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Original article

Effects of thyroid dysfunction on the severity of coronary artery lesions and its prognosis

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ABSTRACT

Background: Abnormal thyroid hormone metabolism influences the occurrence and progress of coronary heart disease (CHD). The aim of the present study was to analyze the severity of coronary artery lesions and the prognosis of thyroid dysfunction patients admitted for coronary angiography (CAG).
Methods: From July 2011 to July 2012, 605 consecutive patients with suspected coronary heart disease admitted for CAG were selected. The patients were divided into three groups, based on their thyroid function prior to CAG: euthyroid group ($n = 455$ patients), low T3 syndrome group ($n = 96$ patients), and hypothyroidism group ($n = 54$ patients). All patients underwent CAG. Then the severity of coronary artery lesions was assessed by Gensini scores. All patients were followed up for major adverse cardiac events.
Results: The prevalence of CHD in low T3 syndrome group and hypothyroidism group was significantly higher than that in the euthyroid group ($p < 0.001$ and $p = 0.004$, respectively). Moreover, the severity of coronary artery lesions in low T3 syndrome group and hypothyroidism group was significantly greater than that in the euthyroid group (all $p < 0.001$). Multinomial logistic regression analysis demonstrated that low T3 syndrome was an independent risk factor of coronary artery moderate [odds ratio (OR) = 4.268, 95% CI: 3.294–7.450, $p = 0.016$] and severe (OR = 4.294, 95% CI: 2.259–9.703, $p < 0.001$) lesions. The mean duration of follow-up was 15.3 ± 3.8 months; patients with thyroid dysfunction had a significantly worse prognosis as compared to those in the euthyroid group for the composite end-point ($p < 0.01$). Moreover, the incidence of the composite end-point (all-cause death, non-fatal myocardial infarction, and coronary revascularization) was significantly higher in low T3 syndrome group and hypothyroidism group compared with that of in the euthyroid group (all $p < 0.001$).
Conclusions: The patients with hypothyroidism and low T3 syndrome had a high prevalence of CHD, increased severity of coronary artery lesions and poor prognosis.

Introduction

The cardiovascular system is one of the main target organ systems on which the thyroid hormones act [1,2]. The active hormone triiodothyronine (T3) 80% of which is derived from peripheral conversion of prohormone thyroxine (T4) exerts its biological effect [3]. The study has shown that T3 plays an important role in regulating the heart rate and cardiac contractility and arterial peripheral resistance [1,2]. Abnormal thyroid hormone metabolism leads to different forms of heart disease: T3 level is negatively correlated with the prevalence of coronary heart disease (CHD) [4]; hypothyroidism could accelerate the process of atherosclerosis and increase the risk of cardiovascular events [5]; low T3 syndrome increases the mortality of acute myocardial infarction patients and is a strong predictor of cardiac death [6]. However, do thyroid dysfunction patients have increased severity of coronary artery lesions and prognosis? Few studies in this aspect were seen in China. The aim of the present study was to assess the severity of coronary artery lesions and the prognosis of thyroid dysfunction patients.

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Methods

Study population

The study enrolled 605 consecutive patients with suspected CHD who were admitted to the Department of Cardiology in Zhengzhou University People's Hospital for coronary angiography (CAG) from July 2011 to July 2012. The exclusion criteria were as follows: (1) previous CAG; (2) therapy with amiodarone; (3) subclinical hypothyroidism, clinical hyperthyroid, subclinical hyperthyroidism; (4) chronic renal insufficiency; (5) clinical signs of sepsis or cachexia or any other severe systemic disease.

The present study was designed as a prospective observational study. All participants signed consent forms, and the approval of the institutional review board was obtained prior to the initiation of the study.

