Journal of Cardiology 73 (2019) 114–119

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Prognostic implications of prealbumin level on admission in patients with acute heart failure referred to a cardiac intensive care unit

Madoka Akashi (MD), Yuichiro Minami (MD, PhD)*, Shintaro Haruki (MD, PhD), Kentaro Jujo (MD, PhD), Nobuhisa Hagiwara (MD, PhD, FJCC)

Department of Cardiology, Tokyo Women's Medical University, Tokyo, Japan

ARTICLE INFO

Article history:
Received 16 May 2018
Received in revised form 11 August 2018
Accepted 14 August 2018
Available online 23 October 2018

Keywords:
Acute heart failure
Inflammation
Nutrition
Prealbumin
Risk stratification

ABSTRACT

Background: Prealbumin is a marker of nutritional and inflammatory status, and low prealbumin level at discharge is associated with poor outcome in hospitalized patients with heart failure. However, the prognostic value of prealbumin level on admission in patients with acute heart failure (AHF) has not been established, especially in an acute care setting. We aimed to clarify the association between prealbumin level on admission and outcome in patients with AHF referred to a cardiac intensive care unit.
Methods: We analyzed 186 hospitalized patients with AHF who had their prealbumin level examined within 24 h of admission.
Results: The mean prealbumin level was 16.6 ± 6.5 mg/dL. Prealbumin effectively predicted all-cause death during the median follow-up period of 276 days, using receiver operating characteristic (ROC) curve analysis (the area under the ROC curve; 0.722, optimal cut-off point; ≤14.0 mg/dL, sensitivity 71.0%; specificity 69.7%; $p < 0.001$). The all-cause mortality and the composite endpoints of all-cause death or readmission for AHF in patients with low prealbumin level (≤14.0 mg/dL) were significantly higher than in patients with high prealbumin level (log-rank $p < 0.001$ and $p = 0.002$). Multivariate analysis adjusted for established markers of AHF severity showed that prealbumin ≤14.0 mg/dL was independently associated with higher mortality (hazard ratio 4.79; 95% confidence interval 1.89–12.2; $p = 0.001$) and with the composite endpoints (hazard ratio 2.38; 95% confidence interval 1.30–4.36; $p = 0.005$).
Conclusions: Prealbumin level on admission may be useful in the risk stratification of patients with AHF in an acute care setting.
© 2018 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

Introduction

Malnutrition is a common problem in hospitalized patients with heart failure, and is associated with adverse outcomes [1–6]. Possible pathophysiologic mechanisms of malnutrition in patients with heart failure include decreased nutritional intake, increased catabolic activity, decreased hepatic synthesis, and chronic inflammation [7,8]. To assess the nutritional status of patients with heart failure, different clinical indicators have been used, including plasma albumin and body mass index (BMI) [3,4,9]. However, anthropometric measures such as BMI are affected by states of fluid overload, especially in patients with the urgent phase of heart failure [i.e. acute heart failure (AHF)] [10]. In contrast, biochemical measurements are more objective markers of nutritional assessment and allow for the early identification of protein-energy malnutrition [11,12]. Although accepted and widely-used biochemical markers of malnutrition are albumin, total cholesterol, and lymphocyte count, it is now recognized that they are relatively insensitive to nutritional variations [13].

Growing interest has been placed on prealbumin for nutritional assessment and risk stratification in multiple settings, including critical care setting such as hemodialysis patients and in intensive care units [13–15]. In addition, prealbumin is a negative acute-phase protein in that its synthesis is suppressed in inflammatory settings in which cytokines stimulate hepatic production of acute-phase proteins. As prealbumin has a shorter average half-life than albumin, it can help estimate with more precision the nutritional and inflammatory status of a patient at the precise moment that it

* Corresponding author at: Department of Cardiology, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan.
E-mail address: yuichiro24@celery.ocn.ne.jp (Y. Minami).

https://doi.org/10.1016/j.jjcc.2018.08.003
0914-5087/© 2018 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

is measured [16]. As for hospitalized patients with heart failure, several previous studies have demonstrated that low prealbumin level at discharge is associated with a higher short-term mortality [17,18]. However, the prognostic value of prealbumin level on admission in patients with AHF has not been established, especially in acute and critical care settings. Therefore, the aim of this study was to clarify the association between prealbumin level on admission and long-term mortality and morbidity in patients with AHF referred to a cardiac intensive care unit.

