A Low-Normal Free Triiodothyronine Level Is Associated with Adverse Prognosis in Euthyroid Patients with Heart Failure Receiving Cardiac Resynchronization Therapy

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Summary
Thyroid dysfunction is prevalent in patients with heart failure (HF) and hypothyroidism is related to the adverse prognosis of HF subjects receiving cardiac resynchronization therapy (CRT). We aim to investigate whether low-normal free triiodothyronine (fT3) level is related to CRT response and the prognosis of euthyroid patients with HF after CRT implantation.

One hundred and thirteen euthyroid patients who received CRT therapy without previous thyroid disease and any treatment affecting thyroid hormones were enrolled. All of patients were evaluated for cardiac function and thyroid hormones (serum levels of fT3, free thyroxine [fT4] and thyroid-stimulating hormone [TSH]). The end points were overall mortality and hospitalization for HF worsening. During a follow-up period of 39 ± 3 weeks, 36 patients (31.9%) died and 45 patients (39.8%) had hospitalization for HF exacerbation. A higher rate of NYHA III/IV class and a lower fT3 level were both observed in death group and HF event group. Multivariate Cox regression analyses disclosed that a lower-normal fT3 level (HR = 0.648, \( P = 0.009 \)) and CRT response (HR = 0.441, \( P = 0.001 \)) were both independent predictors of overall mortality. In addition, they were also both related to HF re-hospitalization event (\( P < 0.01 \) for both). Patients with fT3 < 3.00 pmol/L had a significantly higher overall mortality than those with fT3 ≥ 3.00 pmol/L (\( P = 0.027 \)). Meanwhile, a higher HF hospitalization event rate was also found in patients with fT3 < 3.00 pmol/L (\( P < 0.001 \)).

A lower-normal fT3 level is correlated with a worse cardiac function and adverse prognosis in euthyroid patients with HF after CRT implantation.

Key words: Thyroid hormones, Cardiac dysfunction, Left ventricular dyssynchrony, CRT response, Mortality, Hospitalization

Cardiac resynchronization therapy (CRT) is a considerable treatment for patients with drug-refractory heart failure (HF) and electromechanical dyssynchrony.1,2 Though CRT improves heart failure symptoms and quality of life, and reduces both HF-related morbidity and mortality, non-response to CRT has been reported in nearly one third of patients.3 The reason of non-response to CRT is complicated and remains a question of different opinions.

Thyroid hormones (THs) have cardiac and vascular effects, and they also regulate biochemical reactions in most tissues.4,5 TH consists of thyroxine (T4) and triiodothyronine (T3), and the cardiac myocyte does not convert T4 to T3. In other word, T3 is the bioactive form of thyroid hormone for cardiomyocytes and plays an important role in cardiovascular regulation. Many studies have confirmed that T3 is a prognostic predictor or risk stratification of HF.5,7 Recently, fT3 level was shown to be associated with cardiac function and heart structure in euthyroid subjects without HF.8 In addition, another research reported hypothyroidism was associated with a worse prognosis after CRT implantation, but it did not supply values for complete thyroid panel (fT3 and fT4).9 Is the prognosis of patients with HF after CRT implantation is correlated with lower fT3 levels within a normal reference range? If the above is true, what is the relationship among THs, CRT response and prognosis? Thus, we aim to understand whether changes in fT3 levels within the normal reference range could affect the prognosis in a group of HF subjects with CRT implantation, and investigate the relationship between THs and CRT response.

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Methods

Study population: This original cohort consisted of 138 consecutive HF patients who received CRT implantation in the Sun Yat-sen Memorial Hospital of Sun Yat-sen University, from August 2007 to August 2013. All the devices were implanted according to a combination of 2008 and 2010 ESC guidelines: New York Heart Association (NYHA) functional classification II/III/IV, left ventricular ejection fraction (LVEF) ≤ 35% and sinus rhythm with QRS duration ≥ 120 ms, under optimal medical therapy. Euthyroid status was defined as all thyroid hormones within the normal reference range. Exclusion criteria included fT3 levels beyond the reference range; therapy with amiodarone, thyroid hormone (TH), glucocorticoids, and antithyroid medication within the last 1 month; previous therapy with radiiodine treatment and thyroid surgery; interventional or surgical procedures performed within the last 3 months; acute myocardial infarction within the previous 3 months; and loss of follow-up or data missing.

