J Med Sci 2010;30(6):249-255
http://jms.ndmctsgh.edu.tw/3006249 .pdf

The Influence of Age on the Clinical Features of Primary Hypothyroidism in Hospitalized Patients

Po-Wen Yang[1], Hong-Da Lin[2,3*], Kuan-Hung Lin[4], Lee-Ming Wang[3,5], Nan-Ping Yang[3,6], and Yi-Chun Lin[2]

[1]Department of Internal Medicine, Lo-Sheng Sanatorium, Taipei;
[2]Division of Endocrinology and Metabolism, Department of Medicine, Taipei Veterans General Hospital, Taipei;
[3]School of Medicine, National Yang-Ming University, Taipei;
[4]Department of Internal Medicine, Yang-Ming University Hospital, Ilan;
[5]Department of Emergency Medicine, Taichung Veterans General Hospital, Taichung;
[6]The Biostatistics Office, Tao-Yuan General Hospital, Taoyuan,
Taiwan, Republic of China

Background: The diagnosis of primary hypothyroidism in the elderly hospitalized patients is difficult because of lack of classic symptoms and signs, especially when it is concurrent with other non-thyroid illnesses. The purpose of this analysis was to identify the influence of age on the clinical characteristics of hospitalized patients with hypothyroidism. **Methods:** Using the database of a medical center in northern Taiwan, 121 adult inpatients with newly diagnosed primary hypothyroidism were enrolled from January 1, 1999 to December 31, 2006. The patients were divided to two groups, group A were aged ≤ 75 years and group B were aged > 75 years. The initial clinical presentations, laboratory data, diagnoses at admission and discharge, and outcomes were analyzed. **Results:** Our population consisted of 77 males and 44 females, and the mean age was 73 years. The patients were most often diagnosed in the division of cardiology (36.4%), and 71.1% had coexistent heart diseases. The percentage of diagnosis in hypothyroidism after thyroid screening was significantly improved in group A (p=0.012) but not group B (p=0.121).The percentage of diagnoses of heart and neuro-mental diseases at discharge were significantly decreased when compared to at admission. The mean duration of hospitalization and rate of coexistent heart diseases and 2-year follow-up mortality were significantly higher in group B than group A. The main factors associated with 2-year mortality in the hospitalized patients with hypothyroidism were ages and hyponatremia. **Conclusion:** Hospitalized patients with primary hypothyroidism may present as heart or neuromental diseases. Ages and hyponatremia attributed to 2-year mortality in the hospitalized patients with hypothyroidism.

Key Words: aged, hyponatremia, hypothyroidism

INTRODUCTION

The prevalence of hypothyroidism in the elderly is higher than that in younger subjects. The Whickham Survey reported that the incidence of overt hypothyroidism increased tenfold in women age more than 75 as compared with those in their twenties.[1] The Colorado thyroid disease prevalence study reported that an elevation of serum TSH levels was found in 16% of males and 21% of females more than 74 years.[2] Epidemiology studies have reported higher prevalence rates for both overt and subclinical hypothyroidism in women in comparison to men with advanced age. However, this sex-related difference has not been identified for hospitalized patients.[3]

Hypothyroidism may present as an obvious clinical syndrome. When careful attention is paid to myxedematous changes or organ system dysfunction, especially in older female patients, this may ultimately lead to a correct diagnosis. However, most symptoms and signs of hypothyroidism are usually nonspecific and develop insidiously. Diagnosis of thyroid dysfunction in the elderly is particularly difficult because of the lack of classic symptoms and signs, while neuro-mental and cardiovascular signs are frequent.[4] Moreover, the underlying diseases may mask the symptoms and signs of hypothyroidism, and interpretation of thyroid function tests need to

Received: March 9, 2010; Revised: July 26, 2010; Accepted: September 24, 2010
*Corresponding author: Hong-Da Lin, Division of Endocrinology and Metabolism, Department of Medicine, Taipei Veterans General Hospital, No. 201, Sec. 2, Shih-Pai Road, Taipei 112, Taiwan, Republic of China. Tel: +886-2-28757515; Fax: +886-2-28745674; E-mail: hdlin@vghtpe.gov.tw

be handled cautiously in patients with acute illness or in patients on medication because such factors might affect these tests.

Patients with thyroid dysfunction have a higher mortality rate during hospitalization.[5] Clinicians should be familiar with the clinical manifestations of hypothyroidism so that appropriate treatment can be initiated, which in turn may decrease cardiovascular mortality.[6-8] Physical examination alone is often not reliable when confirming or ruling out hypothyroidism,[8] therefore a high degree of suspicion and a full diagnostic workup are required for the diagnosis of hypothyroidism. Routine screening of all hospitalized patients for hypothyroidism is not indicated. Thyroid screening seems to add little to the diagnostic evaluation of patients hospitalized for acute medical or psychiatric illness,[9,10] but may be indicated for patients > 60 years of age or those who are admitted to specialized geriatric units.[10,11]

No previous study has aimed to analyze aged hospitalized patients with newly diagnosed hypothyroidism in Taiwan. The aim of the present analysis was to investigate the potential clinical characteristics of primary hypothyroidism in elderly hospitalized patients in our area and the association between serum thyroid hormone levels and the clinical parameters; furthermore, the association of these factors with mortality was also investigated.