Methods

Patients

We retrospectively evaluated 322 consecutive hospitalized adult patients with AHF who were referred to the cardiac intensive care unit at Tokyo Women's Medical University Hospital, Tokyo, Japan, between January 2014 and February 2017. The diagnosis of heart failure was defined by the modified Framingham criteria [19]. AHF was defined as new onset of decompensated heart failure or decompensation of chronic established heart failure sufficient to warrant referral to the intensive care unit for urgent therapy. Therefore, all patients had New York Heart Association (NYHA) functional class III or IV symptoms on admission. Patients were enrolled if they were hospitalized for AHF as the primary cause of admission. After excluding patients with missing prealbumin measurements on admission, acute coronary syndrome, a previous diagnosis of malignancy, recent surgery (within the last month of index admission), or recent trauma (total $n = 136$), 186 patients were included in our final analysis (Fig. 1). The excluded patients were similar to the cohort used in the final analysis, and no significant differences were observed in all-cause death and the composite of all-cause death or readmission due to AHF between the two groups ($p = 0.089$ and $p = 0.119$, respectively). This study was performed according to the principles of the Helsinki Declaration, and the review board of Tokyo Women's Medical University Hospital approved the protocol.

Prealbumin measurements

Fasting peripheral venous blood samples were collected within 24 h of admission. The serum prealbumin level was measured using turbidimetric immunoassay (Nittobo Medical, Tokyo, Japan).

Follow-up and endpoints

Follow-up started from the day of admission to the cardiac intensive care unit for AHF, and follow-up data were obtained from the review of in-hospital records or periodical examination of patients in our outpatient clinic. The primary endpoint of this study was all-cause death (including in-hospital and post-discharge) after AHF admission. The secondary endpoint was a composite of all-cause death or readmission due to an episode of AHF.

Statistical analysis

All statistical analyses were performed with SAS ver. 9.4 (SAS Institute, Cary, NC, USA), at an independent biostatistics and data center (STATZ Institute, Inc., Tokyo, Japan). Data are presented as mean ± standard deviation (SD), as median with interquartile range, or as frequency. Receiver operating characteristic (ROC) curves were constructed, and the area under the ROC curve was calculated to assess the usefulness of prealbumin, B-type natriuretic peptide (BNP), C-reactive protein (CRP), and blood urea nitrogen (BUN) for predicting all-cause death. Best cut-off values were identified by ROC curves with the Youden index, and sensitivity and specificity were calculated according to standard definitions. The Student's *t*-test was used to compare normally distributed continuous variables, and the Mann–Whitney *U*-test was used for skewed continuous variables. The chi-square test or Fisher's exact test (when an expected value was less than 5) were used for nominally scaled variables. To evaluate the impact of prealbumin level on the <30 days and in-hospital mortality, univariable logistic regression models were used. Event-free curves were estimated using the Kaplan–Meier method, and differences between curves were assessed by log-rank tests. Univariable and multivariable Cox proportional hazards models were used to evaluate the impact of prealbumin level on the primary and secondary endpoints. Due to the small number of primary and secondary endpoints in this study, we avoided including all potential confounders in one multivariable model. Therefore, multivariable analysis was performed using the following three separate models. Model 1 was adjusted for age and sex. Model 2 was adjusted for established markers of AHF severity such as BUN, serum albumin, BNP level, and left ventricular ejection fraction. Model 3 was adjusted for other

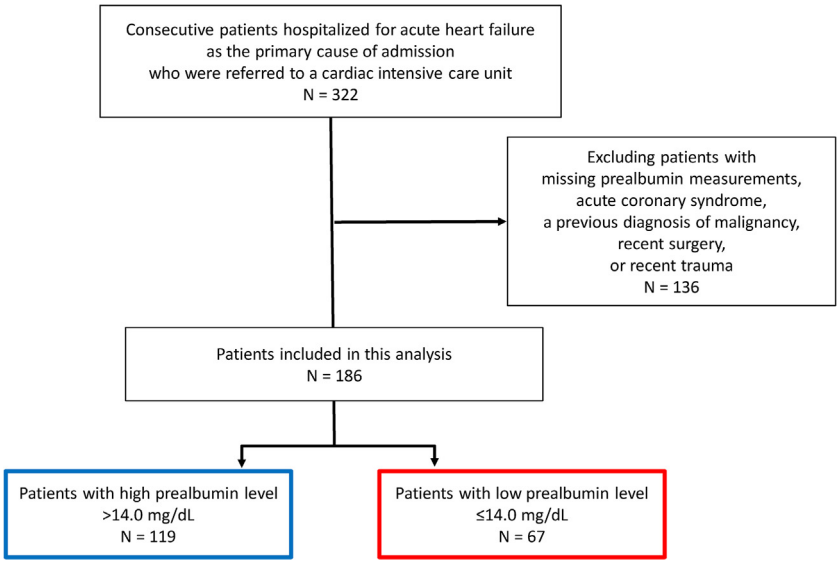

Fig. 1. Disposition of the study population.

imbalanced baseline variables such as total cholesterol, triglyceride, and CRP level. A value of $p < 0.05$ was considered to indicate statistical significance in all analyses of this study.

