Journal of Cardiology 66 (2015) 205–211

Contents lists available at ScienceDirect

Journal of Cardiology

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

Original article

Thyroid function on admission and outcome in patients hospitalized for acute decompensated heart failure

Dai Okayama (MD), Yuichiro Minami (MD)*, Shohei Kataoka (MD), Tsuyoshi Shiga (MD), Nobuhisa Hagiwara (MD, FJCC)

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

ARTICLE INFO

Article history:
Received 26 February 2015
Received in revised form 2 April 2015
Accepted 9 April 2015
Available online 14 May 2015

Keywords:
Acute heart failure
Free triiodothyronine
Outcome
Thyroid function

ABSTRACT

Background: Although thyroid dysfunction is a known prognostic factor for cardiovascular disease, the relationship between thyroid function and prognosis in patients with acute decompensated heart failure (ADHF) is poorly understood. Herein, we investigated the association between thyroid hormone levels and outcome in patients hospitalized for ADHF.

Methods: We evaluated 270 hospitalized ADHF patients with thyroid hormone levels measured at admission between April 2007 and May 2012.

Results: The median (interquartile range) thyroid stimulating hormone, free triiodothyronine (fT3), and free thyroxine were 2.79 (1.49–4.96) μU/ml, 2.32 (1.93–2.75) pg/ml, and 14.0 (12.1–15.7) pg/dl, respectively. Receiver operating characteristic (ROC) curve analysis was applied to assess their prognostic value for in-hospital outcome. The fT3 had the most favorable performance, with an area under the ROC curve of 0.791 (optimal cutoff point ≤2.05; sensitivity 85.0%; specificity 72.0%). Although patients in the low fT3 group (≤2.05) had higher age and lower body mass index, there were no significant differences with respect to systolic blood pressure and heart rate between the groups. In multivariate analysis adjusted for various markers of disease severity and amiodarone use, low fT3 level was independently associated with higher in-hospital mortality (odds ratio 14.4; $p < 0.001$). In addition, the probability of 1-year total death among patients with low fT3 was significantly higher than that among patients with normal fT3 (log-rank $p < 0.001$).

Conclusions: Low fT3 level was associated with adverse outcomes in patients hospitalized for ADHF. Thyroid hormone measurements might be useful in the risk stratification of ADHF patients.

Introduction

Acute decompensated heart failure (ADHF) is a common but poorly defined clinical syndrome in cardiovascular and emergency medicine, and is associated with a poor outcome [1,2]. In addition, ADHF is the most common cause of hospitalization in patients older than 65 years, and rates will continue to increase in the future [1,2]. However, assessment of prognosis in individual ADHF patients remains challenging because of the high variability in the clinical course of the disease [3–7].

Thyroid hormone affects the function of all cells, tissues, and organs, including the heart [8–11]. Previous studies have elucidated that altered thyroid hormone metabolism, such as low serum free triiodothyronine (fT3) concentration, was described in patients with cardiovascular disease including heart failure [8,12,13]. A low fT3 was associated with higher right atrial, pulmonary artery, and pulmonary capillary wedge pressures, and lower ejection fraction and cardiac index [12]. In addition, thyroid dysfunction may influence outcome in patients with cardiovascular disease, because the cardiovascular system is a key target of thyroid hormone [13–23]. However, the relationship between thyroid dysfunction and clinical outcomes in patients with established chronic heart failure remains controversial [14,16–18,20,23]. Furthermore, an association of thyroid function with outcome in patients with acute decompensated phase of heart failure is poorly understood. Thus, we investigated the association between thyroid hormone levels on admission and

DOI of commentary article: http://dx.doi.org/10.1016/j.jjcc.2015.05.001
* Corresponding author at: Department of Cardiology, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan.
Tel.: +81 3 3353 8111; fax: +81 3 3356 0441.
E-mail address: yuichiro24@celery.ocn.ne.jp (Y. Minami).

http://dx.doi.org/10.1016/j.jjcc.2015.04.006
0914-5087/

prognosis (in-hospital and 1-year outcome) in patients hospitalized for ADHF.

Methods

Patients and thyroid function measurements

We retrospectively evaluated 367 consecutive hospitalized patients who suffered from ADHF who were referred to the Cardiac Intensive Care Unit at Tokyo Women's Medical University Hospital, Tokyo, Japan, between April 2007 and May 2012. The diagnosis of heart failure was assessed based on modified Framingham criteria [24]. ADHF was defined as new onset of decompensated heart failure or decompensation of chronic, established heart failure meeting the criteria and sufficient to warrant hospitalization and urgent therapy. Patients were certified for enrollment if they were hospitalized for episodes of ADHF as the primary cause of admission. Patients aged less than 20 years old and those with acute coronary syndrome were excluded. The study was performed according to the principles of the Declaration of Helsinki, and this study protocol was approved by our institutional ethics committee.

Thyroid hormone levels [thyroid stimulating hormone (TSH), fT3, and free thyroxine (fT4)] were measured in hospitalized ADHF patients within 48 h after admission. A total of 97 patients were excluded from this analysis because of missing thyroid hormone measurements ($n = 92$), overt primary hypothyroidism (TSH $>$ 10 μU/ml and fT4 $<$ 6 pg/ml with or without thyroid replacement therapy) ($n = 3$), and overt primary hyperthyroidism (fT3 $>$ 4.5 pg/ml or fT4 $>$ 23 pg/ml with undetectable TSH levels) ($n = 2$) [14]. Therefore, the final study population consisted of 270 patients hospitalized for ADHF.

