

Is hypoalbuminemia a predictor for mortality in Tracheostomized patients transferred from intensive care unit to palliative service?

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ABSTRACT

Objective: Tracheostomy is a bedside surgical procedure that is frequently performed in intensive care units. It allows patients who need a long-term mechanical ventilator to be transferred from intensive care through a home-type mechanical ventilator. In this study, we aimed to evaluate the relationship between serum albumin levels before hospitalization and discharge or before exitus and mortality in patients who were transferred to the palliative care service with a home type mechanical ventilator by opening a tracheostomy in the intensive care unit.

Material-Method: 110 patients with tracheostomy and home ventilator who were transferred from the intensive care unit to the palliative care service between 01/05/2018-11/05/2021 were analyzed retrospectively. Patients' age, gender, diagnosis of hospitalization (chronic obstructive pulmonary disease (COPD) / malignancy), presence of comorbidity, number of days of tracheostomy (on which day the tracheostomy was opened in the intensive care unit admission), Glasgow Coma Scale (GCS) and intensive care severity scores (Acute Physiology and Chronic Health Evaluation Score (APACHE II), Sequential Organ Failure Assessment (SOFA), hospitalization serum albumin (g/dl) values, and recent serum albumin values of those who had exitus or discharge before discharge or exitus were examined retrospectively.

Results: The study's results showed that the 28-day mortality relation with old age is statistically significant. There is a statistically significant relationship between the high SOFA score at admission to the intensive care unit and 28-day mortality. There is no statistically significant difference between gender, presence of comorbidity in patients with COPD and malignancy hospitalization, GCS, APACHE II showing intensive care severity score, number of days of tracheostomy and 28-day mortality. There is a statistically significant difference between the intensive care hospitalization serum albumin value and the low serum albumin values before discharge/death and the mortality rate of 28 days.

Conclusion: In the analysis of this study, it was observed that old age and high SOFA score increased 28-day mortality in tracheostomized patients transferred to the palliative service in the intensive care unit. In addition, the low level of albumin values in intensive care hospitalization and before discharge/death also increases mortality.

Keywords: Albumin, Mortality, Palliative care, Tracheostomy, Intensive care

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INTRODUCTION

Albumin is a protein that is naturally found in plasma. It has high solubility and a negative charge. Up to 9-12 gram Albumin produces in the liver daily (1). Plasma oncotic pressure is very important in albumin synthesis. Insulin, thyroxine, and cortisol also increase albumin synthesis. Under normal conditions, albumin moves from the intravascular space through the capillary wall to the interstitial space. Albumin that passes into the interstitial space returns to the intravascular space via the lymphatic system. Thus, the albumin cycle is formed, which affects the oncotic pressure (2,3).

Studies conducted with inpatients have shown that hypoalbuminemia increases the length of hospital stay, complication rates, and mortality (4). The relationship between hypoalbuminemia and poor prognosis was independent of the patients' inflammation and nutritional status. It has also been observed that low serum albumin increases mortality in intensive care patients (5).

Serum albumin level has been added as one of the evaluation parameters to the APACHE III scoring system as a mortality determinant and is also included in the APACHE IV scoring system. The production and secretion of many plasma proteins, such as antiproteases, C-reactive protein, fibrinogen, α 1-antitrypsin, complement C3 increase in the cytokine-mediated acute phase response of inflammation. In addition, plasma concentrations of constitutive proteins such as albumin and transferrin decrease (6,7).

Sepsis hypoalbuminemia most commonly develops as a result of the change in albumin distribution due to increased capillary permeability. Measurement of colloid osmotic pressures in serum and edema fluid reflects increased capillary permeability in sepsis (8-10). Due to the release of cytokines, the escape rate from the capillary endothelium increases 3 times. The inability of lymphatic functions to compensate for the capillary escape rate also contributes to the development of edema in septic patients (9).

Palliative care is a care service that provides the adaptation of tracheostomy patients to a home-type mechanical ventilator and supports patients and their relatives both physically and psychologically (11). There are many publications in the literature regarding the effect of intensive care albumin level on mortality. In this study, we aimed to study the effect of plasma albumin level on discharge and mortality in home-type mechanical ventilated tracheostomized patients transferred from the intensive care unit to the palliative care service.