Results

Prealbumin level on AHF admission

The distribution of prealbumin levels on admission of the 186 patients with AHF are shown in Fig. 2A. The mean prealbumin level in the study patients was 16.6 ± 6.5 mg/dL. The distribution of prealbumin levels on admission of patients with AHF with the primary and secondary endpoints are also shown in Fig. 2A. During a median [interquartile range] follow-up period of 276 [59–648] days, 31 (16.7%) of all study patients with AHF died, and 61 (32.8%) experienced composite endpoints of all-cause death or readmission for AHF. Prealbumin level on admission was significantly lower in patients who died during the follow-up period (12.5 ± 5.6 mg/dL) than in patients who remained alive during the follow-up period (17.4 ± 6.4 mg/dL) ($p < 0.001$). Prealbumin level on admission was also significantly lower in patients who experienced composite endpoints of all-cause death or readmission for AHF during the follow-up period (14.9 ± 6.6 mg/dL) than in patients without these endpoints (17.4 ± 6.3 mg/dL) ($p = 0.012$). In ROC curve analysis, the area under the ROC curve was 0.722 and the optimal cut-off point of prealbumin level for all-cause death was ≤14.0 mg/dL (sensitivity 71.0%; specificity 69.7%; $p < 0.001$) (Fig. 2B). As a result of comparing the prognostic value for all-cause death of prealbumin level with other established biomarkers for heart failure (i.e. BNP, CRP, and BUN), prealbumin showed the most favorable performance, and the area under the ROC curve for BNP was 0.515, for CRP was 0.704, and for BUN was 0.628.

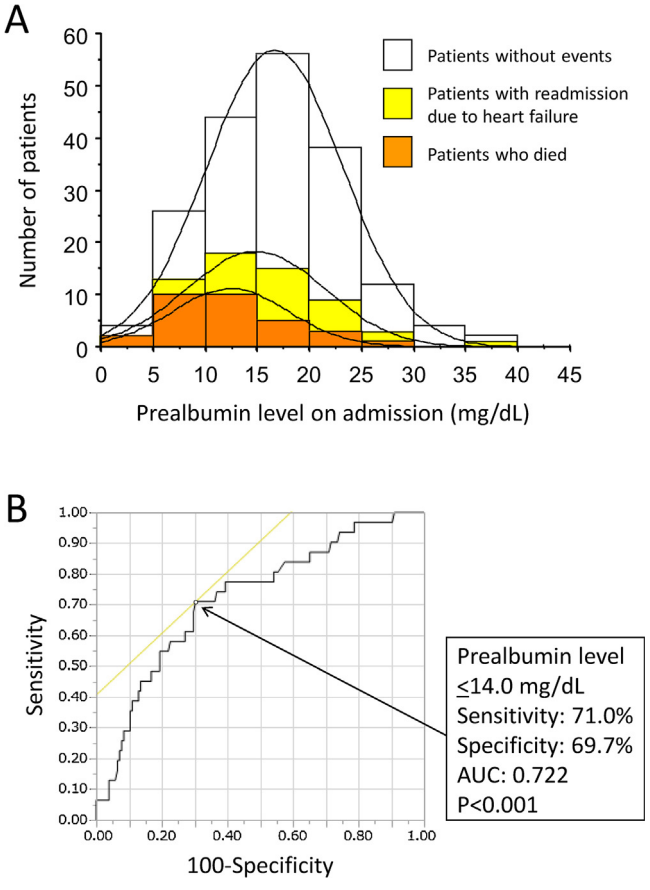

Fig. 2. Distribution of prealbumin levels on admission of study patients with acute heart failure (AHF) (A). Receiver operating characteristic (ROC) curve predicting the all-cause death for prealbumin level on admission in hospitalized patients with AHF (B). AUC, area under the ROC curve.

Baseline characteristics

Baseline clinical characteristics according to prealbumin level on admission are shown in Table 1. Patients with low prealbumin level (≤14.0 mg/dL) had higher CRP levels and lower albumin, total cholesterol, and triglyceride levels than did patients with high prealbumin level (>14.0 mg/dL). A significant negative correlation between prealbumin and CRP levels was found in study patients with AHF ($r = -0.42$, $p < 0.001$). However, there were no significant differences in age, sex, left ventricular ejection fraction, systolic blood pressure, heart rate, BUN, serum creatinine, sodium, hemoglobin, and BNP level.

