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Original Article

Association of Serum Albumin Levels at Admission on Physical Function and Walking Capacity in Patients with Acute Illness

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SUMMARY

Objective: In this retrospective study, we aimed to group the albumin concentrations at the time of hospitalization among elderly patients who were admitted for internal medical care. These concentrations were then used to clarify the relationship between physical function and activities of daily living.
Method: We included 1328 patients aged ≥ 65 years old who were hospitalized between December 2015 and April 2018. Data were collected on prehospital mobility, hand grip strength, balance, activities of daily living, and blood test results. Patients were assigned to low (< 2.5 mg/dL; 270 patients), mild (< 3.5 mg/dL; 796 patients), and normal (≥ 3.5 mg/dL; 262 patients) albumin groups.
Results: The low albumin group had worse outcomes in all evaluations. The risk of having poorer walking ability at discharge was significantly higher in the low albumin group than in the normal albumin group. Compared with the normal group, the OR for the low albumin group that was associated with a change in the level of assistance from independent to assisted walking was 1.7 (95% CI, 1.1–2.4; $p < 0.01$), whereas that for the mildly low albumin group was 1.3 (95% CI, 0.7–2.7; $p = 0.33$). The respective ORs for declining from independent walking to difficulty with walking were 2.4 (95% CI, 1.2–4.8; $p < 0.01$) and 2.1 (95% CI, 0.8–2.8; $p = 0.25$).
Conclusion: We conclude that a relationship exists between low admission albumin levels and poorer physical function at discharge.

1. Introduction

Walking is fundamental to daily life; thus, it is an especially important factor in order to assess the elderly to determine the prognosis for life.[1] Decline in walking ability in the elderly, as well as movement ability,[2] has been applied as a harmful risk marker.

Furthermore, rates of decline in physical function and in activities of daily living (ADLs) were determined to be higher among the elderly when they are admitted to a hospital.[3,4] Hospitalization was considered a risk factor for decreased function.[3,5] Since walking is the basis of daily life, it is speculated that walking ability is also reduced. A strong correlation has been determined between nutritional status and physical function, as reported in many studies.[6–8]

Therefore, albumin levels at admission may reflect a patient's general health status. Although elderly patients who are admitted with acute medical disorders are considered at increased risk of declining walking ability, the extent of the decline may vary depending on the nutritional status at the time of admission. In Japan, a few studies on large hospitalized cohorts of patients with acute medical disorders and multiple comorbidities have been reported.

Therefore, this study examines the relationship between changes in walking ability and albumin levels before admission and after discharge in elderly patients with acute medical disabilities.

We hypothesized that the lower the albumin levels at admission, the lower will be their walking ability, which is the basic movement in ADLs, and the greater the risk of hospitalization.

2. Material and methods

2.1. Study design and participants

This retrospective study has used the data of patients admitted to a 500-bed secondary care emergency medical institution. Patients who received physical therapy when admission in any internal medicine department (e.g., respiratory medicine, cardiovascular medicine, gastroenterology, hematology, diabetes/endocrinology, and kidney medicine) between December 2015 and April 2018 were included. However, those who were younger than 65 years, refused physical therapy, died, and those whose albumin levels were not measured at admission were excluded from the analysis. The patients were then divided into the following three groups based on their albumin levels at admission: the "low albumin" group, which consisted of patients with < 2.5 g/dL; the "mildly low albumin" group, which consisted of those with 2.5–3.4 g/dL; and the "normal albumin" group, which consisted of those with ≥ 3.5 g/dL.[9]

The study was approved by the ethics committee of our hospital (research number 2019-915). This study has received IRB approval

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from the Clinical Research Review Board of Iwata City General Hospital. Furthermore, the study content was disclosed in paper and electronic formats, and individual patients could withdraw their consent on the use of their data at any time.

2.2. Data collection

Six physical therapists provided the patient therapy and obtained the study data by performing a retrospective survey of the patients' electronic medical records. The survey items included basic characteristics (e.g., age, gender, body mass index [BMI], dementia, and diagnosis), comorbidities (e.g., Charlson Comorbidity Index [CCI][10]), prehospital transportation, prehospital activity status, blood test values at admission (e.g., albumin, C-reactive protein [CRP], and hemoglobin [Hb]), grip strength, balance, ADLs (e.g., Barthel Index [BI]), length of hospitalization, and physical therapy time (PTt). The patients' physical function and ADLs were both measured at the start of physical therapy. Walking ability at the time of discharge was examined using the BI walking items. Physical therapy intervention time was expressed as days of hospitalization divided by the total physical therapy intervention time.