Study design: Clinical data included clinical status (e.g., body mass index [BMI], previous hypertension, diabetes, hyperlipidemia, previous heart disease or stroke, NYHA class), electrocardiogram, echocardiogram and blood samples test before CRT implantation. Baseline of renal function was determined by estimated glomerular filtration rate (eGFR). eGFR was estimated with the abbreviated Modification of Diet in Renal disease (MDRD) equation: eGFR (mL/minute) = 186.3 × (serum creatinine)-1.154 × age-0.203 × body mass index [BMI] (0.742 if female). This study was approved by the Hospital’s ethical committee and informed consents were given by all enrolled patients.

Blood chemistry and assays: Fasting blood samples were drawn from each patient during the first two days of admission. Serum fT3, fT4 and TSH levels were measured by Immulite 2000 (Bio DPC, Los Angeles, USA). The reference intervals of our laboratory are as follows: fT3 1.84-7.39 pmol/L, fT4 8.36-29.6 pmol/L and TSH 0.3-4.5 mIU/mL. The patients were further divided into low-normal fT3 group (fT3 1.84-3.00 pmol/L) and high-normal fT3 group (fT3 3.01-7.39 pmol/L) according to lower quartile of fT3. Creatinine was measured by automatic biochemistry analyzer (Hitachi 7600, Japan).

CRT implantation: Before CRT implantation, all patients received a coronary angiography (CAG) to identify coronary artery disease (CAD). CAD was defined as the stenosis of when at least one of three major coronary arteries was more than 50%. Ischemic etiology of HF was determined when CAD was diagnosed. When CRT was implanted, a coronary sinus venogram was performed firstly, and the LV pacing lead was inserted through the coronary sinus and placed in the lateral or posterolateral vein. Both atrial and right ventricular leads were implanted conventionally, and all leads were connected to a dual-chamber biventricular implantable pacemaker.

Follow-up and end points: All patients were followed up via telephone or medical records in our hospital every 1 to 6 months after CRT implantation until the end point. Optimal medical treatment was executed to all patients. Patients were classified as responders when the LVEF increased by more than 5%, and as non-responders if these response criteria were not satisfied. The primary end-point was overall mortality and the secondary end-point was hospitalization for HF worsening. Hospitalization for HF worsening was defined as patients admission with worsening signs and/or symptoms of HF, including dyspnea, peripheral edema, and/or congestion on the chest radiograph and the need for treatment with intravenous diuretics or an increase in oral diuretics.

Statistical analysis: Continuous data with normal distribution were presented as mean ± SD, continuous data with non-normal distribution were presented as median (interquartile range [IQR]), and dichotomous data were presented as numbers and percentages. Independent-samples t test was used to compare normally distributed data, and Mann-Whitney U test was used to compare non-normally distributed data. Chi square (χ²) test or Fisher’s exact test were used for dichotomous variables. To explore the predictors of overall survival and hospitalization admission event, multivariable Cox regression models with forward stepwise approach were constructed with age, sex, etiology of HF, NYHA class, LVEF, QRS width, NT-proBNP, fT3, fT4, TSH and response to CRT as predictive variables, respectively. All analyses were performed with PASW Statistics for Windows, version 18.0 (SPSS Inc, Chicago, Illinois). Level for statistical significance was P-value < 0.05 at 2-sides.

Results

Among the original 138 patients, 15 patients treated with amiodarone (9 patients), thyroid hormone (3 patients) or anti-thyroid medication (3 patients) during the follow-up period and 10 patients who were lost to follow-up were excluded. Finally, 113 patients (85 male and 28 female) completed the entire study. All of the patients were under biventricular pacing after CRT implantation, with 65 CRT responders (57.5%) and 48 non-responders (42.5%). Except for LVEF (29.9% versus 32.9%, P = 0.038), there were no significant differences between patients’ characteristics for CRT responders and non-responders. During a follow-up period of 39 ± 3 weeks, 36 patients (31.9%) died, including 30 (83.3%) of cardiac causes and 45 (39.8%) had hospitalization for HF worsening (Table I). The death group had a higher rate of NYHA III/IV class (80.6% versus 50.6%, P = 0.004), a lower fT3 level (3.35 pmol/L versus 4.06 pmol/L, P < 0.001) than those of the survival group. Compared with event-free group, the hospitalization event group had a significantly higher rate of NYHA III/IV class (77.8% versus 48.5%, P = 0.003) and a lower fT3 level (3.15 pmol/L versus 4.11 pmol/L, P < 0.001).