Thyroid hormone determination

Venous blood samples on empty stomach were performed before the CAG in order to measure the levels of triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), apolipoprotein A1 (Apo-A1), and apolipoprotein B100 (Apo-B100) assayed using the routine laboratory techniques. In addition, 3 mL of venous blood samples on empty stomach were rapidly centrifuged, and plasmatic concentration of free T3 (fT3), free T4 (fT4), and hypersensitive thyroid stimulating hormone (hTSH) was measured by a completely automated ADVIA Centaur XP system (Siemens Medical Solutions Diagnostics, Tarrytown, NY, USA). The reference intervals for our laboratory are as follows: fT3 3.5–6.5 pmol/L, fT4 11.5–22.7 pmol/L, and hTSH 0.55–4.78 uIU/mL. We divided the patients into three groups on the basis of thyroid hormone profile [7]: euthyroid group (patients with normal values of hTSH, fT3 and fT4), low T3 syndrome group (patients with fT3 < 3.5 pmol/L, normal values of hTSH and fT4), hypothyroid group (patients with hTSH > 4.78 uIU/mL, fT3 < 3.5 pmol/L or/and fT4 < 11.5 pmol/L).

CAG and the severity of coronary artery lesions

CAG was done by the Judkins technique via radial or femoral artery. Each examination was reviewed by two interventional cardiologists who were blinded to the study plan and to each other. CHD was defined as a greater than 50% stenosis by visual assessment in at least one major vessel or principal side branch. The Gensini score was used to evaluate the severity of coronary artery lesions. The coronary artery lesions were divided into three categories according to Gensini scores [8]: coronary artery mild lesions (Gensini score 0–20), coronary artery moderate lesions (Gensini score 21–33), and coronary artery severe lesions (Gensini score >33). Contrast media (CM) used for CAG were ultravist solution or histodenz solution.

Clinical follow-up

We obtained follow-up information from a survey of the patients' records, telephone interviews, or medical visits at the outpatient clinic. The end time of follow-up was May 2013. Major adverse cardiac events were carefully recorded, including all-cause death, non-fatal myocardial infarction (MI), and coronary revascularization. All-cause death was defined as a composite of death from any cause. Non-fatal MI was defined as the presence of typical chest pain, electrocardiographic ST-segment elevation with or without Q waves, as well as serum cardiac enzyme elevations at least twofold upper limit of the normal range. Coronary revascularization was defined as a repeat percutaneous coronary intervention during follow-up.

Statistical analysis

Continuous data were expressed as means ± SD, and the differences were analyzed with one-way analysis of variance (ANOVA, normal distribution) or Mann–Whitney *U* test (abnormal distribution or unequal variances). Categorical variables were presented by frequency counts, and the differences were tested using the chi-square test or Fisher exact test. The Kruskal–Wallis test was used for ordered categorical data with the severity of coronary artery lesions, and the risk factors of the severity of coronary artery lesions were estimated by multinomial logistic regression analysis. Cumulative event rates were evaluated using Kaplan–Meier estimates and compared using a log-rank test. A multivariable Cox proportional hazards model was used to evaluate the association between thyroid function and adverse events after adjustment for baseline that differed significantly among the thyroid function groups. Univariable predictors of adverse events with less than 0.05 of p value were allowed to enter the model. We presented the results as hazard ratio (HR) and 95% confidence intervals (CI) and p values. A proportional-hazards model was developed by using enter selection. Statistical significance was considered to be $p < 0.05$ among the three groups and $p < 0.0167$ between two groups. All statistical analyses were performed with SPSS17.0 software (SPSS Inc, Chicago, IL, USA).

Results

We divided the 605 patients into three groups on the basis of thyroid hormone profile: euthyroid group ($n = 455$, 75.2%); low T3 syndrome group ($n = 96$, 15.7%); and hypothyroid group ($n = 54$, 8.9%). Table 1 reports the clinical characteristics of the study population. As compared to euthyroid patients, low T3 syndrome patients and hypothyroid patients had significantly higher prevalence of acute coronary syndrome (ACS), TC, and LDL-C levels (all $p < 0.01$). There were no significant differences in other cardiovascular risk factors.

