Clinical phenotypes and prognosis of thyrotoxic heart failure and cardiomyopathy in patients hospitalized for acute heart failure

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Abstract

Background   We sought to examine clinical characteristics and outcomes in patients hospitalized for acute heart failure (HF) and thyrotoxicosis.

Methods   Patients with thyrotoxic HF were compared with age and gender-matched patients hospitalized for acute HF (controls). Thy-HF was defined by the Framingham criteria for HF and clinical hyperthyroidism. Thyrotoxic cardiomyopathy was defined as left ventricular ejection fraction (LVEF) < 55%.

Results   Of 11 109 consecutive patients hospitalized for acute HF between 1 January 2002 and 1 January 2017, 92 patients (0.8%) had thyrotoxic HF. Clinical and echocardiographic data were available in 87 patients (age 51 ± 16 years; 74% female), representing the study population. Compared with controls, patients with Thy-HF had a smaller body surface area (BSA), a higher LVEF, a lower LV end-diastolic diameter, a higher tricuspid annular plane systolic excursion (TAPSE), higher blood pressure, higher heart rate, and were more likely to have right-sided HF at presentation (P < 0.01 for all). The survival rate among patients with thyrotoxic HF was higher than the control group (HR: 4.3; 95% CI: 2.1–9.5). Fifty-eight percent of patients with thyrotoxic HF had thyrotoxic cardiomyopathy. In multivariate analysis, TAPSE (OR = 46; 95% CI: 1.04–2008.20; P = 0.047) and leukocytosis (OR = 16; 95% CI 1.01–259.39; P = 0.049) correlated with thyrotoxic cardiomyopathy. LV recovery was observed in 69% of these patients.

Conclusions   Thyrotoxic HF was uncommon among patients hospitalized for acute HF. However, after definitive therapy, these patients had a more favourable prognosis than those hospitalized for acute HF without thyrotoxic HF. Clinical phenotypes of thyrotoxic HF include small BSA, middle-aged female, HF-pEF, and right-sided HF. Thyrotoxic cardiomyopathy affected over half of the patients with thyrotoxic HF with a two-third recovery rate.

Keywords   Acute heart failure; Outcome; Thyrotoxicosis; Cardiomyopathy; Thyroid

Introduction

Thyroid hormones regulate key cardiac genes and effects on myocyte and systemic vasculature altering cardiovascular haemodynamics, including tachycardia, increased myocardial contractility/ejection fraction (EF), increased cardiac output, increased blood volume, and lower systemic vascular resistance (SVR).1–4 A recent study found that high-output heart failure (HF) was associated with increased mortality; however, patients with HF and thyrotoxicosis were excluded from the study.5 Thyroid disorders are common problems in patients with HF.6,7 Thyrotoxicosis or hyperthyroidism complicated

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with acute HF has been previously described in case reports. However, there is a paucity on systematic data of clinical phenotypes and prognosis of patients hospitalized for acute HF and thyrotoxicosis. Furthermore, little is known about the effects of the excess circulating thyroid hormones on left and right ventricular (RV) function and pulmonary pressure in those patients. Therefore, we examined the prevalence, clinical, and echocardiographic characteristics, and clinical outcomes of patients hospitalized for acute HF with thyrotoxicosis.