The relationship between thyroid hormones levels and other parameters of cardiac function: Spearman’s correlation was used to analyze the relationship between different levels of THs and other parameters of cardiac function (Table II). When we compared TH levels in patients with different NYHA classes, a lower fT3 was found in NYHA III/IV patients compared with those with NYHA II (r = -0.254, P = 0.007). However, no difference was detected between NYHA classes in terms of fT4 and TSH. After
| Variables                        | Response to CRT | Overall survival | HF worsening event |
|---------------------------------|-----------------|-----------------|-------------------|
|                                 | n = 68          | n = 45          | n = 68            | n = 45          | n = 68            | n = 45          | n = 68            | n = 45          |
|                                 | Male, n (%)     | Survival group  | Death group       | Event-free group | Event group       | P     | P       |
| Age (years)                     | 59.3 ± 12.4     | 60.3 ± 11.5     | 63.0 ± 13.5       | 69.4 ± 12.1     | 63.9 ± 11.9       | 0.055 |
|                                 | 47 (72.3)       | 58 (75.3)       | 27 (75.0)         | 52 (76.5)       | 33 (73.3)         | 0.824 |
| BMI (kg/m²)                     | 23.9 ± 3.7      | 24.2 ± 3.5      | 23.6 ± 3.5        | 24.5 ± 3.5      | 23.3 ± 3.4        | 0.075 |
| Ischemic etiology, n (%)        | 16 (24.6)       | 19 (24.7)       | 10 (27.8)         | 18 (26.5)       | 11 (24.4)         | 0.830 |
| Hypertension, n (%)             | 28 (43.1)       | 30 (39.0)       | 21 (58.3)         | 29 (42.6)       | 22 (48.9)         | 0.565 |
| Diabetes, n (%)                 | 19 (29.2)       | 18 (23.4)       | 12 (33.3)         | 17 (25.0)       | 13 (28.9)         | 0.669 |
| NYHA III/IV, n (%)              | 37 (56.9)       | 39 (50.6)       | 29 (80.6)         | 33 (48.5)       | 35 (77.8)         | 0.003 |
| QRS width ≥ 120ms, n (%)        | 44 (67.7)       | 47 (61.0)       | 26 (72.2)         | 42 (61.8)       | 31 (68.9)         | 0.547 |
| LVEF (%)                        | 29.9 ± 7.8      | 31.1 ± 6.9      | 31.1 ± 8.8        | 31.2 ± 7.2      | 31.0 ± 8.1        | 0.892 |
| NT-proBNP (pg/mL)               | 2517 (1333, 5058) | 2451 (1164, 4593) | 2866 (1785, 5625) | 2254 (1126, 4489) | 2927 (1672, 5452) | 0.074 |
| eGFR (mL/minute)                | 64.7 ± 23.5     | 66.4 ± 25.5     | 59.4 ± 19.3       | 66.3 ± 23.1     | 57.9 ± 23.2       | 0.122 |
| fT3 (pmol/L)                    | 3.82 (2.96, 4.57) | 4.06 (3.31, 4.62) | 3.35 (2.23, 3.77) | 4.11 (3.67, 4.64) | 3.15 (2.37, 3.81) | < 0.001 |
| fT4 (pmol/L)                    | 18.70 (16.55, 21.10) | 18.50 (16.30, 20.80) | 18.08 (16.00, 20.25) | 18.75 (16.20, 21.25) | 18.40 (16.20, 21.30) | 0.091 |
| TSH (mIU/L)                     | 1.43 (1.01, 2.62) | 1.50 (0.99, 2.62) | 1.33 (0.99, 2.04) | 1.41 (0.91, 2.57) | 1.43 (1.07, 2.37) | 0.318 |
| β-blockers, n (%)               | 13 (20.8)       | 20 (55.6)       | 66 (97.1)         | 74 (96.1)       | 74 (96.1)         | 0.500 |
| ACEIs/ARBs, n (%)               | 53 (81.5)       | 63 (88.9)       | 40 (88.9)         | 55 (80.9)       | 44 (97.8)         | 1.000 |
| Furosemide, n (%)               | 62 (95.4)       | 72 (93.5)       | 36 (100.0)        | 64 (94.1)       | 45 (100.0)        | 0.647 |