Dementia scores were not calculated, and we relied on "Yes" and "No" answers, using the Mini-Cog© test, which is a simple cognitive screening test.[11]

Prehospital transportation: The methods of prehospital transportation were classified as "self-walking," "cane," "walker/walking trolley," and "wheelchair." In addition, the BI walking items were scored (0–15 points). The patients' activity status before hospitalization was evaluated into seven stages ranging from very healthy to severely frail, using the Clinical Frailty Scale© (CFS). Grip strength was measured in bed with a grasping motion at an elbow extension position of 60° G-up. The averages of the left and right values were then used. Balance was evaluated using the standing test for imbalance and disequilibrium (SIDE), which is identified as a discriminative measure of static standing balance. The SIDE score has been shown to be highly correlated with the Berg Balance Scale among patients, in acute and convalescent hospitals, having high inter-rater reliability.[12]

2.3. Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences, version 21 (IBM Japan Ltd., Tokyo, Japan). Continuous variables are expressed as medians (first to third quartiles), while qualitative variables are expressed as percentages (number). The comparisons between groups were then performed using χ^2 tests or the Mann-Whitney *U* tests, with the significance level adjusted using the Bonferroni correction. Statistical superiority was defined for levels < 1%.

Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using multiple logistic regression analyses in order to assess the relationship between the patients' albumin level and their walking ability at discharge. Walking ability was defined as a BI score of 15, assisted walking as a BI of 10, and difficulty walking as a BI of ≤ 5 items. Items were then compared between admission and discharge. The ORs were calculated using dependent walking and difficulty walking as dependent variables, with adjustments made for age, gender, BMI, dementia, CCI, and PTt.

3. Results

3.1. Patient characteristics

We identified 1,802 admitted patients with acute medical illnesses. Among these patients, we have included 1,328 of them (Figure 1). The patients that were included were then grouped as follows: 270 patients (20.3%) in the low albumin group, 796 (60.0%) in the mildly low albumin group, and 262 (19.7%) in the normal group (Table 1 and Figure 1).

The median age of the cohort was 84 years, (range, 78–89 years), and 722 patients (54.4%) were women. The main reasons for admission were heart diseases (25.2%), kidney diseases (10%), gastrointestinal diseases (28.2%), respiratory diseases (10.7%), cancers (7.5%), and diabetes mellitus (4.2%), with other diseases accounting for the remaining 14.2%. In total, 609 patients walked independently before admission. The number of days from admission to the start of physical therapy was 4.2 ± 5.5 days, and the patients were admitted for an average of 18 days (range, 12–28 days), and PTt was determined to be on an average 11.6 minutes (range, 9.4–13.7 minutes). The median assessment values were as follows: BMI, 20.4 kg/m^2 (range, 18.2–23 kg/m^2); CFS, 4 (range, 2–6); grip strength, 13.4 kg (range, 9.3–18 kg); SIDE, 2a (range, 1–2b); BI, 45 (20–70); albumin, 3 g/dL (range, 2.6–3.4 g/dL); CRP, 2.2 mg/dL (range, 0.5–7.1 mg/dL);

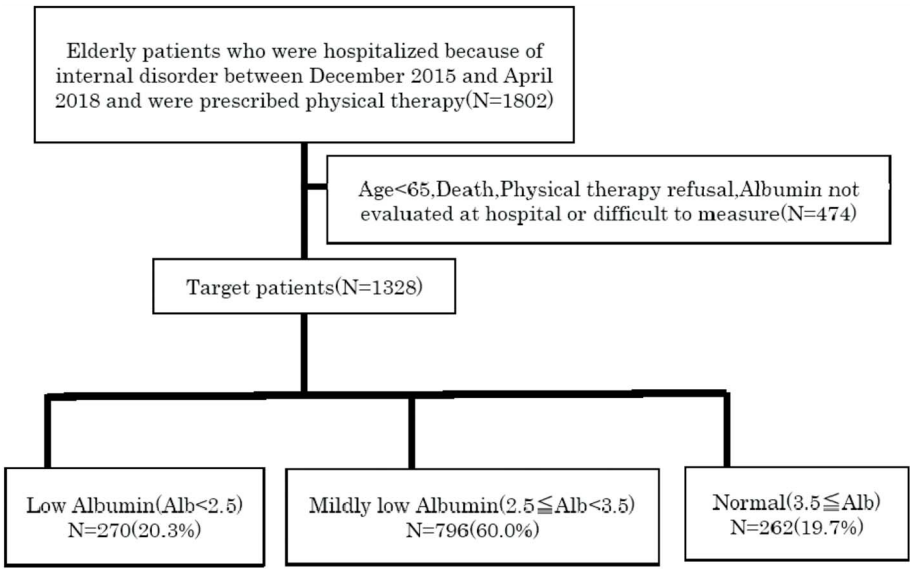

Figure 1. Study flow chart.