MATERIAL and METHODS

Permission was obtained from the hospital ethics committee for the study (date: 14.01.2021 and decision no: 709). Written and signed consents of the patients or their relatives are available in the patient files to evaluate and use the patients' data for scientific purposes and studies.

This study includes patients who were transferred from the anesthesia intensive care unit of the hospital to the palliative care service with a tracheostomized home-type ventilator with any diagnosis between 01/05/2018-11/05/2021 and received inpatient treatment.

These patients are over the age of 18 and patient data were scanned retrospectively. The values recorded retrospectively from the hospital database and patient files are as follows: Patients' age, gender, diagnosis of hospitalization (chronic obstructive pulmonary disease (COPD)/malignancy), presence of comorbidity, number of days of tracheostomy (on which day the tracheostomy was opened in the intensive care unit admission), Glasgow Coma Scale (GCS) and intensive care severity scores (Acute Physiology and Chronic Health Evaluation Score (APACHE II),

Sequential Organ Failure Assessment (SOFA), hospitalization serum albumin (g/dl) values, and recent serum albumin values

of those who had exitus or discharge before discharge or exitus. The relationship between albumin value and mortality was examined by accessing the 28-day mortality of the patients from the death notification system.

Statistical Analyses: Data analyses were performed by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). Whether the distribution of continuous variables was normal or not was determined by the Kolmogorov-Smirnov test. The Levene test was used for the evaluation of homogeneity of variances. Continuous data were described as mean $\pm$ SD and median (interquartile range). Categorical data were described as number of cases (%). Student's t-test compared statistical analysis differences in normally distributed variables between two independent groups, Mann Whitney U test was applied for comparisons of the not normally distributed data. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to assess the association between and the risk factors findings. It was accepted p -value < 0.05 as a significant level in all statistical analyses.

RESULTS

Patients who tracheostomized home ventilators transferred from intensive care to palliative care between 01/05/2018-11/05/2021 were retrospectively analyzed.

The relationship between old age and 28-day mortality was statistically significant in patients who were transferred to the palliative care service with a home mechanical ventilator by opening a tracheostomy in the intensive care unit. A statistically significant correlation between the high SOFA score at admission to the intensive care unit and the 28-day mortality was found. No statistically significant relationship was found between gender, diagnosis of COPD and malignancy hospitalization, presence of comorbidity, GCS, APACHE II intensive care unit severity score, number of days of tracheostomy and 28-day mortality. A statistically significant correlation was found between the low serum albumin values of intensive care hospitalization and the serum albumin values before discharge/death and 28-day mortality (**Table 1**). Ages and SOFA scores of patients with 28-day mortality were statistically significantly higher than the group without mortality ($p < 0.05$).

Hospitalization albumin and final albumin values (before discharge/exitus) of patients with 28-day mortality were found to be statistically significantly lower than patients without mortality ($p < 0.05$). Univariate logistic regression analysis was applied for factors affecting mortality. As a result of univariate logistic regression analysis, it was evaluated that age, malignancy, APACHE II, SOFA and albumin (discharged or ex) ($p < 0.25$) could be factors affecting mortality, and these factors were included in the multivariate logistic regression analysis (**Table 2**).

Enter method was used in multivariate logistic regression analysis. According to the results, a decrease in serum albumin value (discharged or ex) (OR(95% CI):0.025 (0.006-0.110) was considered to be a factor increasing the risk of mortality (**Table 2**) (**Figure 1**).