LVEF indicates left ventricular ejection fraction; NT-proBNP, N-terminal pro brain natriuretic peptide; fT3, free triiodothyronine; fT4, free thyroxin; TSH, thyroid-stimulating hormone; ACEIs, angiotensin-converting enzyme inhibitors; and ARBs, angiotensin receptor blockers. * Fisher’s test
fT3 indicates free triiodothyronine; fT4, free thyroxin; TSH, thyroid-stimulating hormone; BMI, body mass index; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro brain natriureticpeptide; and eGFR, estimated glomerular filtration rate.

| Variables | FT3 | FT4 | TSH |
|-----------|-----|-----|-----|
| Age       | 0.297 | 0.001 | -0.058 | 0.545 | -0.034 | 0.719 |
| Male      | -0.150 | 0.112 | -0.137 | 0.149 | 0.083 | 0.381 |
| BMI       | 0.207 | 0.028 | 0.007 | 0.939 | 0.130 | 0.170 |
| Hypertension | -0.140 | 0.140 | -0.165 | 0.080 | 0.023 | 0.805 |
| Diabetes mellitus | -0.168 | 0.075 | 0.084 | 0.375 | -0.101 | 0.288 |
| NYHA III/IV | -0.254 | 0.007 | 0.001 | 0.995 | -0.037 | 0.697 |
| LVEF      | 0.019 | 0.842 | -0.058 | 0.545 | 0.014 | 0.880 |
| logNT-proBNP | -0.261 | 0.005 | -0.033 | 0.730 | -0.019 | 0.838 |
| eGFR      | 0.321 | 0.001 | 0.175 | 0.063 | -0.175 | 0.064 |
| CRT response | 0.113 | 0.232 | 0.066 | 0.490 | 0.059 | 0.537 |

HR indicates hazard ratio; CI, confidence interval; LVEF, left ventricular ejection fraction; fT3, free triiodothyronine; fT4, free thyroxin; TSH, thyroid-stimulating hormone; ACEIs, angiotensin-converting enzyme inhibitors; and ARBs, angiotensin receptor blockers.

Table III. Univariate and multivariate Cox regression models of HF patients receiving CRT for overall mortality and HF worsening event

| Variables | Univariate (95% CI) | P | Multivariate (95% CI) | P | Univariate (95% CI) | P | Multivariate (95% CI) | P |
|-----------|---------------------|---|-----------------------|---|---------------------|---|-----------------------|---|
| Age (per 1 year) | 1.008 (0.980-1.038) | 0.565 | - | - | 1.020 (0.993-1.048) | 0.147 | - | - |
| Male | 1.174 (0.546-2.524) | 0.681 | - | - | 1.029 (0.529-2.002) | 0.932 | - | - |
| Ischemic etiology | 0.795 (0.383-1.654) | 0.540 | - | - | 1.075 (0.544-2.124) | 0.835 | - | - |
| Hypertension | 2.133 (1.086-4.190) | 0.028 | 2.234 (1.105-4.513) | 0.025 | 1.321 (0.735-2.373) | 0.352 | - | - |
| Diabetes mellitus | 1.363 (0.678-2.740) | 0.385 | - | - | 1.046 (0.547-2.001) | 0.892 | - | - |
| NYHA III/IV | 2.084 (0.896-4.844) | 0.088 | - | - | 2.474 (1.220-5.015) | 0.012 | - | - |
| QRS width ≥ 120ms | 1.613 (0.777-3.350) | 0.200 | - | - | 1.496 (0.794-2.819) | 0.213 | - | - |
| logNT-proBNP | 1.979 (0.917-4.274) | 0.082 | - | - | 1.827 (0.944-3.537) | 0.074 | - | - |
| LVEF (per 1%) | 0.987 (0.942-1.035) | 0.602 | - | - | 0.993 (0.952-1.036) | 0.743 | - | - |
| fT3 (per 1 pmol/L) | 0.645 (0.484-0.866) | 0.003 | 0.648 (0.469-0.895) | 0.009 | 0.538 (0.407-0.712) | <0.001 | 0.533 (0.402-0.705) | <0.001 |
| fT4 (per 1 pmol/L) | 0.913 (0.839-0.994) | 0.036 | - | - | 0.967 (0.896-1.044) | 0.397 | - | - |
| TSH (per 1 mU/L) | 0.962 (0.850-1.088) | 0.533 | - | - | 0.992 (0.940-1.048) | 0.785 | - | - |
| CRT response | 0.430 (0.221-0.837) | 0.013 | 0.441 (0.221-0.880) | 0.020 | 0.433 (0.237-0.790) | 0.006 | 0.425 (0.229-0.787) | 0.007 |
| β-blockers | 0.450 (0.233-0.870) | 0.018 | - | - | 0.488 (0.268-0.889) | 0.019 | - | - |
| ACEIs/ARBs | 0.355 (0.137-0.919) | 0.033 | 0.178 (0.063-0.499) | 0.001 | 0.835 (0.259-2.719) | 0.770 | - | - |
| Spironolactone | 2.154 (0.253-21.270) | 0.458 | - | - | 2.020 (0.277-14.711) | 0.488 | - | - |