**Methods**

**Patients and definitions**

Between 1 January 2002 and 1 January 2017, consecutive patients hospitalized for acute HF and thyrotoxicosis were identified. The study population includes patients hospitalized with a diagnosis of HF (International Classification of Disease-10th [ICD-10] I 500–504, I 508–509), who met the Framingham criteria for HF and a diagnosis of thyrotoxicosis (ICD-10 E05). Thyrotoxic HF was defined by the Framingham criteria for the diagnosis of HF coupled with the presence of a clinical syndrome characterized by hyper-metabolism and hyperactivity due to excess circulating free thyroid hormones, including serum-free thyroxine (FT4) > 1.8 ng/dL, free triiodothyronine (FT3) > 4 pg/mL, and serum thyroid-stimulating hormone (TSH) level < 0.3 μIU/mL. Thyroid hormones were measured by electrochemiluminescence immunoassay on a Cobas analyser (Roche Diagnostics, Thailand). Those cut-off values for thyroid hormones were based on an internal validation of a previous cohort in the Thai population. Graves' disease was diagnosed based on the clinical presentation of diffuse goitre and biochemical tests consisting of primary hyperthyroidism. Thyroid storm was diagnosed by the Burch and Warsofsky’s score of 45 or greater. Patients with thyrotoxic HF were compared with age and gender-matched patients hospitalized for acute HF in the corresponding periods (controls) in a 1:1 ratio. Clinical and echocardiographic data were taken from medical records review and reanalysis of echocardiographic data in the Echo PAC system. A transthoracic echocardiogram was performed in hospitalized patients using commercially available ultrasound machines, Vivid 7 GE-Vingmed (Milwaukee, WI), and IE-33 Philips (Philips Medical System, Andover, MA). The echocardiographic images were digitally stored in the EchoPAC and QLAB software packages for off-line analysis. Right-sided HF was determined by the presence of one of the following signs of HF resulting from RV dysfunction: elevated jugular venous pulse (JVP), lower extremity oedema, or positive hepatojugular reflex. Thyrotoxic cardiomyopathy was defined as left ventricular ejection fraction (LVEF) < 55% and the clinical syndrome of thyrotoxicosis. Recovery of thyrotoxic cardiomyopathy was defined as LVEF ≥ 55%, with an improvement of LVEF of 15% or greater. Heart failure with reduced EF (HF-rEF), mid-range EF (HF-mEF), and preserved EF (HF-pEF) were defined according to the ESC guidelines for acute and chronic HF. Pulmonary hypertension (PH) was defined as peak pulmonary systolic pressures (PASP) > 35 mmHg estimated by Doppler echocardiography. The study protocol was approved by the Institutional Review Board, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (IRB No. 253/61).

**Clinical outcomes**

Overall mortality was determined by medical records, death certificates, or telephone interviews. Five (6%) and two (2%) patients were lost to follow-up in the thyrotoxic HF group and control group, respectively.

**Statistical analysis**

Descriptive data were presented by frequency, percentage, median, and mean ± standard deviation (SD). Differences in continuous variables were determined by a student’s t-test or a Wilcoxon–rank-sum test. Categorical variables were compared using a χ² test or a Fisher’s exact test. To identify the predictors of thyrotoxic cardiomyopathy, univariate analysis was performed comparing the presence of thyrotoxic cardiomyopathy with demographic, clinical, and echocardiographic characteristics. Multivariate analysis was performed to identify if the addition of variables improved the prediction of thyrotoxic cardiomyopathy. The first model included age and gender followed by the addition of each variable with a P-value of ≤0.1 based on the univariate analysis. Kaplan–Meier curves were plotted to estimate survival between groups, based on the log-rank test. P values <0.05 were considered statistically significant.

**Results**

**Patient characteristics and clinical phenotypes of thyrotoxic HF**

Of 11 109 consecutive patients hospitalized for acute HF between 1 January 2002 and 1 January 2017, 92 patients (1%) had thyrotoxic HF. Clinical and echocardiographic data were available in 87 patients, representing the study population. Of study patients (age, 51 ± 16 years; 74% female) with thyrotoxic HF, 84%, 52%, and 24% had Graves’ disease, thyroid storm, and HF-rEF, respectively. Eighty patients (93%)