Outcomes

Of the 67 patients with low prealbumin level (≤14.0 mg/dL), 5 (7.5%) died <30 days during hospitalization. In contrast, of 119 patients with high prealbumin level (>14.0 mg/dL), 2 (1.7%) died <30 days in hospital. Patients with low prealbumin level showed a higher risk of all-cause death in acute phase (<30 days) than did those with high prealbumin level, but the difference was not statistically significant [odds ratio (OR) 4.72; 95% confidence interval (CI) 0.89–25.0; $p = 0.068$). Among the 67 patients with low prealbumin level, 10 (14.9%) died during hospitalization. In contrast, of 119 patients with high prealbumin level, 5 (4.2%) died in hospital. Patients with low prealbumin level showed a significantly higher risk of in-hospital all-cause death than did those with high prealbumin level (OR 4.00; 95% CI 1.31–12.3; $p = 0.015$). Among the 67 patients with low prealbumin level, 21 (31.3%) died during a median follow-up period of 189 [45–454] days after admission. In contrast, of 119 patients with high prealbumin level, 10 (8.4%) died during a median follow-up period of 280 [103–690] days after admission. Kaplan–Meier survival curves showed that patients with low prealbumin level were at significantly greater risk of all-cause death (log-rank $p < 0.001$, Fig. 3A) and the composite endpoints of all-cause death or readmission for AHF (log-rank $p = 0.002$, Fig. 3B) than patients with high prealbumin level. Univariable analysis showed that low prealbumin level on admission was associated with a higher all-cause death rate [crude hazard ratio (HR) 4.48; 95% CI 2.11–9.54; $p < 0.001$] and the composite endpoints of all-cause death or readmission for AHF (crude HR 2.17; 95% CI 1.31–3.59; $p = 0.003$) (Table 2). Multivariable analysis showed that low prealbumin level was independently associated with higher all-cause mortality (adjusted HR 4.46; 95% CI 2.09–9.51; $p < 0.001$) and with the composite endpoints (adjusted HR 2.16; 95% CI 1.31–3.58; $p = 0.003$) adjusted for age and sex (Table 2, Model 1). In addition, low prealbumin level was independently associated with higher all-cause mortality (adjusted HR 4.79; 95% CI 1.89–12.2; $p = 0.001$) and the composite endpoints (adjusted HR 2.38; 95% CI 1.30–4.36; $p = 0.005$) in multivariable analysis adjusted for established markers of AHF severity, such as BUN, serum albumin, BNP level, and left ventricular ejection fraction (Table 2, Model 2). Furthermore, low prealbumin level was also independently associated with higher all-cause mortality (adjusted HR 3.66; 95% CI 1.55–8.64; $p = 0.003$) and the composite endpoints (adjusted HR 1.90; 95% CI 1.03–3.49; $p = 0.039$) in multivariable analysis adjusted for other imbalanced baseline variables, such as total cholesterol, triglyceride, and CRP level (Table 2, Model 3).

Table 1
Baseline characteristics according to prealbumin level on admission in patients who were hospitalized for acute heart failure.

Variables	Prealbumin >14 mg/dL (*N* = 119)	Prealbumin ≤14 mg/dL (*N* = 67)	*p*-Value
Age, years	68.4 ± 17.3	72.4 ± 15.3	0.120
Women, *n* (%)	34 (28.6)	24 (35.8)	0.390
Medical history, *n* (%)			
Ischemic etiology	29 (24.4)	16 (23.9)	0.999
Hypertension	82 (69.5)	43 (64.2)	0.562
Dyslipidemia	73 (61.9)	33 (49.3)	0.130
Diabetes mellitus	52 (44.1)	28 (41.8)	0.883
Smoking	71 (61.2)	38 (58.5)	0.840
Echocardiographic parameters			
Left ventricular ejection fraction, %	37.3 ±13.5	40.5 ±13.2	0.118
Left atrial dimension, mm	44.5 ± 9.6	42.9 ± 9.6	0.307
Pulmonary artery systolic pressure, mmHg	39.0 ± 12.9	41.5 ± 12.2	0.249
Heart rate, beats/min	92.7 ± 23.7	97.1 ± 28.7	0.270
Systolic blood pressure, mmHg	130.4 ± 33.4	131.1 ± 29.8	0.877
Diastolic blood pressure, mmHg	71.7 ± 20.3	71.7 ± 19.7	0.991
B-type natriuretic peptide, pg/mL[a]	774 [408–1342]	721 [385–2020]	0.610
Blood urea nitrogen, mg/dL	32.7 ± 21.6	32.7 ± 24.3	0.988
Serum creatinine, mg/dL[a]	1.28 [0.92–2.39]	1.12 [0.83–1.79]	0.243
Serum sodium, mEquiv./L	137.2 ± 12.4	138.4 ± 6.2	0.480
Hemoglobin, g/dL	12.2 ± 2.4	11.5 ± 2.3	0.058
C-reactive protein, mg/dL[a]	0.41 [0.19–1.59]	2.74 [0.80–6.59]	<0.001
Total bilirubin, mg/dL	1.0 ± 0.8	1.1 ± 0.7	0.422
White blood cell, μL^{-1}	7896.6 ± 3769.8	8628.7 ± 3908.2	0.211
Uric acid, mg/dL	6.9 ± 2.1	6.9 ± 3.0	0.977
Total cholesterol, mg/dL	167.3 ± 51.3	141.8 ± 37.4	0.001
Triglyceride, mg/dL	103.8 ± 73.9	81.1 ± 44.8	0.030
Albumin, mg/dL	3.58 ± 0.5	3.06 ± 0.5	<0.001

