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Original article

Hemodynamic correlates of nutritional indexes in heart failure

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ABSTRACT

Background: Malnutrition in heart failure (HF) is related to altered intestinal function, which could be due to hemodynamic changes. We investigated the usefulness of novel nutritional indexes in relation to hemodynamic parameters.

Methods: We retrospectively analyzed 139 HF patients with reduced ejection fraction who underwent right heart catheterization. We investigated correlations between right side pressures and nutritional indexes, which include controlling nutritional (CONUT) score and geriatric nutritional risk index (GNRI). Receiver operating characteristic (ROC) curves were generated to investigate the prognostic accuracy of CONUT score and GNRI for a composite of death or HF hospitalization in 12 months. Logistic regression analysis was performed to investigate whether hemodynamic correlates were associated with malnutrition, which was defined based on CONUT sore or GNRI.

Results: Higher right side pressures were positively correlated with worse nutritional status according to CONUT score, but were negatively correlated with worse nutritional status according to GNRI. Area under ROC curve for the composite endpoint was 0.746 in CONUT score and 0.576 in GNRI. The composite endpoint occurred in 40% of CONUT score ≥ 3 and in 11% of CONUT score < 3 ($p < 0.001$). These relationships were also investigated with GNRI (40% of GNRI < 95 vs. 17% of GNRI ≥ 95, $p = 0.002$). In multivariate analysis, higher right atrial pressure was significantly associated with higher CONUT score, while no hemodynamic parameter was related to GNRI.

Conclusions: CONUT score was associated with right side congestion, while no association between GNRI and right side congestion was noted. CONUT score had better predictive value than GNRI.

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Introduction

Malnutrition is common in heart failure (HF). Cardiac cachexia, an involuntary non-edematous weight loss within 6–12 months [1–4], is observed in 5–15% of patients with HF and is associated with poor prognosis [5,6]. The malnutrition in HF is related to altered intestinal function, which could be due to hemodynamic changes. Intestinal hypoperfusion and congestion lead to bowel edema and increased adherent bacteria, resulting in chronic inflammation and malnutrition [7–12]. These findings were mainly investigated in HF patients with reduced ejection fraction (EF), which is associated with more severe hemodynamic deteriorations than HF with preserved EF.

Several nutritional indexes have been utilized in HF. Controlling nutritional (CONUT) score is calculated using serum albumin, total cholesterol, and the number of lymphocytes [13]. Serum albumin reflects protein reserve, total cholesterol reflects caloric depletion, and the number of lymphocytes reflects immune defense. These three variables have a prognostic effect in HF [14–17]. Higher CONUT score indicates worse nutritional status [13]. A post hoc analysis of 3421 patients in a prospective registry of chronic HF showed that 3-year survival in patients with CONUT score 0–1, 2, and ≥ 3 was 95.5%, 92.3%, and 73.2%, respectively ($p < 0.001$) [18].

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Geriatric nutritional risk index (GNRI) is another nutritional index, which is calculated using serum albumin and body weight [19]. Contrary to CONUT score, lower GNRI indicates worse nutritional status [19]. Although patients with obesity were associated with higher risks of developing HF, previous studies reported a survival advantage for obese and overweight patients compared with patients with normal or low weight [20,21]. Cardiovascular death or HF hospitalization at 28 months occurred in 15%, 23%, 38%, and 54% within 28 months in a cohort of 388 HF patients with GNRI > 98, 98–92, 82–91, and <82, respectively [22]. Another study reported that HF patients with GNRI < 92 had higher mortality at 2 years than those with GNRI ≥ 92 [hazard ratio 2.667, 95% confidence interval (CI) 1.527–4.651, $p < 0.001$] [23].

CONUT score and GNRI, which are novel nutritional indexes, are objective and useful in predicting prognosis [18,22,24]. However, whether they are associated with hemodynamic parameters and further reflect the pathophysiology of malnutrition in patients with HF remains uncertain. Therefore, we investigated the usefulness of these nutritional indexes in relation to hemodynamic parameters in the prognosis of HF patients with reduced EF.

Methods

Study population

Consecutive HF patients who underwent right heart catheterization (RHC) have been prospectively registered in our institutional database since January 2012. Of these patients, those with reduced EF (EF ≤ 40%) were analyzed from January 2012 to December 2015. We excluded patients with brain natriuretic peptide (BNP) level < 100 pg/ml, with acute coronary syndrome (ACS), or undergoing hemodialysis. We also excluded patients without echocardiography data of EF.