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presented with clinical right-sided HF, including elevated JVP in 65 patients (74%), positive hepatojugular reflux in seven patients (8%), and bilateral pitting oedema of lower extremities in 63 patients (72%). Mean serum FT3, serum FT4, and serum TSH was 12.6 pg/mL, 5.0 ng/dL, and 0.01 μIU/mL, respectively. The median duration of symptoms before HF admission was 10 (1–365) days. Thyrotoxicosis was treated with antithyroid drugs in all patients, radionuclide iodine (I131) therapy in 55%, and surgical thyroidectomy in 3%. Table 1 shows baseline characteristics in patients with thyrotoxic HF and controls. Compared with controls, patients hospitalized for thyrotoxic HF had smaller body surface area (BSA), smaller body mass index (BMI), higher blood pressure, higher heart rate, higher LVEF, lower LV end-diastolic diameter, higher PASP, higher tricuspid annular plane systolic excursion (TAPSE), lower serum creatinine, and were more likely to have PH and right-sided HF at presentation (P < 0.01 for all).

Thyrotoxic cardiomyopathy

Of the 87 patients with thyrotoxic HF, 50 patients (58%) had thyrotoxic cardiomyopathy. Table 2 shows the clinical and echocardiographic characteristics of study patients with and without thyrotoxic cardiomyopathy. Serum thyroid hormones, heart rate, atrial fibrillation, age, or gender were not different between patients with and without thyrotoxic cardiomyopathy, while greater white blood counts (8429 vs. 6598 cells/mL, P = 0.002), greater proportion of propylthiouracil (PTU) use as an antithyroid drug (44% vs. 20%, P = 0.024), greater dilated LV end-diastolic diameter (57 vs. 48 mm, P < 0.001), and lower TAPSE (15 vs. 21 mm, P = 0.0004) were observed in patients with thyrotoxic cardiomyopathy compared with those without thyrotoxic cardiomyopathy. In multivariate analysis, TAPSE (OR = 46, 95% CI: 1.01–259.39, P = 0.04) and leukocytosis (OR = 16, 95% CI: 1.04–20820, P = 0.049) were associated with thyrotoxic cardiomyopathy in patients hospitalized for thyrotoxic HF (Table 3). Among patients with thyrotoxic cardiomyopathy, 32 (64%) had a complete follow-up echocardiographic study for analysis. Over the mean follow-up period of 18 months, 22 patients (69%) had recovery of LV systolic function. Heart rate, atrial fibrillation, thyroid hormone levels, or TSH levels were not different between patients with and without LV recovery at the follow-up periods.

Clinical outcomes

During the 5-year follow-up period, nine patients (10%) with thyrotoxic HF and 47 controls (54%) died. One patient (1%) with thyrotoxic HF died in-hospital from ventricular

Table 1  Baseline characteristics

| Parameters | Thyrotoxic heart failure requiring hospitalization (n = 87) | Acute heart failure requiring hospitalization (n = 87) | P value |
|------------|----------------------------------------------------------|-----------------------------------------------------|---------|
| Age (years) | 51 ± 16                                                  | 49 ± 15                                              | 0.794   |
| Sex (female) | 64 (74%)                                               | 61 (70%)                                             | 0.613   |
| Body surface area (m²) | 1.56 ± 0.19                                      | 1.69 ± 0.24                                         | <0.001* |
| Body mass index (kg/m²) | 22.5 ± 4.7                         | 23.9 ± 5.0                                          | 0.040*  |
| Clinical features |                                             |                                                     |         |
| Right heart failure (n, %) | 84 (97%)                                             | 60 (69%)                                            | <0.001* |
| Systolic blood pressure (mmHg) | 133 ± 27                                               | 117 ± 19                                            | <0.001* |
| Heart rate (b.p.m.) | 109 ± 34                                             | 82 ± 16                                             | <0.001* |
| Atrial fibrillation (n, %) | 32 (37%)                                             | 35 (40%)                                            | 0.427   |
| Laboratories |                                             |                                                     |         |
| Creatinine (mg/dL) | 0.71 ± 0.43                                         | 1.27 ± 0.73                                         | <0.001* |
| White blood cells (cells/mm³) | 7718 ± 3239                                        | 7488 ± 3864                                        | 0.805   |
| Potassium (mEq/L) | 3.9 ± 0.7                        | 4.1 ± 0.6                                           | 0.125   |
| NT-pro BNP (pg/mL) | 4062 ± 3556                                      | 8760 ± 1071                                         | 0.588   |
| Echocardiography |                                             |                                                     |         |
| LVESD (mm) | 53 ± 8                                                  | 56 ± 10                                              | 0.006*  |
| LVEF (%) | 51 ± 17                                                  | 38 ± 24                                              | <0.001* |
| TAPSE (mm) | 18 ± 5                                                  | 14 ± 4                                               | 0.009*  |
| PASP (mmHg) | 48 ± 15                                                  | 43 ± 14                                              | 0.008*  |
| PASP > 35 mmHg | 52/60 (87%)                                     | 50/72 (69%)                                         | 0.002*  |
| HF phenotype (n, %) |                                             |                                                     |         |
| HF-rEF | 21 (24%)                                                | 56 (64%)                                             | <0.001* |
| HF-mEF | 15 (17%)                                                | 2 (2%)                                               |         |
| HF-pEF | 51 (59%)                                                | 29 (33%)                                             |         |

