Journal of Cardiology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Journal of Cardiology

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

Original article

Risk stratification based on nutritional screening on admission: Three-year clinical outcomes in hospitalized patients with acute heart failure syndrome

Masashi Fujino (MD)[a,b], Hiroyuki Takahama (MD, PhD)[a,*], Toshimitsu Hamasaki (PhD)[c], Kenichi Sekiguchi (MD, PhD)[a], Kengo Kusano (MD, PhD, FJCC)[a,b], Toshihisa Anzai (MD, PhD, FJCC)[a,b], Teruo Noguchi (MD, PhD)[a,b], Yoichi Goto (MD, PhD, FJCC)[a], Masafumi Kitakaze (MD, PhD, FJCC)[a], Hiroyuki Yokoyama (MD, PhD)[a], Hisao Ogawa (MD, PhD, FJCC)[a,d], Satoshi Yasuda (MD, PhD, FJCC)[a,b]

[a] *Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, Suita, Japan*
[b] *Division of Advanced Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan*
[c] *Office of Biostatistics and Data Management, Department of Advanced Medical Technology Development, National Cerebral and Cardiovascular Center, Suita, Japan*
[d] *Division of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan*

ARTICLE INFO

Article history:
Received 4 January 2016
Received in revised form 17 April 2016
Accepted 7 May 2016
Available online xxx

Keywords:
Nutrition
Acute heart failure
Albumin
Lymphocyte counts
Prognosis

ABSTRACT

Background: Several blood tests are commonly used to assess nutritional status, including serum albumin levels (SAL) and lymphocyte counts (LC). The aim of this study is to investigate whether nutritional screening on admission can be used to determine risk levels for adverse clinical events in acute heart failure syndrome (AHFS) patients.

Methods: In 432 consecutive AHFS patients, we measured SAL and LC and prospectively followed the patients for their combined clinical events (all-cause death and re-hospitalization for heart failure) for three years from admission. The classification and regression tree (CART) tool identified the cut-off criteria for SAL and LC to differentiate among patients with different risks of clinical events as 3.5 g/dl and 963/mm^3, respectively.

Results: The CART tool classified 15.5% patients as high risk, 15.7% as intermediate risk, and 68.8% as low risk. The CART for nutritional status (CART-NS) values were strongly correlated with combined clinical events [hazard ratio of 2.13 (low vs high risk), 95% confidence interval of 1.42–3.16, $p < 0.001$], even after adjusting for plasma brain natriuretic peptide levels. The CART-NS analysis improved the specificity (89.5%) of predictions of clinical outcomes with the comparable sensitivity (36.3%) compared with the use of a single criterion (SAL <3.5 g/dl: 70.2, 42.4% or LC <963/mm^3: 73.4, 41.7%, respectively).

Conclusion: A substantial proportion of AHFS patients are at risk of malnutrition, and this risk is associated with poor clinical outcomes. We demonstrate that this algorithm for nutritional screening, even in emergency clinical settings, can determine risk levels for further adverse events in AHFS patients.

Introduction

Malnutrition is often observed in patients with heart failure (HF) and associated with adverse clinical outcomes [1–3]. Several studies have demonstrated the significance of malnutrition in chronic HF because of its association with long-term clinical outcomes [4]. However, the clinical significance of identification of malnutrition on admission in patients with acute heart failure syndrome (AHFS) has not been fully recognized in the clinical setting.

Several examinations have been proposed to assess nutritional status in a clinical setting, including serum albumin levels, which are widely used for the assessment of nutritional status. Because

* Corresponding author at: Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, Suita 565-8565, Osaka, Japan.
Tel.: +81 6 6833 5012; fax: +81 6 6872 7486.
E-mail address: takahama@ncvc.go.jp (H. Takahama).

http://dx.doi.org/10.1016/j.jjcc.2016.05.004
0914-5087/

the half-life of albumin is 14–18 days, serum albumin levels can provide information on nutrition status related to prolonged malnutrition [5]. Horwich et al. reported that the presence of hypo-albuminemia (≤3.4 g/dl) was significantly associated with one-year survival in HF patients with systolic dysfunction [6]. Recently, a relationship between long-term mortality and hypo-albuminemia in HF patients has been reported [7]. However, serum albumin levels are influenced by multiple factors, such as hepatic synthesis [8]. Rapid and simple, but accurate, screening for nutritional status is necessary for the management of HF in emergency clinical settings, such as in patients with AHFS. Lymphocyte counts are also used as a standard measure of nutritional status [3,9–12] that is independent of hepatic synthesis. Therefore, we combined two variables for nutritional screening in AHFS patients. To obtain maximal accuracy of risk stratification within a short time, we used the classification and regression tree (CART) for nutritional status (CART-NS) tool and analyzed serum albumin levels and lymphocyte counts. Several studies for risk stratification of AHFS patients are reported [13–15]; however, little has been known about the risk stratification of AHFS using assessment for nutritional status. The primary aim of the present study was to investigate the extent to which AHFS patients are at risk of malnutrition on admission and to determine whether the CART-NS algorithm can differentiate among high-risk patients with AHFS with regard to their long-term mortality and likelihood of re-hospitalization for HF.