Table 1: Mortality Relationship of Variables of 28-Day Mortality Patients

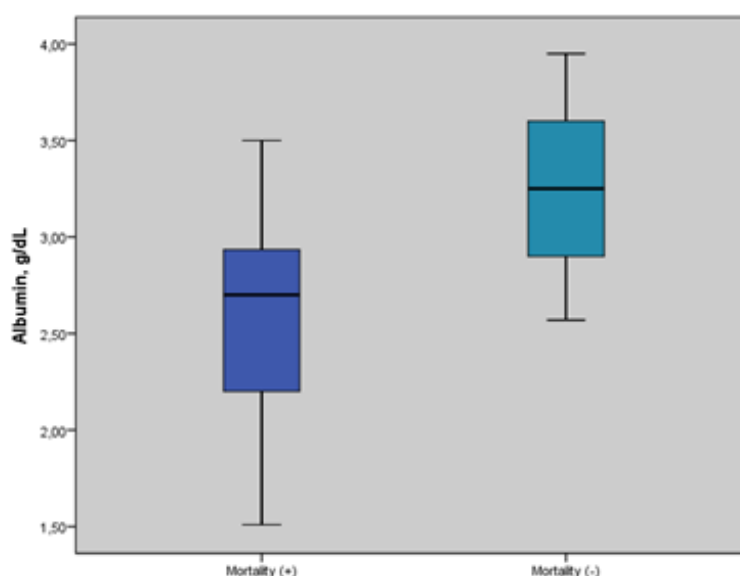
		28-Day Mortality (+) (n:68)	28-Day Mortality (-) (n:42)	P
		$\bar{X} \pm SD$ med(IQR) or n(%)	$\bar{X} \pm SD$ med(IQR) or n(%)	
Age*		73,37 $\pm$ 13,17	65,67 $\pm$ 16,62	0,004
Gender ^Φ	Male	42(61,8%)	26(63,4%)	0,575
	Female	26(38,2%)	15(36,6%)	
Presence of comorbidity ^Φ	No	35(51,5%)	23(54,8%)	0,737
	Yes	33(48,5%)	19(45,2%)	
COPD ^Φ	No	28(41,2%)	13(31,0%)	0,281
	Yes	40(58,8%)	29(69,0%)	
Malignancy ^Φ	No	55(80,9%)	39(92,9%)	0,084
	Yes	13(19,1%)	3(7,1%)	
APACHI*		25,53 $\pm$ 7,70	23,36 $\pm$ 8,33	0,077
		24,00(8,00)	21,00(10,00)	
GCS*		9,81 $\pm$ 3,80	10,05 $\pm$ 4,13	0,634
		11,00(5,50)	11,00(7,00)	
SOFA*		8,15 $\pm$ 2,19	7,14 $\pm$ 1,87	0,021
		8,00(3,50)	6,50(3,00)	
Tracheotomy Day *		9,62 $\pm$ 5,90	10,14 $\pm$ 8,18	0,815
		9,00(7,50)	8,50(11,00)	
Albumin Admission ^β		2,73 $\pm$ 0,58	2,99 $\pm$ 0,59	0,022
		2,80(0,77)	2,94(0,96)	
Albumin (Discharged or Ex)*		2,58 $\pm$ 0,49	3,23 $\pm$ 0,39	<0,001
		2,70(0,74)	3,25(0,70)	

Continuous variables are expressed as either the mean $\pm$ standard deviation (SD) and median (interquartile range) and categorical variables are expressed as either frequency (percentage). Continuous variables were compared with student t test, mann-whitney u test*, and categorical variables were compared using Pearson's chi-square test or Fisher's exact test^Φ. Statistically significant p-values are in bold.

Table 2: Factors Affecting Mortality with Logistic Regression Analysis

	Univariate Logistic Regression					Multivariate Logistic Regression				
	Wald	OR	%95 C for OR	p		Wald	OR	%95 C for OR	p	
Age	6,274	1,036	1,008	1,066	0,012	1,632	1,022	0,989	1,056	0,201
Gender	0,030	1,073	0,481	2,393	0,863					
Presence of comorbidity	0,113	1,141	0,528	2,469	0,737					
COAH	1,154	0,640	0,284	1,444	0,283					
Malignancy	2,775	3,073	0,820	11,511	0,096	1,522	2,593	0,571	11,785	0,217
APACHE II	1,904	1,037	0,985	1,091	0,168	0,243	0,979	0,898	1,067	0,622
GCS	0,098	0,984	0,891	1,087	0,755					
SOFA	5,607	1,276	1,043	1,562	0,018	0,035	1,032	0,744	1,430	0,851
Tracheotomy Day	0,155	0,989	0,935	1,046	0,694					
Albumin Discharge/ Ex	23,637	0,025	0,006	0,110	<0,001	19,836	0,027	0,005	0,132	<0,001

Wald : test statistics, OR: odds ratio, CI: Confidence interval. Statistically significant p-values are in bold.