Table 1
Comparison of basic characteristics among the three albumin groups.

	Total (n = 1328)	Low albumin (n = 270)	Mildly low albumin (n = 796)	Normal (n = 262)	p[a]	p[b]	p[c]
Age	84 (78–89)	84 (77–88)	84 (79–89)	81 (74–86)	0.07	0.02	< 0.01
Female % (n)	54.4 (722)	47.1 (127)	56.9 (453)	54.2 (142)	< 0.01	0.1	0.43
BMI (kg/m^2)	20.4 (18.2–23)	20.5 (18.4–22.6)	20.4 (17.8–22.9)	21.1 (18.6–23.5)	0.60	0.12	0.03
How to walk before hospitalization %					0.16	< 0.01	< 0.01
No aids % (n)	43.4 (576)	38.5 (104)	39.8 (317)	59.6 (156)			
Cane % (n)	15.7 (208)	14.8 (40)	16.1 (128)	15.1 (40)			
Walker % (n)	11 (147)	7.4 (20)	12.5 (100)	10.1 (26)			
Wheelchair % (n)	29.9 (397)	39.3 (106)	31.5 (251)	15.1 (40)			
CFS	4 (2–6)	5 (3–7)	4 (3–6)	3 (2–5)	0.02	< 0.01	< 0.01
Hand Grips (kg)	13.4 (9.3–18)	12.3 (9.2–16.1)	13 (9.1–18)	16.5 (11.4–21.3)	0.14	< 0.01	< 0.01
Balance (SIDE)	2a (1–2b)	1 (0–2a)	2a (1–2b)	2a (2a–3)	< 0.01	< 0.01	< 0.01
ADL (BI)	45 (20–70)	35 (10–55)	45 (20–65)	68 (40–80)	< 0.01	< 0.01	< 0.01
CRP (mg/dL)	2.2 (0.5–7.1)	6 (1.6–12.2)	2.2 (0.6–6.8)	0.4 (0.1–1.8)	< 0.01	< 0.01	< 0.01
Hb (g/dL)	10.7 (9.5–12)	9.6 (8.4–11)	10.8 (9.5–12.1)	12.2 (10.9–13.5)	< 0.01	< 0.01	< 0.01
Length of stay (day)	18 (12–28)	25 (17–40)	18 (12–27)	12 (9–18)	< 0.01	< 0.01	< 0.01
Heart disease % (n)	25.2 (335)	12.2 (33)	29.0 (231)	27.1 (71)	< 0.01	< 0.01	0.58
Renal disease % (n)	10.0 (133)	14.4 (39)	9.4 (75)	6.9 (19)	0.02	< 0.01	0.32
Digestive disease % (n)	28.2 (375)	30.4 (82)	27.3 (217)	27.5 (76)	0.35	0.78	0.63
Respiratory disease % (n)	10.7 (142)	11.1 (30)	11.8 (94)	6.5 (18)	0.83	0.09	0.03
Other % (n)	14.2 (189)	17.8 (48)	13.7 (109)	11.6 (32)	0.11	0.09	0.62
Diabetes mellitus % (n)	4.2 (54)	1.5 (4)	2.2 (18)	11.6 (32)	0.48	< 0.01	< 0.01
Heart failure % (n)	18.6 (247)	8.5 (23)	19.7 (157)	20.3 (56)	< 0.01	< 0.01	0.93
Renal failure % (n)	6.6 (88)	10.4 (28)	6.9 (55)	4.3 (12)	0.68	0.15	0.19
Pneumonia % (n)	9.1 (121)	10.4 (28)	10.2 (81)	4.3 (12)	0.99	0.02	< 0.01
Cancer % (n)	7.5 (100)	12.6 (34)	6.5 (52)	5.1 (14)	< 0.01	< 0.01	0.56
CCI	1 (1–3)	2 (1–3)	1 (1–3)	1 (0–2)	< 0.01	< 0.01	< 0.01
PTt (mins/day)	11.6 (9.4–13.7)	11.5 (9.2–13.4)	11.7(9.3–13.9)	11.9(10–13.3)	0.29	0.28	0.87

Median (first–third quartile), expressed as % (n).
BI: Barthel Index, BMI: body mass index, CCI: Charlson Comorbidity Index, CFS: Clinical Frailty Scale, CRP: C-reactive protein, Hb: hemoglobin, SIDE: The Standing Test for Imbalance and Disequilibrium. PT: physical therapy, PT t: Total PT time/Length of stay.
* $p < 0.01$.
[a] Low vs. mild low albumin. [b] Low vs. normal albumin. [c] Mild low vs. normal albumin.

and Hb, 10.7 g/dL (range, 9.5–12 g/dL).

