study has some limitations. One of these is that the study was performed in a single center. Although the study was conducted on patients receiving geriatric palliative care, another limitation is that we did not include assessment of other geriatric syndromes such as frailty and falling, which we believe may also be associated with mortality. Performing an extensive geriatric assessment for palliative care in the elderly population may be especially beneficial.

5. Conclusion

In conclusion, CKD and low albumin were found to be independent risk factors for shorter in-hospital survival time. Independent risk factors for shorter 12-month post-discharge survival time included presence of solid organ malignancy, high APACHE II score, high CCI, and low albumin level.

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