Data are presented as mean ± SD or count (percentage).
*Statistical significance (P < 0.05).
*Of 87 patients, 60 patients had a complete spectral Doppler of tricuspid regurgitation for analysis.
*Of 87 patients, 72 patients had a complete spectral Doppler of tricuspid regurgitation for analysis.
EF, ejection fraction; HF, heart failure; HF-mEF, heart failure with mid-range ejection fraction; HF-pEF, heart failure with preserved EF; HF-rEF, heart failure with reduced EF; LVESD, left ventricular end-diastolic diameter; LVEF, left ventricular EF; NT-pro BNP, N-terminal pro B-type natriuretic peptide; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid annular plane systolic excursion.
arrhythmia and multiorgan failure. The rate of survival among survivors of in-hospital death in patients with thyrotoxic HF was higher than that in controls (hazard ratio: 4.3; 95% CI: 2.1–9.5; P < 0.001) (Figure 1A). There was no difference in survival between thyrotoxic HF patients with and without cardiomyopathy (hazard ratio: 1.2; 95% CI: 0.3–3.6; P = 0.967) (Figure 1B).

Discussion

The major findings of our study are (i) the prevalence of thyrotoxic HF in patients hospitalized for acute HF was uncommon, only 1%; (ii) the most common cause of thyrotoxic HF in hospitalized patients was Graves’ disease, accounting for 84%; (iii) key clinical features of thyrotoxic HF included small middle-aged female, right-sided HF, tachycardia, and HF-preserved EF; (iv) thyroid storm was found in approximately half of the patients hospitalized for thyrotoxic HF; (v) thyrotoxic cardiomyopathy was present in half of the hospitalized patients with thyrotoxic HF with a 69% chance of recovery after definitive treatment; and (vi) in-hospital mortality of overall thyrotoxic HF was 1%; however, patients with thyrotoxic HF who received definitive treatment had a more favourable prognosis compared with general patients hospitalized for acute HF.

Table 2 Clinical and echocardiographic characteristics of patients hospitalized for thyrotoxic HF with and without thyrotoxic cardiomyopathy