**Figure 1:** 28-Day Mortality developing and Non-Developing Albumin Levels

DISCUSSION

In this study, it was found that old age, high SOFA score, low serum albumin values before hospitalization and discharge / death were associated with 28-day mortality in patients who were transferred to the palliative care service with a home type mechanical ventilator by opening a tracheostomy in the intensive care unit. No correlation was found between gender, diagnosis of COPD and malignancy hospitalization, presence of comorbidity, GCS, APACHE II intensive care severity score, number of days of tracheostomy and 28-day mortality.

Albumin is the most abundant protein in plasma and is the main carrier of many compounds in the blood. Because this protein also acts as a negative acute phase reactant, it can be affected by many acute and chronic disease processes (12). The effects of serum albumin on protein metabolism during the disease process allow it to be considered as a prognostic factor. There are many causes of hypoalbuminemia. In acute disease, inflammation, increased capillary leakage and decreased synthesis due to underlying malnutrition and/or hepatic synthesis dysfunction cause hypoalbuminemia. Due to all these reasons, it has been suggested that albumin can be used as a biomarker in the prognosis follow-up of critically ill patients treated in hospital (1).

Patkins et al. showed that patients with hypoalbuminemia (albumin < 3.5 g/dL), including patients in septic shock treated in the intensive care unit, had higher APACHE and SOFA scores and increased 30-day all-cause mortality (13). In our study, although a correlation between 28-day mortality and high SOFA scores was found, it could not be found with APACHE scores.

Some studies have shown that a decrease of approximately 1 gram in serum albumin levels in patients aged 80 and over increases the risk of cardiac disease, cancer, and mortality (14). Supporting this, some studies have reported that decreased albumin levels increase cardiovascular risk in patients (13-14). Our study found that low albumin value before admission to the intensive care unit and discharge/exitus was associated with 28-day mortality, similar to the literature.

Albumin values below 2.5 g/dl were found to be significant in terms of mortality in studies (15,16). However, there was no cut-off value for albumin in our study. In general, in patients with 28-day mortality, albumin levels were significantly lower at hospitalization and at the recent values before discharge or death. Albumin values were significantly higher in patients who did not develop 28-day mortality compared to those who did not.

It has been shown in the literature that there is a relationship between albumin value and gender and mortality (17). It has been stated that the negative change in plasma albumin increases mortality in patient groups of all ages and genders. However, in our study, no significant relationship was found between gender and albumin value, nor could it be associated with mortality.

It has not been fully proven whether interventions designed to increase the albumin value, such as nutritional supplements, have the potential to improve outcomes in patients with hypoalbuminemia (13). In particular, intravenous hyperoncotic albumin supplementation targeting an albumin

level ≥ 3 g/dL in hypoalbuminemic patients with sepsis or septic shock has not been shown to provide an improvement in clinical outcomes (19). Therefore, the routine use of albumin-containing solutions is not supported, although there is a relationship between acute hypoalbuminemia and increased mortality in critically ill patients. Prospective, randomized studies in critically ill patients failed to show a positive effect of albumin supplementation on mortality and morbidity (13, 17). We also avoid making unnecessary albumin replacements to our patients in intensive care.

Albumin is a sensitive marker that also shows the nutritional status of patients. Studies have shown that a low albumin level is associated with intensive care, mechanical ventilation, vasopressor need and mortality of patients (19, 20). All patients in our study had tracheostomy and already had mechanical ventilator needs, so we found that albumin deficiency was associated with mortality.

CONCLUSION

In tracheostomy patients transferred from the intensive care unit to the palliative service, old age, high SOFA score, low albumin value before hospitalization, and discharge or death in the intensive care unit increase 28-day mortality.

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Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study.

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