CAG showed that there were 280 (61.5%) patients with CHD in the euthyroid group, 80 (83.3%) patients with CHD in the low T3 syndrome group, and 44 (81.5%) patients with CHD in the hypothyroid group, respectively. Statistical analysis showed that the prevalence of CHD in three groups had a significant difference ($p < 0.01$). The prevalence of CHD in the low T3 syndrome group and hypothyroidism group was significantly higher than that in the euthyroid group ($p < 0.001$ and $p = 0.004$, respectively); the total amount of CM administered with CAG in the three groups was 31.9 ± 12.3 g, 30.6 ± 11.1 g, and 30.0 ± 9.7 g, in groups 1, 2, and 3, respectively, and no significant difference was found among the three groups ($p > 0.05$). All patients had no thyroid crisis during their hospitalization.

Table 2 shows the severity of coronary artery lesions according to the Gensini score in the three groups, the severity of coronary artery lesions in the three groups had a significant difference ($p < 0.05$), the severity of coronary artery lesions in the low T3 syndrome group and the hypothyroidism group were significantly greater than that in the euthyroid group (all $p < 0.001$). Table 3 shows the significant results of multinomial logistic regression analysis about the severity of coronary artery lesions. In the model, we have included clinical variables in Table 1; coronary artery mild lesion was regarded as a reference category. Results showed that low T3 syndrome was an independent risk factor of moderate (OR = 4.268, 95% CI: 3.294–7.450, $p = 0.016$) and severe (OR = 4.294, 95% CI: 2.259–9.703, $p < 0.001$) coronary artery lesions.

Table 1
Clinical characteristics of study population.

	Euthyroid (n = 455, 72.8%)	Low T3 syndrome (n = 96, 15.4%)	Hypothyroid (n = 54, 8.6%)	p value
Age, years, mean ± SD	64.5 ± 11.3	67.2 ± 9.2	64.4 ± 17.1	0.14
Sex, female, n (%)	139 (30.5%)	35 (36.5%)	22 (40.7%)	0.21
Smoker, n (%)	141 (30.9%)	27 (28.1%)	11 (20.4%)	0.26
Hypertension, n (%)	198 (43.5%)	46 (47.9%)	28 (51.9%)	0.42
Diabetes, n (%)	76 (16.7%)	19 (19.8%)	10 (18.5%)	0.75
Arrhythmias, n (%)	68 (14.9%)	10 (10.4%)	8 (14.8%)	0.51
ACS, n (%)	143 (31.4%)	44 (45.8%)*	26 (48.1%)*	<0.01
TC, mmol/L, mean ± SD	4.21 ± 1.05	4.42 ± 1.05*	4.38 ± 0.96*	<0.01
TG, mmol/L, mean ± SD	2.01 ± 1.62	2.24 ± 1.66	2.47 ± 1.94	0.26
HDL-C, mmol/L, mean ± SD	1.05 ± 0.27	0.96 ± 0.21	1.12 ± 0.28	0.09
LDL-C, mmol/L, mean ± SD	2.29 ± 0.51	2.69 ± 0.67*	2.42 ± 0.81*	<0.01
Apo-A1, g/L, mean ± SD	1.22 ± 0.12	1.26 ± 0.16	1.38 ± 0.23	0.16
Apo-B100, g/L, mean ± SD	0.78 ± 0.02	0.98 ± 0.21	0.84 ± 0.11	0.34

ACS, acute coronary syndrome; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Apo-A1, apolipoprotein A1; Apo-B100, apolipoprotein B100.
* p < 0.001 for comparison with euthyroid group.

Table 2
The analysis of the severity of coronary artery lesions.

	Euthyroid	Low T3 syndrome*	Hypothyroidism*
Mild, n (%)	157 (34.5)	16 (16.7)	11 (20.4)
Moderate, n (%)	208 (45.7)	38 (39.6)	23 (42.6)
Severe, n (%)	90 (19.8)	42 (43.8)	20 (37.0)

* p < 0.001 for comparison with euthyroid group.