| Parameters                      | Thyrotoxic cardiomyopathy | P value |
|---------------------------------|---------------------------|---------|
| Present (n = 50)                | Absent (n = 37)           |         |
| Age (years)                     |                           | 0.283   |
| Female (n, %)                   | 35 (70%)                  | 0.613   |
| Thyroid storm (n, %)            |                           | 0.850   |
| Right heart failure (n, %)      |                           | 0.619   |
| Systolic blood pressure (mmHg)  |                           | 0.332   |
| Heart rate (b.p.m.)             |                           | 0.126   |
| Atrial fibrillation (n, %)      |                           | 0.537   |
| Treatment (n, %)                |                           | 0.291   |
| Antithyroid drugs               |                           | 0.283   |
| Iodine131 therapy               |                           | 0.967   |
| Surgery                         | 2 (4%)                    | 0.046*  |
| PTU: methylazol                   | 29: 21 (58:42%)           | 0.175   |
| ACE-I/ARB                        | 22 (44%)                  | 0.520   |
| MRA                              | 3 (5%)                    | 0.009   |
| Diuretics                        | 24 (48%)                  | 0.714   |
| Laboratory FT3 (pg/mL)          |                           | 0.476   |
| FT4 (ng/dL)                     | 4.9 ± 2.1                 | 0.795   |
| TSH (μIU/mL)                    | 0.012 ± 0.032             | 0.144   |
| Creatinine (mg/dL)              | 0.78 ± 0.48               | 0.075   |
| White blood cells (cells/mm3)   | 8429 ± 3297               | 0.002*  |
| Potassium (mEq/L)               | 4.0 ± 0.8                 | 0.349   |
| Echocardiography LVEDD (mm)      |                           | <0.001* |
| LVET (%)                        | 40 ± 13                   | <0.001* |
| TAPSE (mm)                      | 15 ± 5                    | 0.0004* |
| PASP (mmHg)                     | 46 ± 12                   | 0.146   |
| HF phenotype (n, %)             |                           | 0.576   |
| HF-rEF                           | 22 (44%)                  | <0.001* |
| HF-mEF                           | 14 (28%)                  |         |
| HF-pEF                           | 14 (28%)                  |         |

Data are presented as mean ± SD or count (percentage). *Statistical significance (P < 0.05).

ACE-I, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; EF, ejection fraction; FT3, free triiodothyronine; FT4, free thyroxine; HF, heart failure; HF-mEF, heart failure with mid-range ejection fraction; HF-pEF, heart failure with preserved EF; HF-rEF, heart failure with reduced; LVEDD, left ventricular end-diastolic diameter; LVET, left ventricular EF; MRA, mineralocorticoid receptor antagonists; NT-pro BNP, N-terminal pro b-type natriuretic peptide; PASP, pulmonary artery systolic pressure; PTU, propylthiouracil; TAPSE, tricuspid annular plane systolic excursion; TSH, thyroid stimulating hormone.
Prevalence and clinical phenotype of thyrotoxic HF

We demonstrated that thyrotoxic HF was uncommon (1%) among patients hospitalized for acute HF. The prevalence of thyrotoxic HF in patients with acute HF was less than that reported in the chronic HF population. Previous studies observed that clinical hyperthyroidism was found in about 6–19% of outpatient patients with HF. The prevalence of thyrotoxic HF in patients hospitalized for acute HF has not been described. We found that up to 90% of patients hospitalized for thyrotoxic HF presented with right-sided HF. These findings were consistent with previous case reports demonstrating that right-sided HF was common in thyrotoxicosis. Paran et al. and Thurnheer et al. suggested that PH was the major mechanism linked to right-sided HF in thyrotoxicosis. Marvasi et al. reported that 65% of ambulatory patients with hyperthyroidism caused by Graves’ disease had PH. In the present study, the mean PASP estimated by echocardiogram was 48 mmHg, which was higher than that observed in patients hospitalized for acute HF. Furthermore, we found that 87% of patients