Values are mean ± standard deviation or number (%), unless indicated otherwise.
[a] Median [interquartile range].

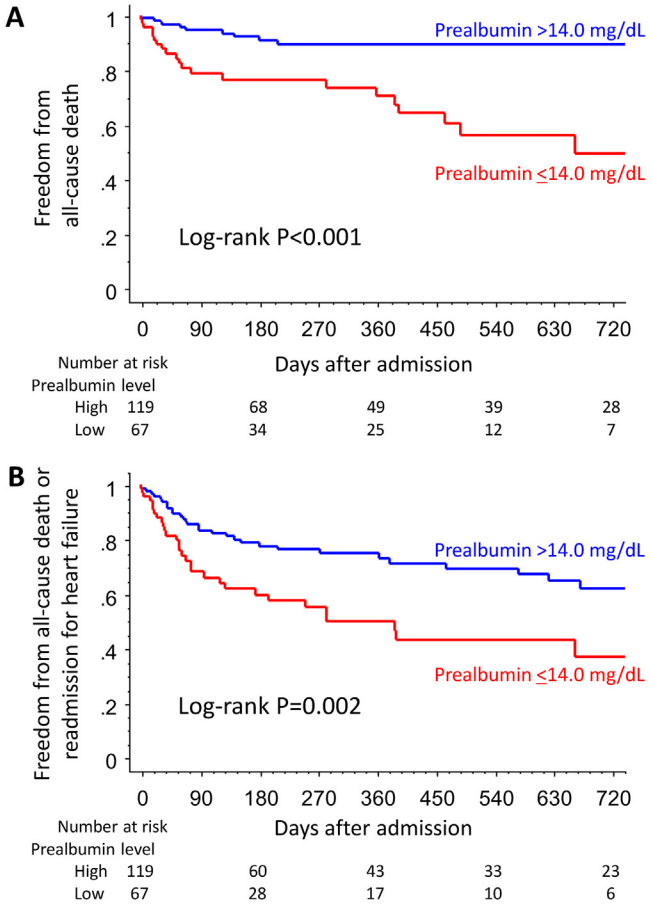

Fig. 3. Kaplan–Meier survival curves for all-cause death (A) and composite endpoints of all-cause death or readmission for acute heart failure (AHF) (B) according to prealbumin level on AHF admission to cardiac intensive care unit.

Discussion

In this study, the mean prealbumin level on admission was 16.6 mg/dL in patients with AHF referred to a cardiac intensive care unit. Patients with low prealbumin level had higher inflammatory and lower nutritional status, and had higher risk of mortality and morbidity. Multivariable analysis adjusted for various markers of disease severity and imbalanced baseline variables showed that low prealbumin level on admission was independently associated with higher long-term all-cause mortality and readmission due to AHF.

In previous studies, the mean (median) serum prealbumin level at discharge in hospitalized heart failure cohort was 18 (20) mg/dL [17,18]. These values are higher than those reported in the present study, indicating that prealbumin may be lower on admission than at discharge in patients with AHF. In addition, a previous study revealed that the mean prealbumin level on admission to Internal Medicine ward (including NYHA class II patients) in hospitalized heart failure patients was 18 mg/dL [20]. In our cohort from a cardiac intensive care unit, only patients with NYHA class III and IV symptoms were included; therefore, malnutrition may be more severe and prealbumin lower than in previous studies. Despite being based on a highly selective cohort of patients from a single tertiary referral intensive care unit, our results may have generalizability to some extent, providing additional epidemiological information about the prealbumin level on admission in patients with AHF.

In this study, low prealbumin level on admission (≤14 mg/dL) was independently associated with higher all-cause mortality and the composite endpoints of all-cause death or readmission for AHF. A previous study also demonstrated that patients with low prealbumin level at discharge (≤15 mg/dL) had a significant increase in all-cause mortality [17]. In addition, in the prospective study enrolling 514 patients, Lourenço et al. demonstrated that patients with discharge prealbumin ≤15 mg/dL had a significant excess risk of AHF readmission [18]. Therefore, low prealbumin level may be a useful marker for not only all-cause death but also readmission due to AHF.