Table 3
The analysis of multinomial logistic regression about the severity of coronary artery lesions.

	b	p value	OR	95% CI for OR
Moderate				
Low T3 syndrome	1.362	0.016	4.268	3.294–7.450
ACS	1.263	0.003	3.466	1.347–6.912
LDL-C	1.437	<0.001	3.540	1.641–5.643
Severe				
Low T3 syndrome	1.472	<0.001	4.294	2.259–9.703
ACS	1.768	<0.001	5.967	2.436–10.902
LDL-C	1.142	0.006	3.257	1.428–7.503

Coronary artery mild lesion was regarded as reference category.
b, regression coefficient; OR, odds ratio; ACS, acute coronary syndrome; LDL-C, low-density lipoprotein cholesterol.

The follow-up included 580 (92.8%) out of the overall 625 patients. The mean duration of follow-up was 15.3 ± 3.8 months. Table 4 shows the major events of the three groups in this study. Fig. 1 shows the Kaplan–Meier survival curves for the composite end-point (all-cause death, non-fatal MI, and coronary revascularization). Patients with thyroid dysfunction had a significantly poorer prognosis as compared to the euthyroid group (p < 0.01). The group analysis showed that the low T3 syndrome group and hypothyroidism group had a significant difference in survival as regards composite end-point compared to the euthyroid group (all p < 0.001).

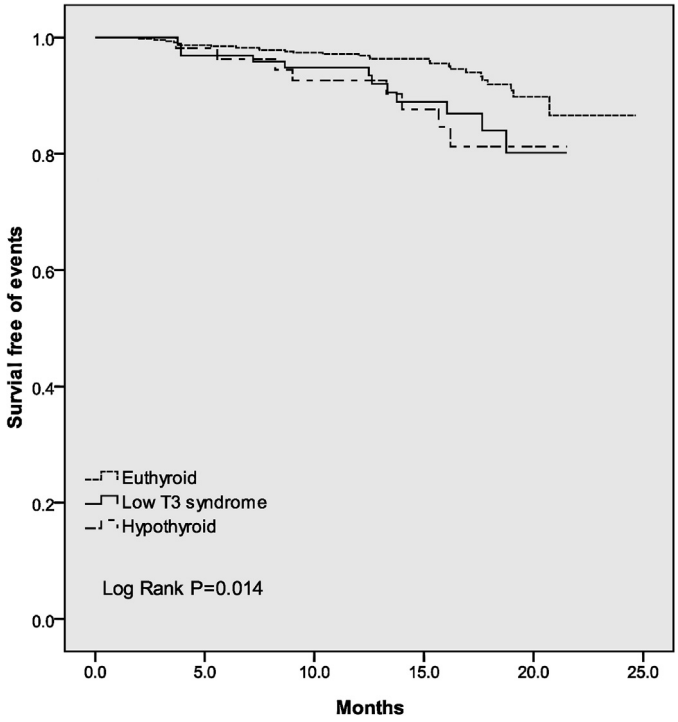

Fig. 1. Survival curves related to composite event (all-cause death, non-fatal myocardial infarction, and coronary revascularization) in three groups.

Table 5 shows the results of the analysis of COX for composite end-point. In the model, we included clinical variables in Table 1 that resulted in significant correlation with the events in the univariate analysis. The presence of the low T3 syndrome, hypothyroidism group, ACS, and LDL were independent prognostic factors for the composite end-point.

Table 4
The analysis of follow-up events.

	Euthyroid (n = 426, 73.4%)	Low T3 syndrome (n = 88, 19.6%)	Hypothyroidism (n = 48, 10.7%)	p value
All-cause death, n (%)	5 (1.2)	2 (2.3)	1 (2.0)	0.716
Non-fatal MI, n (%)	14 (3.3)	6 (6.8)	4 (8.3)	0.071
Revascularization n (%)	8 (1.9)	4 (4.5)	3 (6.3)	0.116
The composite end-point, n (%)	27 (6.3)	12 (13.6)*	8 (16.7)*	0.014

The composite end-point includes all-cause death, non-fatal MI, and coronary revascularization.
MI, myocardial infarction.
* p < 0.001 for comparison with euthyroid group.