Follow-up and end-points

Follow-up started from the day of ADHF admission. Follow-up data were obtained from the following sources: reviewing our hospital records, periodically examining patients in the outpatient clinic, contacting patients' physicians, or interviewing the patients by phone. Complete information on the follow-up data was ascertained for 362 (98.6%) of the total 367 patients. The end-point of this study was in-hospital and 1-year all-cause death, cardiac death, and non-cardiac death. All end-points were ascertained by two experienced physicians who were not study investigators.

Statistical analysis

Analyses were performed with the SAS ver. 9.1 (SAS Institute, Cary, NC, USA) by an independent biostatistics and data center (STATZ Institute, Inc., Tokyo, Japan). Results are presented as the mean with standard deviation (SD), median with interquartile range, or frequencies (%). Student's *t*-test was used to compare normally distributed continuous variables between groups.The Mann–Whitney *U*-test was used for skewed continuous or ordinal variables. The chi-square test or Fisher's exact test (when an expected value was less than 5) was used to compare nominal variables. Sensitivity and specificity were calculated according to standard definitions. Receiver operating characteristic (ROC) curves were constructed and the area under the ROC curve was calculated to assess the usefulness of the thyroid hormone levels for predicting the in-hospital outcome. Best cutoff values were identified by ROC curves with Youden index. To evaluate the impact of low fT3 on the in-hospital prognosis, univariate and multivariate logistic regression models were used. Multivariate models included the age, sex, body mass index, systolic blood pressure, B-type natriuretic peptide, serum sodium, creatinine, blood urea nitrogen, hemoglobin, C-reactive protein, and amiodarone use before admission. The probability of 1-year all-cause, cardiac, and non-cardiac death was estimated by the Kaplan–Meier method, after which the log-rank test was used to compare survival curves. Two-tailed *p*-values of less than 0.05 were considered to indicate statistical significance.

Results

Thyroid function profile

The median (interquartile range) serum concentrations of TSH, fT3, and fT4 were 2.79 (1.49–4.96) μU/ml, 2.32 (1.93–2.75) pg/ml, and 14.0 (12.1–15.7) pg/ml, respectively, in 270 hospitalized patients with ADHF. ROC curve analysis was applied to assess their prognostic value for in-hospital all-cause death (Fig. 1). As a result, fT3 showed the most favorable performance, and the area under the ROC curve for TSH was 0.580 (optimal cutoff point $>$2.78; sensitivity 70.0%; specificity 51.6%, Fig. 1A), for fT3 was 0.791 (optimal cutoff point $\leq$2.05 pg/ml; sensitivity 85.0%; specificity 72.0%, Fig. 1B), and for fT4 was 0.552 (optimal cutoff point $\leq$16.1; sensitivity 95.2%; specificity 19.6%, Fig. 1C). Box-and-whisker plots of fT3 levels at admission in ADHF patients with or without end-point (in-hospital all-cause death) are shown in Fig. 2. In patients who died during hospitalization, fT3 at admission

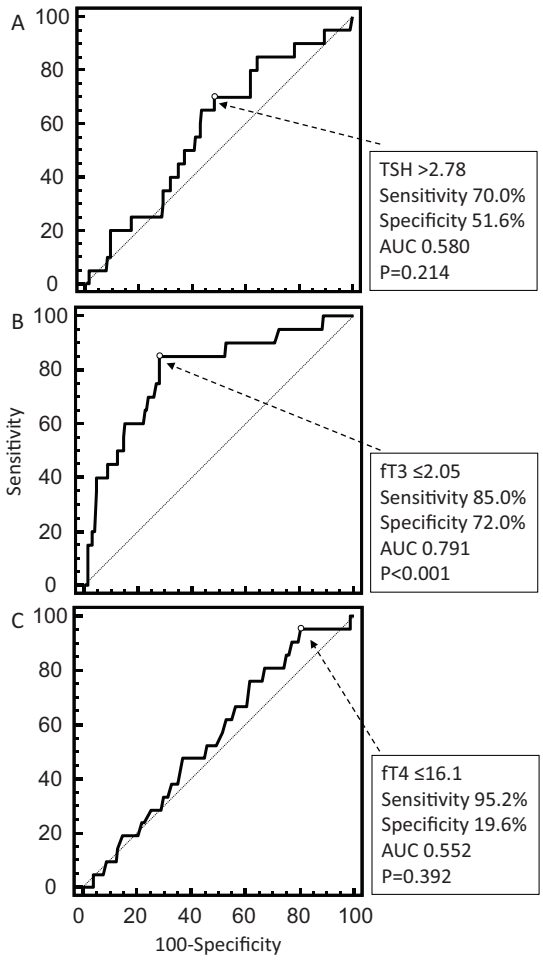

Fig. 1. Receiver operating characteristic (ROC) curves predicting the in-hospital all-cause death for hospitalized patients with acute decompensated heart failure. The area under the ROC curve (AUC) for thyroid stimulating hormone (TSH) (A) was 0.580, for free triiodothyronine (fT3) (B) was 0.791, and for free thyroxine (fT4) (C) was 0.552.