3.2. Comparison between the three albumin groups

The normal albumin group was found to be significantly younger than the other two groups; and the functional level, CFS, grip strength, SIDE, and BI scores were all determined to be significantly different between the normal albumin group and the other two groups. The normal albumin group was significantly different from the low albumin group. Consequently, CRP and Hb values were also found to significantly differ between the three groups, with CRP and Hb being higher and lower in the low albumin group, respectively. The low albumin group also had significantly lower rates of heart disease and diabetes mellitus but had significantly higher rates of kidney disease and cancer. In the normal albumin group, significantly fewer patients had pneumonia, and more patients were identified to have diabetes mellitus ($p < 0.01$).

3.3. Decrease in walking ability during hospitalization

The results regarding the relationship between albumin levels and decreased walking ability during hospitalization were as follows: the rate of decline from walking independently (a BI of 15 points) to assisted walking (a BI of 10 points) was 16.7%; the rate of gait independence (a BI of ≤ 5 points) was determined to be a t6.2%; in each group, the rate of decline from walking independently (a BI of 15 points) to assisted walking (a BI of 10 points) was 38.1% in the low albumin group, 22.6% in the mildly low albumin group, and 14.5% in the normal albumin group. The rate of gait independence (a BI of ≤ 5 points) was 12.4% in the low albumin group, 6.3% in the mildly low albumin group, and 2.3% in the normal albumin group.

3.4. Multiple logistic regression analysis

Compared with the normal albumin group, the OR for the low albumin group that was associated with a change in the level of assistance from independent to assisted walking was 1.7 (95% CI, 1.1–2.4; $p < 0.01$), while that for the mildly low albumin group was 1.3 (95% CI, 0.7–2.7; $p = 0.33$). The respective ORs for the decline from independent walking to difficulty walking were 2.4 (95% CI, 1.2–4.8; $p < 0.01$) and 2.1 (95% CI, 0.8–2.8; $p = 0.25$) (Table 2).

4. Discussion

We focused on the albumin levels at admission of elderly patients who were admitted for acute medical illnesses and had disabilities that required physical therapy. Approximately 20% of inpatients in acute hospitals were determined to have low albumin levels; however, approximately 80% do not have normal albumin levels and are considered at high risk of undernutrition. Kaiser et al.[13] and Hsin-Yin et al.[9] have suggested that many hospitalized elderly patients were undernourished. In contrast to these reports, Akirov et al.[14] have found that only 30% of patients had albumin levels of < 3.5 g/dL. However, the mean age of their patients was 60 years, and their overall population is found to be relatively younger. Jellinge et al.[15] have reported that few patients had albumin levels of

Table 2
Relationship between albumin level and reduction in walking ability during hospitalization (N = 609).

	Total (N = 609)	Low albumin (N = 105)	Mildly low albumin (N = 332)	Normal (N = 172)	P[b]	P[c]
Walking independence → Assisted walking % (BI 15 points → 10 points)	16.7	38.1	22.6	14.5		
OR (95% CI)		1.7 (1.1–2.4)	1.3 (0.7–2.7)	1.0	< 0.01	0.33
Walking independence → Walking difficulty % (BI 15 points → 0 or 5 points)	6.2	12.4	6.3	2.3		
OR (95% CI)		2.4 (1.2–4.8)	2.1 (0.5–7.8)	1.0	< 0.01	0.25

BI: Barthel Index; CI: confidence interval; OR: odds ratio; CCI: Charlson Comorbidity Index; PT: physical therapy; PT t: Total PT time/Length of stay.
* $p < 0.01$.
[b] Low vs. normal albumin. [c] Mild low vs. normal albumin.
Adjustment factors: age, gender, BMI, presence of dementia, CCI, PT t.

< 3.5 g/dL. Given that the mean age of subjects in the current study was more than 80 years, it is perhaps to be expected that more patients had albumin levels below normal.

The length of hospitalization was also found to be significantly longer in the low albumin group; this finding is consistent with the results of other studies.[14,16]

Overall, the normal albumin group had significantly better preadmission mobility, chronic fatigue syndrome, muscle strength, balance, and ADL than the other two groups.