adjusting for potential confounders (age, sex, hypertension, diabetes mellitus), fT3 showed a significant correlation with BMI (r = 0.207, P = 0.028) and eGFR (r = 0.321, P = 0.001). On the other hand, fT4 and TSH had no significant relationship with BMI and eGFR. Besides, none of THs was associated with CRT response.

Association between THs and prognosis of patients with CRT implantation: Table III showed the variables for the prognosis of patients with CRT implantation. In univariate Cox regression analysis, a lower fT3 level (HR = 0.645, 95% CI 0.484-0.866, P = 0.003), a lower fT4 (HR = 0.913, 95% CI 0.839-0.994, P = 0.036) and CRT response (HR = 0.430, 95% CI 0.221-0.837, P = 0.013) were associated with a higher risk of overall mortality. Multivariate Cox regression analysis adjusting for age, sex, ischemic etiology, hypertension, diabetes mellitus, NYHA class, QRS width, LVEF, NT-proBNP, CRT response, use of β-blockers, ACEIs/ARBs and spironolactone revealed that only a lower fT3 level (HR = 0.648, 95% CI 0.469-0.895, P = 0.009) and response to CRT (HR=0.441, 95% CI 0.221-0.880, P = 0.020) remained independent predictors of overall mortality. On the other hand, only a lower fT3 level (HR = 0.533, 95% CI 0.402-0.705, P < 0.001) rather than fT4 or TSH was an independent predictor of HF readmission, as well as CRT response (HR = 0.425, 95% CI 0.229-0.787, P = 0.007). Therefore, the prognosis of patients with CRT implantation was significantly associated with a lower fT3 level before CRT implantation and CRT response.

All patients were grouped into two subgroups according to lower quartile (3.00), of fT3 level: low-normal fT3 group (fT3 1.84-3.00 pmol/L) and high-normal fT3 group (fT3 3.01-7.39 pmol/L). The overall survival rate and event-free survival between two subgroups were both compared using Kaplan-Meier curves with log-rank test. Figure A showed that patients in low-normal fT3 group had a significantly lower overall survival rate than high-normal group (log-rank test, χ² = 4.896, P = 0.027). Meanwhile, lower event-free survival rate was also observed in low-normal fT3 group (log-rank test, χ² = 2.084, 95% CI 0.896-4.844, P = 0.088) and response to CRT (fT3 1.84-3.00 pmol/L) and high-normal fT3 group.
Figure. Kaplan-Meier survival curves showing the differences in overall survival (A) and event-free survival rate (B) between those with lower-normal fT3 levels (fT3 < 3.00 pmol/L) and higher-normal fT3 levels (fT3 ≥ 3.00 pmol/L).
Discussion

As we had known, CRT proved to be beneficial for the LV dysfunction with electromechanical dyssynchrony. However, mortality still remains high due to frequent comorbidities. Hypothyroidism and “low T3 syndrome,” which represent decreased level of fT3 in common, are both the frequent comorbidities resulting to poor prognosis for patients with HF. Our study demonstrated that even the low-normal level of fT3 (less than lower quartile) could influence the prognosis of HF patients after CRT implantation. It was an interesting result that fT3 might be a sensitive biomarker to detect the prognosis of HF patients receiving CRT.