Table 5
Multivariate survival COX proportional hazards analysis.

	b	SE(*b*)	Wald	*p* value	Exp(*b*)	95% CI for Exp(*b*)
Low T3 syndrome vs. euthyroid	0.683	0.159	4.126	0.022	1.892	1.381–2.558
Hypothyroid vs. euthyroid	0.932	0.406	5.927	0.004	1.334	1.073–1.806
ACS	1.066	0.306	12.160	<0.001	2.904	1.595–5.287
TC	−0.112	0.160	0.491	0.483	0.894	0.653–1.224
HDL-C	0.136	0.117	1.145	0.084	1.145	0.818–1.602
LDL-C	0.543	0.217	6.263	0.012	1.721	1.125–2.633

b, regression coefficient; CI, confidence interval; Exp(*b*), risk according to prognostic variables; SE(*b*), standard error of *b*; Wald, coefficient of the Wald test; ACS, acute coronary syndrome; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Discussion

The present study demonstrated that low T3 syndrome and hypothyroidism were associated with a higher prevalence of CHD, more serious coronary artery lesions, and poorer prognosis compared to euthyroidism. The reason could be dyslipidemia and endothelial dysfunction affected by thyroid hormone.

Thyroid hormones could regulate blood lipid levels, and then influence the occurrence and progress of CHD. The promoter of the LDL receptor gene contains a thyroid hormone responsive element which can promote fT3 to increase the expression of LDL receptors, therefore increasing the clearance of LDL [9]. Several studies found that hypothyroidism could increase the levels of TC and LDL-C [10], and accelerate the development of atherosclerosis and the progress of CHD [2,11]. Several studies also have pointed out a relationship between the serum thyroid hormone levels and the development of atherosclerosis. Tatar et al. [12] confirmed that serum fT3 levels were inversely correlated with carotid atherosclerosis and low serum fT3 level was an important determinant of carotid atherosclerosis. Coceani et al. [4] reported that serum fT3 levels were inversely correlated with the presence of CHD and the low T3 syndrome indicated an adverse prognosis, even after adjusting for the traditional coronary risk factors.

In addition to dyslipidemia, hypothyroidism may also lead to endothelial dysfunction, hypercoagulability, impaired fibrinolysis, hyperhomocysteinemia, systemic inflammation, and platelet abnormalities [5]. Low thyroid hormones altered the arterial muscle structure, and then caused thickening of the vessel wall. Several reports indicated that hypothyroidism was an independent risk factor for atherosclerosis and MI [13], even when hypothyroidism was treated, a residual increased risk of cardiovascular diseases may persist [14]. These changes in arterial muscle structure and vessel wall were independent of hypercholesterolemia and emerged rapidly after hypothyroidism took shape [15].

Ertas et al. [16] found that T3 levels within the physiological range were inversely correlated with the presence and severity of CHD. And free T3 was significantly lower in subjects with CHD compared to those without CAD (4.0 ± 0.7 pmol/L vs. 4.6 ± 0.6 pmol/L, $p < 0.001$). Moreover, fT3 was lower in patients with severe compared to mild CAD (3.9 ± 0.7 pmol/L vs.4.5 ± 0.6 pmol/L, $p < 0.001$). Logistic regression analysis demonstrated that the lower FT3 levels were associated with the presence (OR = 0.266, 95% CI: 0.097–0.731, $p = 0.01$) and severity (OR = 0.238, 95% CI: 0.083–0.685, $p = 0.008$) of CHD. Low T3 syndrome may produce a hypothyroid-like syndrome that contributes to the worsening or exacerbation of the intrinsic cardiac diseases [1,17]. In our study, hypothyroidism and low T3 syndrome, whose T3 levels were below the physiological range, increased the incidence of CHD and the severity of coronary artery lesions. Moreover, multinomial logistic regression analysis demonstrated low T3 syndrome was an independent risk factor of moderate (OR = 4.268, 95% CI: 3.294–7.450, $p = 0.016$) and severe (OR = 4.294, 95% CI: 2.259–9.703, $p < 0.001$) coronary artery lesions.