Table 2
Crude and adjusted hazard ratios for all-cause death and composite endpoints associated with low prealbumin level in patients with acute heart failure.

Endpoints	Model type	Hazard ratio	95% confidence interval	*p*-Value
All-cause death				
Prealbumin >14.0 mg/dL	Reference	1.00		
Prealbumin ≤14.0 mg/dL	Univariable	4.48	2.11–9.54	<0.001
	Multivariable model 1[a]	4.46	2.09–9.51	<0.001
	Multivariable model 2[b]	4.79	1.89–12.2	0.001
	Multivariable model 3[c]	3.66	1.55–8.64	0.003
Composite endpoints of all-cause death or readmission for acute heart failure				
Prealbumin >14.0 mg/dL	Reference	1.00		
Prealbumin ≤14.0 mg/dL	Univariable	2.17	1.31–3.59	0.003
	Multivariable model 1[a]	2.16	1.31–3.58	0.003
	Multivariable model 2[b]	2.38	1.30–4.36	0.005
	Multivariable model 3[c]	1.90	1.03–3.49	0.039

Hazard ratios were obtained by univariable and multivariable Cox proportional hazards models.
[a] Model 1 is adjusted for age and sex.
[b] Model 2 is adjusted for established markers of acute heart failure severity such as blood urea nitrogen, serum albumin, B-type natriuretic peptide level, and left ventricular ejection fraction.
[c] Model 3 is adjusted for other imbalanced baseline variables such as total cholesterol, triglyceride, and C-reactive protein level.

As indicators of general nutritional status, there are anthropometric measures such as body weight and BMI. However, BMI does not discriminate fat from fat-free mass, and is a very late indicator of malnutrition [21]. In clinical conditions coursing with hyperhydration such as the urgent phase of AHF, BMI can be challenging to interpret [10,22]. Furthermore, accurately measuring BMI at the time of admission is challenging for patients with AHF with NYHA IV symptoms. In contrast, biochemical measurements are more objective markers of nutritional assessment than anthropometric measurements. However, accepted and widely-used biochemical markers of malnutrition, such as albumin, are recognized as relatively late and insensitive to nutritional variations [13]. Prealbumin is a homotetrameric protein that carries thyroid hormones and retinol, and is a rapid turnover visceral protein that is considered to reflect the status of whole-body N metabolism and the metabolic N pool of rapid turnover proteins [13,23]. The short 2-day half-life, small body pool, and reduced sensitivity to patient's hydration status favor its ability to detect early nutritional deficit [13,24]. Early diagnosis of malnutrition is an important issue in the evaluation and management of patients with AHF. In a previous study, a specific nutritional program improved the quality of life of patients with heart failure [25]. The nutritional treatment of malnourished patients with AHF (e.g. detected by low prealbumin level) requires additional interventional studies to demonstrate its impact on the quality of life and prognosis. This remains an important area for future research to improve the management of patients with AHF.

Patients with low prealbumin level had higher CRP levels than those with high prealbumin level in our AHF cohort. An inverse relationship between prealbumin and CRP has been documented previously [26]. Also, in this study, a significant negative correlation was observed between prealbumin and CRP levels on admission. In patients with AHF, systemic inflammation has long been recognized to contribute in its pathogenesis [27,28]. Although the factor responsible for triggering this systemic inflammatory response is unclear, monocyte-macrophage and lymphocyte activation, the renin–angiotensin–aldosterone system, the sympathetic nervous system, and enhanced bacterial translocation from the intestine are possible candidates [27,29,30]. Prealbumin is a negative acute-phase protein in that its synthesis is suppressed in inflammatory settings in which cytokines stimulate hepatic production of CRP and other acute-phase proteins [13,31]. There is also a component of increased vascular permeability and protein leakage in inflammatory conditions that can contribute to lower levels of prealbumin [23]. In this respect, prealbumin in the acute phase may not accurately reflect the nutritional status in patients with AHF. In a recent systematic review and meta-analysis, it was reported that prealbumin reflects the degree of inflammation, but not nutritional status, especially in an acute care setting [32]. Careful interpretation of the significance of prealbumin level may thus be necessary in the acute phase of AHF hospitalization. On the other hand, identifying the patients with low prealbumin on admission may enable physicians to optimize nutritional and inflammatory status during AHF hospitalization. Providing opportunities for early intervention for malnutrition and systemic inflammation may be an advantage of measurement of prealbumin on admission rather than at discharge. In addition, prealbumin measured in the acute phase affected not only short-term outcome during hospitalization, but also long-term prognosis in this study. Furthermore, prealbumin showed the most favorable performance as a result of comparing the prognostic value for all-cause death of prealbumin level with other established biomarkers for heart failure (i.e. BNP, CRP, and BUN). Thus, prealbumin level on admission may be a comprehensive marker including nutritional status and acute inflammatory response, and could be a useful prognostic marker in the acute phase of AHF hospitalization. However, there are many unanswered questions about the relationships among prealbumin level, malnutrition, inflammation, and adverse outcome in patients hospitalized for AHF, and further study is needed.