Methods

Study population

From July 2006 to June 2009, 662 consecutive AHFS patients who met the Framingham criteria [16] were prospectively enrolled in our database. In this single-center registry [17], AHFS patients with acute coronary syndromes and patients who were admitted to our institute during this follow-up period more than twice ($n = 117$) were excluded. Additionally, patients whom we could not follow-up ($n = 10$) and for whom laboratory data were unavailable ($n = 17$) were not included in the present study. Because we used lymphocyte counts to build CART-NS, it was necessary to exclude the patients with abnormal values of white blood cell (WBC) counts, indicating the presence of infectious disease. Based on the previous study [18], we excluded the patients with either high WBC counts (≥12,000/mm^3) or low WBC counts (<4000/mm^3).

Data collection and definition of nutritional impairment

For each patient, baseline clinical data were collected, including (1) demographic, (2) etiological, and (3) comorbidity data, (4) laboratory tests and (5) echocardiographic findings. In addition to the echocardiographic examination, biochemical tests following blood sampling were performed on admission, including tests to determine the WBC count, lymphocyte count, and hemoglobin, albumin, C-reactive protein, creatinine, and blood urea nitrogen levels, which were obtained in the first 24 h after admission. Plasma brain natriuretic peptide (BNP) levels were obtained in the first three days after admission. All of the biochemical analyses were performed using routine hospital analytical facilities. An echocardiograph was also performed on admission, and the body mass index (BMI) was calculated as the body weight in kilograms divided by the square of the height in meters. The estimated glomerular filtration rate was calculated according to the following published equation: $194 \times \text{serum creatinine}^{-1.094} \times \text{age}^{-0.287} \times 0.739$ (for females) [19].

Clinical follow-up and data analysis

In the present study, we prospectively followed clinical events in AHFS patients for three years. Combined clinical events were defined as either all-cause death or re-hospitalization for HF, and such information for HF patients was obtained via medical records or communication by telephone and written correspondence.

Risk stratification

Risk stratification by the CART tool has been described previously [15]. Briefly, risk was allocated through a series of two binary decisions based on lymphocyte counts and serum albumin levels on patient admission (Fig. 1). The first allocation was for lymphocyte counts ≥963/mm^3 vs lymphocyte counts <963/mm^3, which was followed by serum albumin levels ≥3.5 g/dl vs serum albumin levels <3.5 g/dl, and these threshold values were identified through a recursive partitioning analysis (CART method) [15,20,21].

Ethics

This study was approved by the National Cerebral and Cardiovascular Centre Institutional Ethics Committee and conducted in accordance with the ethical principles of the Declaration of Helsinki.

Statistical analysis

Data are expressed as the median and interquartile range (IQR), or percentages as appropriate. The Wilcoxon's rank sum test was used for the comparison of continuous variables between the two groups; categorical variables were compared with χ^2 statistics or Fisher's exact test as appropriate. For analysis of survival and hospitalization for HF, Kaplan–Meier method was used to estimate

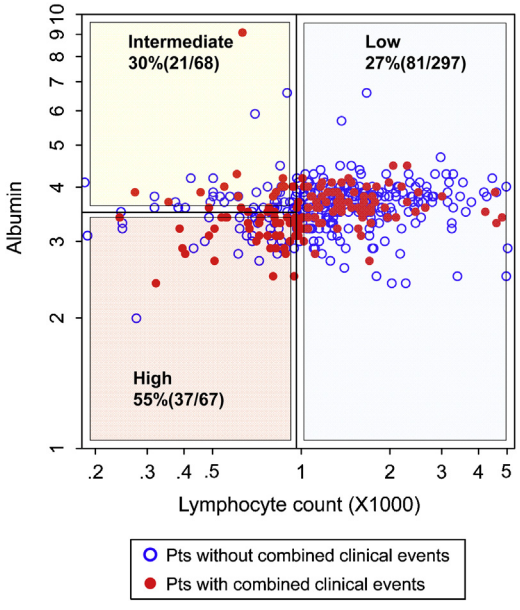

Fig. 1. The relationship of serum albumin levels and lymphocyte counts with clinical outcomes. The figure shows the values of serum albumin levels and lymphocyte counts in acute heart failure syndrome patients and indicates the presence of combined clinical outcomes, which are indicated by red closed circles for combined clinical events and blue open circles for no occurrence of events. A classification and regression tree for nutritional status analysis determined the cut-off values for lymphocyte counts and serum albumin levels, which were 963/mm^3 and 3.5 g/dl, respectively.

Please cite this article in press as: Fujino M, 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), http://dx.doi.org/10.1016/j.jjcc.2016.05.004