Patient characteristics and medical history were recorded upon admission. Ischemic etiology was defined as the presence of at least one of the following: previous myocardial infarction, previous percutaneous coronary intervention, or previous coronary bypass grafting. Left ventricular EF was calculated using the modified Simpson method. Ultrasonographers performed echocardiography, and specialists of the Japanese Society of Echocardiography approved the findings. Vital signs, laboratory data, and medication at the time of RHC were also recorded.

All patients provided written informed consent. All data were anonymized throughout the analysis. The study was conducted in accordance with the Declaration of Helsinki.

Right heart catheterization

RHC was performed after optimal treatment with diuretics, angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin II receptor blocker (ARB), β-blocker, and other pharmacologic therapies, which are based on the physician's discretion. RHC was performed in the supine position and was conducted using a 6-F balloon-tipped catheter (Swan-Ganz Thermodilution Catheter, Edwards Lifesciences, Irvine, CA, USA). Transducers were zeroed at the mid-axilla and measured by calipers. Under fluoroscopic guidance, the catheter was inserted through a femoral vein to a pulmonary artery. Wedge position of the catheter was confirmed by fluoroscopy and pressure wave forms. Hemodynamic data were measured at the end of expiration and represent the mean of ≥3 beats. Cardiac output was measured using the thermodilution method and indexed to body surface area (cardiac index). Right ventricle stroke work index (RVSWI) was calculated as follows: (cardiac index/heart rate) × [mean pulmonary artery pressure - mean right atrium pressure (RAP)] × 13.6.

Nutritional indexes

Nutritional indexes were calculated based on the data at the time of RHC. CONUT score consists of three variables: serum albumin, total cholesterol, and total lymphocyte count (Table 1) [13]. GNRI is calculated as follows: GNRI = 14.98 × serum albumin (g/dl) + 41.7 × present body weight (BW) (kg)/ideal BW. Ideal BW is calculated as follows: body height (BH; cm) – 100 – [(BH – 150)/4] for males and BH (cm) – 100 – [(BH – 150)/2.5] for females [19].

Clinical endpoints

The endpoints were death, cardiovascular (CV) death, HF hospitalization, and composite of death or HF hospitalization within 12 months. CV death was defined as fatal myocardial infarction, pump failure, sudden death, stroke, pulmonary embolism, or CV procedural death. HF hospitalization was defined as an unexpected hospitalization with at least one of the following symptoms: increasing dyspnea on exertion, worsening orthopnea, paroxysmal nocturnal dyspnea, increasing fatigue/worsening exercise tolerance, or altered mental status, and at least two of the following symptoms: peripheral edema, elevated jugular venous pressure, radiologic signs of HF, increasing abdominal distension or ascites, pulmonary edema or crackles, rapid weight gain, hepatojugular reflux, S3 gallop, or elevated BNP. These endpoints were evaluated by retrospective medical record review.

Statistical analysis

Normally distributed continuous variables were described as mean ± standard deviation, and non-normally distributed data were expressed as medians and interquartile ranges. Categorical variables were described as percentages. Missing values (not more than 20%) were imputed by multivariate imputation method.

Pearson's correlation analysis was conducted to investigate the association between the nutritional indexes (CONUT score and GNRI) and hemodynamic correlates, including pulmonary capillary wedge pressure (PCWP), pulmonary artery systolic pressure (PASP), pulmonary artery diastolic pressure (PADP), RAP, cardiac index, and RVSWI.

Receiver operating characteristic (ROC) curves were generated to investigate the prognostic accuracy of CONUT score and GNRI for the endpoints. The optimal cut-off point for death or HF hospitalization within 12 months was determined using ROC curve analysis. Patients were divided to malnourished group defined as CONUT ≧ cut-off point and well-nourished group defined as CONUT < cut-off point. They were also divided to malnourished group defined as GNRI < cut-off point and well-nourished group defined as GNRI ≧ cut-off point. To compare the characteristics of the malnourished and well-nourished patients, we used Student's *t*-test for continuous variables and chi-square test for categorical variables. Kaplan–Meier curves and 12-month event-free rates were estimated. The log-rank test was also used to compare the two groups. A p-value < 0.05 was considered statistically significant.

Table 1
CONUT score calculation.

Variables				
Serum albumin (g/ml)	≥3.5	3.0–3.49	2.50–2.99	<2.50
Score	0	2	4	6
Total cholesterol (mg/dl)	≥180	140–179	100–139	<100
Score	0	1	2	3
Lymphocytes (count/ml)	≥1600	1200–1599	800–1199	<800
Score	0	1	2	3

CONUT, controlling nutritional.

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