This was a retrospective observational study in a single center, which may have resulted in certain inherent selection biases. In addition, the measurement of prealbumin level was not performed in all patients with AHF, and was dependent on the physician's judgment, which introduces the potential for serious selection bias. Even with adjustments by multivariable analysis, we cannot exclude the possibility that residual measured or unmeasured confounders may have influenced our results. Although prealbumin level is a dynamic measurement, we measured it at only one time point (on admission) and it was not measured at discharge. Therefore, the prognostic effect of serial prealbumin measurements in patients with AHF is unclear. Data showing severity of acute phase hemodynamics were not included in our analysis, because invasive hemodynamic assessments (i.e. pulmonary artery catheterization) were not performed in all study AHF patients. Furthermore, patients with concomitant infectious diseases were not completely excluded and these may have affected the prealbumin level on admission in this study. We only included patients in whom an episode of AHF was the primary cause of admission, and patients with severe concomitant infections as the primary cause of admission were not included from the initial evaluation for eligibility. However, only obvious,

severe infections on admission were considered, and the possibility that some patients may have had undetected infectious diseases cannot be discarded. Moreover, the number of patients with AHF included in this study was relatively small. Further larger-scale, multicenter or multinational, prospective cohort studies are thus required to confirm and extend the current findings on the relationship between prealbumin level on admission and outcome in patients with AHF.

Conclusions

Low prealbumin level on admission is potentially associated with poor long-term outcome in hospitalized patients with AHF treated in a cardiac intensive care unit. Prealbumin level on admission may be useful in the risk stratification of patients with AHF in an acute care setting.

Contribution (statistical analysis and data center)

Katsunori Shimada, PhD (STATZ Institute Inc., Tokyo, Japan).

Funding

This research received no grant from any funding agency in the public, commercial, or not-for profit sectors.

Conflicts of interest

The authors declare that there is no conflict of interest.

Acknowledgments

We thank Yuki Iijima, Issei Ishida, MD, Keiko Mizobuchi, MD, Hiromu Kadowaki, MD, Kazuki Tanaka, MD, Yoshiaki Minami, MD, and Tsuyoshi Shiga MD, PhD, for support and assistance.