Some studies [18–20] have observed a relationship between the fT4 and TSH levels and the presence or severity of the CHD, but Ertas et al. [16] took the opposite view. In the present study, T4 and TSH were not found to be related to the presence and severity of CHD. Some possible reasons may be those of differences in sample sizes, study populations, various ethnic groups, and laboratory methods.

Many studies [6,21–23] concluded that hypothyroidism and low T3 syndrome were associated with the increased risk in deaths and the composite end-point (cardiac death and non-fatal MI). Marraccini et al. [23] indicated that hypothyroidism and low T3 syndrome had a significantly worse prognosis both for the overall and cardiac death as compared to euthyroidism, and also the incidence of the composite end-point (cardiac death and nonfatal MI). In addition, low T3 had an independent prognostic value both for the total mortality and for the composite end-point (nonfatal MI and cardiac death). In the present study, hypothyroidism and low T3 syndrome had a significantly worse prognosis only for the composite end-point (all-cause death, non-fatal MI, and coronary revascularization) as compared to euthyroidism. Moreover, hypothyroidism and low T3 syndrome were independent risk factors for the composite end-point.

In non-pathological conditions, there is a Wolff–Chaikoff effect [24] that the thyroid gland has the ability to handle an acute iodide overload by inhibition of iodide organification, which leads to a transient reduction in hormone synthesis. In pathological conditions, the Wolff–Chaikoff effect is insufficient to protect the thyroid gland and thyreotoxicosis may ensue [25]. In our study, all patients with thyroid dysfunction did not appear to have thyreotoxicosis. This was possibly because the symptomatic patients of thyroid dysfunction were treated with medicines before CAG.

Study limitations

The main limitation of this study is being a single center of clinical research which has a limited number of study subjects. These subjects were not selected from the general population. It is also not an ideal method to identify the severity of coronary artery lesions by Gensini scores. In addition, the follow-up time is not as long as in previous studies.

Conclusion

In the present study, we demonstrated that low T3 syndrome and hypothyroidism had a high prevalence of CHD, increased severity of coronary artery lesions, and poor prognosis.