There was a high prevalence of abnormal thyroid hormone metabolism in patients with advanced HF. The most prominent abnormality was a decrease in T3 levels due to a diminished conversion of T4 to T3. Our study also confirmed that lower fT3, rather than fT4 or TSH, was associated with the prognosis, which was in line with most of the research results. The reasons for this phenomenon might be that cytokines such as tumor necrosis factor, IL-1 and IL-6, had been implicated in the pathogenesis of low-T3 syndrome in HF patients through reduced peripheral conversion of T4 into T3 and by inhibiting 5′-deiodinase activity. Hepatic congestion caused by volume overload in the setting of right ventricular dysfunction was another contributing factor to the decreased hepatic conversion of T4 to T3. Several potential mechanisms might explain the association between low serum fT3 levels and higher mortality and HF exacerbation rate in euthyroid subjects. Firstly, a lower fT3 level was more frequently seen in NYHA III/IV class patients and fT3 level had a negative correlation, both with NYHA class and NT-proBNP, in our study. It suggested that fT3 level was correlated to the severity of HF in patients receiving CRT, which agreed with the previous studies. Low fT3 level in HF reduced metabolic demand, which was seen as an adaptive process for HF: But persistently low fT3 represented a maladaptive mechanism in favor of structural and functional cardiac remodeling, which had a key role in the pathogenesis of HF. Secondly, low fT3 was correlated to deteriorative hemodynamic status and had been proved in catheterization-based studies. Worse hemodynamic status and low ejection fraction were clearly associated with low fT3 level. Low fT3 reduced ejection fraction, and further caused enlarged heart chambers, lower velocity in the left atrial appendage and severe mitral regurgitation, which finally reduced cardiac systolic function. Thirdly, low-normal fT3 could affect several arteriosclerotic risk factors, such as diabetes mellitus, insulin resistance, serum lipid levels and artery stiffness, all of them above had been proved to have adverse effects on progress of HF. Fourthly, low fT3 status was independently correlated to peak oxygen uptake and functional exercise capacity in severe HF, which made recurrence of HF more frequent and remission period shorter than those with normal range of fT3. As for the euthyroid population without HF, fT3 is also associated with heart rate and echocardiographic heart function and structure. Roef et al found that fT3 level was positively associated with the peak velocity of systolic mitral annulus and late ventricular filling, whereas negatively with left ventricular end-diastolic diameter. It suggested that euthyroid subjects with low-normal fT3 levels had an increased risk to suffer relatively reduced heart function, decreased fT3 level within the low-normal range might be associated with the severity of cardiac insufficiency. On the other hand, CRT can improve fT3 levels after a reverse of cardiac remodeling. Celikyurt et al reported that the fT3 levels increased from 2.67 pg/mL to 2.97 pg/mL and the fT3/fT4 ratio increased from 1.81 to 2.34 in the reverse remodeling group (P < 0.05 for both), which indicated that the increase of fT3 levels after CRT device implantation might be a potential biomarker for identification of CRT response.

Despite adverse outcome of HF with a lower level of fT3, the relationship between fT3 level and CRT response remained unclear. Sharma AK found that hypothyroidism was related to adverse outcome for CRT patients, but there was no significant difference between echocardiographic responses to CRT implantation in hypothyroid subjects compared with patients with euthyroid. Our results also showed that there was no correlation between thyroid hormones (fT3, fT4 and TSH) before CRT implantation and CRT response. Therefore, we thought that adverse outcomes might result from decrease in fT3, which did not affect CRT response. Baseline thyroid hormones before CRT implantation and the changes of thyroid hormones after CRT implantation should be studied together, and further large sample studies could be carried out to deal with the complicated relationship.

This study had some limitations. Firstly, the sample size of this study was relatively small, which might increase the sampling error and reduce the statistical power. Secondly, the thyroid hormones were only measured at the time of admission before CRT device implantation, but not at the period of follow-up, whereas it could be affected by many confounders. The changes of thyroid hormones may reflect the real effect of CRT. Thirdly, the span of years in enrolling was large, and the periods of follow-up were significantly different.

Conclusions

Our study demonstrates that low-normal fT3 level was found to be associated with poor prognosis of HF patients receiving CRT. HF patients receiving CRT with low-normal fT3 levels had a higher mortality rate than patients with high-normal fT3 levels. Patients receiving CRT with low-normal fT3 levels are vulnerable to suffer HF again compared to those with high-normal fT3 levels. A low-normal fT3 level may affect the response of CRT in patients through their association with HF process.

Disclosures

Conflicts of interest: The authors report no relationships that could be construed as a conflict of interest.
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