References

[1] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37:2129–200.
[2] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey Jr DE, Colvin MM, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Am Coll Cardiol 2017;70:776–803.
[3] Agra Bermejo RM, Gonzalez Ferreiro R, Varela Roman A, Gomez Otero I, Kreidieh O, Conde Sabaris P, et al. Nutritional status is related to heart failure severity and hospital readmissions in acute heart failure. Int J Cardiol 2017;230:108–14.
[4] Iwakami N, Nagai T, Furukawa TA, Sugano Y, Honda S, Okada A, et al. Prognostic value of malnutrition assessed by controlling nutritional status score for long-term mortality in patients with acute heart failure. Int J Cardiol 2017;230:529–36.
[5] Fujino M, Takahama H, Hamasaki T, Sekiguchi K, Kusano K, Anzai T, et al. Risk stratification based on nutritional screening on admission: three-year clinical outcomes in hospitalized patients with acute heart failure syndrome. J Cardiol 2016;68:392–8.
[6] Horiuchi Y, Tanimoto S, Okuno T, Aoki J, Yahagi K, Sato Y, et al. Hemodynamic correlates of nutritional indexes in heart failure. J Cardiol 2018;71:557–63.
[7] Pasini E, Opasich C, Pastoris O, Aquilani R. Inadequate nutritional intake for daily life activity of clinically stable patients with chronic heart failure. Am J Cardiol 2004;93:41A–3A.
[8] Pasini E, Aquilani R, Gheorghiade M, Dioguardi FS. Malnutrition, muscle wasting and cachexia in chronic heart failure: the nutritional approach. Ital Heart J 2003;4:232–5.
[9] Narumi T, Arimoto T, Funayama A, Kadowaki S, Otaki Y, Nishiyama S, et al. Prognostic importance of objective nutritional indexes in patients with chronic heart failure. J Cardiol 2013;62:307–13.
[10] Gastelurrutia P, Lupon J, Domingo M, Ribas N, Noguero M, Martinez C, et al. Usefulness of body mass index to characterize nutritional status in patients with heart failure. Am J Cardiol 2011;108:1166–70.
[11] Kattel S, Kasai T, Matsumoto H, Yatsu S, Murata A, Kato T, et al. Association between elevated blood glucose level on admission and long-term mortality in patients with acute decompensated heart failure. J Cardiol 2017;69:619–24.
[12] Fukushima A, Kinugawa S. Hyponatremia as a surrogate marker for optimal diuretic selection in acute heart failure. J Cardiol 2018;71:547–9.
[13] Beck FK, Rosenthal TC. Prealbumin: a marker for nutritional evaluation. Am Fam Physician 2002;65:1575–8.
[14] Sreedhara R, Avram MM, Blanco M, Batish R, Avram MM, Mittman N. Prealbumin is the best nutritional predictor of survival in hemodialysis and peritoneal dialysis. Am J Kidney Dis 1996;28:937–42.
[15] Devakonda A, George L, Raoof S, Esan A, Saleh A, Bernstein LH. Transthyretin as a marker to predict outcome in critically ill patients. Clin Biochem 2008;41:1126–30.
[16] Ingenbleek Y, Young V. Transthyretin (prealbumin) in health and disease: nutritional implications. Annu Rev Nutr 1994;14:495–533.
[17] Franco J, Formiga F, Trullas JC, Salamanca Bautista P, Conde A, Manzano L, et al. Impact of prealbumin on mortality and hospital readmission in patients with acute heart failure. Eur J Intern Med 2017;43:36–41.
[18] Lourenco P, Silva S, Frioes F, Alvelos M, Amorim M, Couto M, et al. Low prealbumin is strongly associated with adverse outcome in heart failure. Heart 2014;100:1780–5.
[19] McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. N Engl J Med 1971;285:1441–6.
[20] Lourenco P, Silva S, Frioes F, Alvelos M, Amorim M, Torres-Ramalho P, et al. Does pre-albumin predict in-hospital mortality in heart failure? Int J Cardiol 2013;166:758–60.
[21] Romero-Corral A, Somers VK, Sierra-Johnson J, Thomas RJ, Collazo-Clavell ML, Korinek J, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. Int J Obes 2008;32:959–66.
[22] Colin-Ramirez E, Orea-Tejeda A, Castillo-Martinez L, Montano-Hernandez P, Sanchez-Ramirez A, Pineda-Juarez JA, et al. Malnutrition syndrome, but not body mass index, is associated to worse prognosis in heart failure patients. Clin Nutr 2011;30:753–8.
[23] Ingenbleek Y, Young VR. Significance of transthyretin in protein metabolism. Clin Chem Lab Med 2002;40:1281–91.
[24] Brugler L, Stankovic A, Bernstein L, Scott F, O'Sullivan-Maillet J. The role of visceral protein markers in protein calorie malnutrition. Clin Chem Lab Med 2002;40:1360–9.
[25] Rozentryt P, von Haehling S, Lainscak M, Nowak JU, Kalantar-Zadeh K, Polonski L, et al. The effects of a high-caloric protein-rich oral nutritional supplement in patients with chronic heart failure and cachexia on quality of life, body composition, and inflammation markers: a randomized, double-blind pilot study. J Cachexia Sarcopenia Muscle 2010;1:35–42.
[26] Pinilla JC, Hayes P, Laverty W, Arnold C, Laxdal V. The C-reactive protein to prealbumin ratio correlates with the severity of multiple organ dysfunction. Surgery 1998;124:799–805.
[27] Peschel T, Schonauer M, Thiele H, Anker SD, Schuler G, Niebauer J. Invasive assessment of bacterial endotoxin and inflammatory cytokines in patients with acute heart failure. Eur J Heart Fail 2003;5:609–14.
[28] Minami Y, Kajimoto K, Sato N, Hagiwara N, Takano T, ATTEND Study Investigators. C-reactive protein level on admission and time to and cause of death in patients hospitalized for acute heart failure. Eur Heart J Qual Care Clin Outcomes 2017;3:148–56.
[29] Krack A, Sharma R, Figulla HR, Anker SD. The importance of the gastrointestinal system in the pathogenesis of heart failure. Eur Heart J 2005;26:2368–74.
[30] Werdan K. The activated immune system in congestive heart failure – from dropsy to the cytokine paradigm. J Intern Med 1998;243:87–92.
[31] Kalantar-Zadeh K, Anker SD, Horwich TB, Fonarow GC. Nutritional and anti-inflammatory interventions in chronic heart failure. Am J Cardiol 2008;101:89E–103E.
[32] Zhang Z, Pereira SL, Luo M, Matheson EM. Evaluation of blood biomarkers associated with risk of malnutrition in older adults: a systematic review and meta-analysis. Nutrients 2017;9. pii:E829.