Table 3 Predictors of thyrotoxic cardiomyopathy

| Variables                        | Univariate                      | Multivariate                   |
|----------------------------------|---------------------------------|--------------------------------|
|                                  | Odds ratio 95% CI P value | Odds ratio 95% CI P value |
| Age <60 years                    | 3.44 1.22–9.76 0.02 | 2.22 0.24–20.18 0.480         |
| Female                           | 0.64 0.24–1.73 0.61 | 3.99 0.24–66.86 0.340         |
| Clinical features                |                                 |                                |
| Thyroid storm                    | 0.92 0.39–2.16 0.85 |                                |
| Right heart failure              | 0.64 0.11–3.71 0.62 |                                |
| Atrial fibrillation              | 0.76 0.31–1.82 0.53 |                                |
| Treatment                        |                                 |                                |
| Iodine131 therapy                | 1 0.08–12.16 1.00 |                                |
| Surgery                          | 0.50 0.20–1.22 0.13 |                                |
| PTU: methimazole                 | 0.38 0.15–1.00 0.05 | 2.34 0.24–23.06 0.470         |
| Beta-blocker                     | 1.10 0.46–2.62 0.84 |                                |
| ACE-I/ARB                        | 1.86 0.76–4.56 0.18 |                                |
| Laboratories                     |                                 |                                |
| FT3 ≥ 9 pg/mL                    | 0.54 0.23–1.30 0.17 |                                |
| FT4 ≥ 8 ng/dL                    | 0.88 0.32–2.40 0.80 |                                |
| White blood cells >6300 cells/mm3| 5.69 2.18–14.88 <0.01 | 16.21 1.01–259.39 0.049        |
| Potassium ≤4 mEq/L               | 0.52 0.21–1.28 0.16 |                                |
| Echocardiography                 |                                 |                                |
| TAPSE <18 mm                     | 11.25 1.17–108.41 0.036 | 45.8 1.04–2008.2 0.047         |
| PASP >35 mmHg                    | 0.65 0.14–3.00 0.58 |                                |

ACE-I, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; FT3, free triiodothyronine; FT4, free thyroxine; LVEDD, left ventricular end-diastolic diameter; PASP, pulmonary artery systolic pressure; PTU, propylthiouracil; TAPSE, tricuspid annular plane systolic excursion.

Figure 1 (A) Kaplan–Meier survival curves for patients hospitalized for thyrotoxic HF and hospitalized patients with general acute HF. (B) Kaplan–Meier survival curves for thyrotoxic heart failure patients with and without thyrotoxic cardiomyopathy.

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with thyrotoxic HF had PH. The greater prevalence of PH in our study was likely explained by the larger number of critically ill patients compared with those studied in the ambulatory HF setting. The common phenotypes of thyrotoxic HF were small middle-aged females with normal EF. These phenotypes stand in contrast to those described in classic HF-pEF, typically older women with high BMI and BSA.5,31 Patients with thyrotoxic HF had a higher heart rate and higher blood pressure than controls.32 The effects of the T3 hormone on cardiovascular haemodynamics have been well described in previous literature.1,2,33 Thyroid hormone increases basal metabolism in almost all tissue and organ systems, leading to an increase in preload, myocardial contractility, and cardiac output.1 Additionally, the genomic effects of the T3 hormone regulate the beta-1 adrenergic receptor and affect the action potential in cardiac pacemaker through accelerated diastolic depolarization secondary to an increase in cyclic adenosine monophosphate (cAMP).1,2 In our study, 37% of patients had atrial fibrillation. The prevalence of atrial fibrillation in patients with hyperthyroidism has been shown to range from 2% to 39%.1,2,3 It is unclear as to how the thyroid hormone predisposes to atrial fibrillation.2 Notably, about half of the patients hospitalized for thyrotoxic HF had thyroid storm at presentation. This proportion was considerably higher than previously reported. A study in Japan showed that 5.4% of patients hospitalized for thyrotoxicosis had thyroid storm.18 The possible explanation of the high proportion of thyroid storm in our study may be that the study population consisted of patients hospitalized for acute HF, representing a sicker patient population and underscreeing before the presentation.