Nutritional status is often evaluated using serum albumin levels, which are widely used as an index of long-term nutritional status, regardless of whether a disease is acute or chronic.[9,16]

Albumin levels are affected by various factors, such as diet, muscle mass, inflammatory response, and complications, and are found to be associated to physical function, risk of infection, length of hospital stay, and mortality.[9,14,16]

Visser[17] has reported that low albumin levels (< 3.8 mg/dL) in the healthy elderly population is associated with a risk of lower skeletal muscle mass and that albumin affects muscle strength. The possibility of giving is suggested. Furthermore, it has been shown that grip strength and albumin levels are related correlated; low albumin levels are associated with decreased ADLs, and the progression of ADL decrease is faster in this group individuals with low albumin levels than in those with well-maintained albumin levels.[7,18,19] Moreover, chronic decreases in albumin levels are often associated with functional decline, and below normal albumin levels strongly predict functional decline.[20] In this study, the mean age of the included patients was 80 years, which is often associated with numerous comorbidities, thus suggesting that the chronic decreases in albumin levels may be associated with a loss of muscle strength and a decrease in ADLs including walking ability. In conclusion, there is a correlation between albumin levels at admission and decline in walking ability.

A chronic decrease in albumin levels was found to be associated with reduced dietary intake and chronic inflammation due to aging; this leads to a persistent increase in protein catabolism, leading to muscle weakness and a decrease in ADLs.[16,21,22] Regarding the blood test values in the current study, CRP levels were significantly elevated even in the mildly low albumin group compared with those in the normal group. This finding is consistent with the hypothesis that inflammatory reactions affect albumin levels. Furthermore, Hb levels were found to be significantly lower in the low albumin group. This may be symptomatic or causative of low albumin levels. Hb levels are observed to be affected by an individual's nutritional status and by chronic inflammation;[23] however, anemia may also cause decrease in albumin levels. Conversely, studies have shown that reduced walking ability exacerbated the increasing albumin levels.[24] One similarity between this study and the current study was that the age groups were almost the same or slightly higher in the current study.

In addition, they pointed out that serum albumin reflect the potential adverse effects of glycated serum albumin, although no specific disease has been specified in studies.

In the current study, the disease rate was 4.2% for patients with diabetes (Table 1). Therefore, the target disease may be different. Furthermore, hypoalbuminemia was caused by the combination of acute inflammatory albumin decline and age-related albumin decline. Serum albumin levels decrease with age and acute inflammation. The decline with aging starts at the age of 20 years; then, it gradually decreases thereafter.[25] In the case of acute inflammation, particularly high concentrations of IL-6 and TNF-α are the main influencing factors of hypoalbuminemia.[16]

In this study, the prolonged decline in albumin levels led to muscle weakness and a decrease in the patients' walking ability, suggesting a different result from other studies.

Regarding the presenting diseases, the proportions of patients with kidney disease, pneumonia, and cancer were significantly higher in the low albumin group than in the normal albumin group. In addition, the proportion of patients with cancer was significantly higher in the low albumin group than that in the mildly low albumin group.

Many patients with renal dysfunctions were put on a restricted protein diet.[23] Given that protein intake from diet is important for albumin synthesis, patients with renal dysfunction are at increased risk of their albumin levels gradually decreasing because of protein malnutrition.[26]

In patients with cancer, fat and skeletal muscle tissues are easily lost because of increased energy consumption due to cachexia and increased insulin resistance, thus resulting in weight loss, malnutrition, and weakness.[27]

The results of multiple logistic regression analysis indicated that low albumin levels were associated with higher odds of walking ability deterioration during admission compared with normal albumin levels. A chronic decline in albumin levels is seen to reduce muscle mass and strength,[18,19] and this may reflect systemic functions on the basis of the preadmission nutritional status. Consequently, it is speculated that the degree of movement during hospitalization is affected. In elderly patients with medical disorders requiring physical therapy, we showed that albumin levels at admission were related to walking ability at discharge.

This study has several limitations, notable among which are the numerous medical disorders and internal medical departments that were included. Moreover, we did not consider the specific diseases, specific differences in physical therapy, or any occupational interventions. In addition, the study was conducted in a single facility, which focused on albumin levels at admission only. In the future, it is necessary to consider the characteristics, symptoms, and medical management of each disease.

5. Conclusions

In this study, we showed that albumin levels at admission were

correlated with the decline in walking ability during hospitalization. In Japan, few studies have been conducted on inpatients regarding albumin levels and physical therapy, and there have been a few large-scale studies in acute settings. Therefore, the results of this study should prove to be useful for risk management and for promoting physical therapy.

Conflicts of interest

We declare that there are no conflicts of interest relevant to this study.

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