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References

[1] Polikar R, Burger AG, Scherrer U, Nicod P. The thyroid and the heart. Circulation 1993;87:1435–41.
[2] Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med 2001;344:501–9.
[3] Pilo A, Iervasi G, Vitek F, Ferdeghini M, Cazzuola F, Bianchi R. Thyroidal and peripheral production of 3,5,3′-triiodothyronine in humans by multicompartmental analysis. Am J Physiol 1990;258:E715–26.
[4] Coceani M, Iervasi G, Pingitore A, Carpeggiani C, L'Abbate A. Thyroid hormone and coronary artery disease: from clinical correlations to prognostic implications. Clin Cardiol 2009;32:380–5.
[5] Cappola AR, Ladenson PW. Hypothyroidism and atherosclerosis. J Clin Endocrinol Metab 2003;88:2438–44.
[6] Iervasi G, Pingitore A, Landi P, Raciti M, Ripoli A, Scarlattini M, L'Abbate A, Donato L. Low-T3 syndrome: a strong prognostic predictor of death in patients with heart disease. Circulation 2003;107:708–13.
[7] De Alfieri W, Nistico F, Borgogni T, Riello F, Cellai F, Mori C, Nante N, Di Bari M. Thyroid hormones as predictors of short- and long-term mortality in very old hospitalized patients. J Gerontol A Biol Sci Med Sci 2013;68:1122–8.
[8] Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol 1983;51:606.
[9] Bakker O, Hudig F, Meijssen S, Wiersinga WM. Effects of triiodothyronine and amiodarone on the promoter of the human LDL receptor gene. Biochem Biophys Res Commun 1998;249:517–21.
[10] Mayer Jr O, Simon J, Filipovsky J, Plaskova M, Pikner R. Hypothyroidism in coronary heart disease and its relation to selected risk factors. Vasc Health Risk Manage 2006;2:499–506.
[11] Klein I. Endocrine disorders and cardiovascular disease. In: Zipes DP, Libby P, Bonow R, Braunwald E, editors. Braunwald's heart disease: a textbook of cardiovascular medicine. 7th ed. Philadelphia: W.B. Saunders; 2005. p. 2051–65.
[12] Tatar E, Kircelli F, Asci G, Carrero JJ, Gungor O, Demirci MS, Ozbek SS, Ceylan N, Ozkahya M, Toz H, Ok E. Associations of triiodothyronine levels with carotid atherosclerosis and arterial stiffness in hemodialysis patients. Clin J Am Soc Nephrol 2011;6:2240–6.
[13] Imaizumi M, Akahoshi M, Ichimaru S, Nakashima E, Hida A, Soda M, Usa T, Ashizawa K, Yokoyama N, Maeda R, Nagataki S, Eguchi K. Risk for ischemic heart disease and all-cause mortality in subclinical hypothyroidism. J Clin Endocrinol Metab 2004;89:3365–70.
[14] Flynn RW, Macdonald TM, Jung RT, Morris AD, Leese GP. Mortality and vascular outcomes in patients treated for thyroid dysfunction. J Clin Endocrinol Metab 2006;91:2159–64.
[15] Giannattasio C, Rivolta MR, Failla M, Mangoni AA, Stella ML, Mancia G. Large and medium sized artery abnormalities in untreated and treated hypothyroidism. Eur Heart J 1997;18:1492–8.
[16] Ertas F, Kaya H, Soydinc MS. Low serum free triiodothyronine levels are associated with the presence and severity of coronary artery disease in the euthyroid patients: an observational study. Anadolu Kardiyol Derg 2012;12:591–6.
[17] Klein I, Ojaama K. The cardiovascular system in hypothyroidism. In: Braverman LE, Utiger RD, editors. Werner and Ingbar's the thyroid. Philadelphia: Lippincott-Raven Press; 1996. p. 799–804.
[18] Auer J, Berent R, Weber T, Lassnig E, Eber B. Thyroid function is associated with presence and severity of coronary atherosclerosis. Clin Cardiol 2003;26:569–73.
[19] Yun KH, Jeong MH, Oh SK, Lee EM, Lee J, Rhee SJ, Yoo NJ, Kim NH, Ahn YK, Jeong JW. Relationship of thyroid stimulating hormone with coronary atherosclerosis in angina patients. Int J Cardiol 2007;122:56–60.
[20] Jung CH, Rhee EJ, Shin HS, Jo SK, Won JC, Park CY, Kim BJ, Sung KC, Kim BS, Lee WY, Oh KW, Kang JH, Park SW, Lee MH, Kim SW. Higher serum free thyroxine levels are associated with coronary artery disease. Endocr J 2008;55:819–26.
[21] Ascheim DD, Hryniewicz K. Thyroid hormone metabolism in patients with congestive heart failure: the low triiodothyronine state. Thyroid 2002;12:511–5.
[22] McQuade C, Skugor M, Brennan DM, Hoar B, Stevenson C, Hoogwerf BJ. Hypothyroidism and moderate subclinical hypothyroidism are associated with increased all-cause mortality independent of coronary heart disease risk factors: a PreCIS database study. Thyroid 2011;21:837–43.
[23] Marraccini P, Bianchi M, Bottoni A, Mazzarisi A, Coceani M, Molinaro S, Lorenzoni V, Landi P, Iervasi G. Prevalence of thyroid dysfunction and effect of contrast medium on thyroid metabolism in cardiac patients undergoing coronary angiography. Acta Radiol 2013;54:42–7.
[24] Wolff J, Chaikoff IL. The inhibitory action of excessive iodide upon the synthesis of diiodotyrosine and of thyroxine in the thyroid gland of the normal rat. Endocrinology 1948;43:174–9.
[25] Braverman LE. Effects of iodine on thyroid function in man. Trans Am Clin Climatol Assoc 1991;102:143–51.