**Thyrotoxic cardiomyopathy and heart failure with recovered ejection fraction**

Previous studies have described LV dysfunction among outpatients with hyperthyroidism and chronic HF.23,32 However, there are limited data on the prevalence of thyrotoxic cardiomyopathy in patients hospitalized for acute HF. We demonstrated that 58% of hospitalized patients with thyrotoxic HF had cardiomyopathy. This prevalence rate was higher than previously reported in ambulatory patients with hyperthyroid.23,32 Siu et al. studied the clinical characteristics of 34 patients with primary hyperthyroidism presenting with HF in a thyroid clinic.32 About half of their patients with thyrotoxic HF had Graves’ disease. They found that 47% had LV systolic dysfunction.32 A more recent study by Oliveros-Ruiz et al. examined the recovery of thyrotoxic cardiomyopathy in ambulatory patients with hyperthyroidism.23 Although they did not include HF syndrome in the inclusion criteria, the authors showed that 37% of patients with hyperthyroidism had persistent LV dysfunction on 6 months follow-up. Siu et al. demonstrated that 31% of patients with HF and hyperthyroidism had persistent LV dysfunction at 12 month follow-up.32 Similarly, we found that 31% of patients hospitalized for thyrotoxic HF had persistent cardiomyopathy at 18 months. The possible pathomechanisms of thyrotoxic cardiomyopathy include tachycardia-induced cardiomyopathy, direct myopathic effect caused by T3 hormone, and concomitant auto-immune myocarditis associated with Graves’ disease.1,2,3,4,33 However, heart rate and thyroid hormone levels in patients with and without LV recovery were not different in this study. These findings were consistent with those reported by Siu et al.32 Therefore, the key mechanism of thyrotoxic cardiomyopathy remains elusive. Interestingly, we found that lower TAPSE was associated with thyrotoxic cardiomyopathy, suggesting that RV dysfunction was concordant with the degree of LV systolic dysfunction in the setting of acute thyrotoxic HF. Furthermore, we demonstrated that leukocytosis was another independent factor associated with thyrotoxic cardiomyopathy. It is likely that leukocytosis is attributed to the stress response from the critical hyperthyroid state or concomitant myocarditis. Incorporating cardiac magnetic resonance data could further define this aspect.

**Prognosis of patients hospitalized for acute thyrotoxic heart failure**

One patient with HF and thyroid storm died in the hospital because of refractory ventricular arrhythmia and multiorgan failure. This equates to an in-hospital mortality of 1% and 2% among patients hospitalized with thyrotoxic HF and thyroid storm, respectively. The in-hospital mortality rate of thyroid storm in this study was lower than those reported by previous studies.18,34 Akamizu et al. suggested that the overall mortality rate of thyroid storm was 10%.18,19 In our cohort, patients with thyrotoxic HF who were survivors from in-hospital deaths had a more favourable prognosis than general patients hospitalized with acute HF. Recently, Yogesh et al. demonstrated increased mortality in high-output HF.5 However, they excluded patients with thyrotoxicosis and anaemia from the study population. Our findings highlight that not every high-output HF carried a poor prognosis. Thyrotoxic HF had a favourable prognosis if the definitive treatment was timely commenced. The recovery and reversibility of LV systolic function may play a pivotal role in determining prognosis in this entity of HF.

**Study limitations**

First, the care of thyroidal disease in the present study was conducted in a tertiary care academic centre setting where the I131 ablative therapy is preferable, which could limit the applicability and generalizability of our findings. Second, data of treatment and echocardiogram after hospital discharge.
were not available for every patient. Third, the causes of death were not available. Fourth, PH was mainly defined by echocardiographic estimation of pulmonary artery systolic pressure, instead of right heart catheterization. Lastly, this study is limited by its retrospective nature. We recommend a multi-centre cohort with a larger number of patients to clarify and expand these initial findings.

Conclusions

Thyrotoxic HF was uncommon among patients hospitalized for acute HF. However, after definitive treatment for hyperthyroidism and HF, these patients had a more favourable prognosis than general patients hospitalized for acute HF. Thyrotoxic cardiomyopathy was present in half of the hospitalized patients with thyrotoxic HF with a two-thirds rate of treatment recovery. Thyrotoxic HF should be considered in the differential diagnosis in patients presenting with clinical phenotypes of small middle-aged females with HF-pEF and the clinical syndrome of right-sided HF, tachycardia, and relatively hypertensive manifestation.

Conflict of interest

None declared.

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