METHODS

We conducted a retrospective analysis of patients with newly diagnosed primary hypothyroidism (ICD-9 code: 244) at a 2,800-bed medical center in northern Taiwan from January 1, 1999 to December 31, 2006. Patients with histories of hypothyroidism under levo-thyroxine treatment, previous thyroidectomy, or previous radioiodine treatment were excluded from the analysis. Serum thyroid stimulating hormone (TSH), triiodothyronine (T3) and free thyroxine (free T4) were analyzed by immunochemiluminometric assays (ICMA) or immunoradiometric assays (IRMA). Using ICMA and IRMA, the reference ranges for TSH were 0.4-4.0 μIU/mL and 0.25-4.0 μIU/mL, respectively; for T3 were 82-179 ng/dL and 95-205 ng/dL, respectively; and for free T4 were 0.8-1.9 ng/dL and 0.59-1.81 ng/dL, respectively. The presence of anti-thyroglobulin (anti-TG) and anti-thyroperoxidase (anti-TPO) antibodies were analyzed by ICMA. Patients with TSH levels > 4.0 μIU/mL excluding other causes of an elevated TSH were considered to have primary hypothyroidism, which was subclinical if the free T4 was normal and overt if free T4 was low.[12] All data were obtained by reviewing the patients' histories, current medications, physical examination results, body mass index (BMI), levels of TSH, T3, free T4, anti-TG and anti-TPO antibodies, blood biochemical analysis, and outcomes.

The subjects were divided into two different groups, those ≤ 75 years (group A) and those > 75 years (group B). Student t-tests or Mann-Whitney rank sum tests where appropriate were employed to compare the normally distributed or non-normal distribution clinical data between these two groups. The Fisher's exact test was used for ratio comparisons. Pearson product moment correlation was employed to assess the relationships between serum TSH, free T4 and T3 levels and clinical factors. The prognostic power of clinical factors for death was analysed by the Cox's proportional hazards regression. Hazard ratios (HRs) with 95% confidence interval (CI) were used to estimate the adjusted relative risk of subjects with hypothyroidism. The relative risk of death from all causes associated with hypothyroidism was calculated at 2 years after baseline measurement. All significant tests were two-side and a value of $p<0.05$ was considered statistically significant. All statistical analyses were performed using the Statistical Package for Social Sciences for Windows (SPSS for Windows 13.0). This study was approved by the Institutional Review Board of the hospital.

RESULTS

Patients

We reviewed 135 cases of newly diagnosed hypothyroidism, of which seven had central hypothyroidism resulting from pituitary or hypothalamus pathology and seven with TSH levels below 10 μIU/mL and thus were excluded. As a result, 121 patients with primary hypothyroidism and serum TSH levels above 10 μIU/mL were enrolled in the analysis. The clinical characteristics of the primary hypothyroidism, including coexistent diseases, clinical symptoms and signs, and the results of blood biochemical analyses, were summarized in Table 1. Nineteen of the 121 patients (15.7%) had subclinical hypothyroidism. Seventy-seven patients (63.6%) were male. The mean age was 73 years (range 34-91 years). The average hospital stay was 20 days (range 1-127 days). The mean age, male ratio, and duration of hospitalization in group B were significantly higher than in group A, while the BMI of group B was significant lower than group A.

The most common coexistent disease was hypertension (53.7%), followed by chronic kidney disease

Table 1 Clinical characteristics of all patients with primary hypothyroidism

	Group A ≤ 75 year-old (n=53)	Group B > 75 year-old (n=68)	All (n=121)
Age (years)	61±12	82±5*	73.0±13.2
Male, n (%)	22	55*	77 (63.6)
Body mass index (kg/m^2)	25.8±4.9	21.3±4.0*	23.5±5.0
Coexistent diseases			
Heart diseases, n (%)	32	54*	86 (71.1)
Cerebrovascular accidents, n (%)	7	15	22 (18.2)
Chronic kidney diseases, n (%)	13	19	32 (26.4)
Symptoms/signs			
Drowsiness, n (%)	6	12	18 (14.9)
Dementia, n (%)	1	2	3 (2.5)
Nausea/Vomiting, n (%)	6	6	12 (9.9)
Constipation, n (%)	0	3	3 (2.5)
Poor appetite, n (%)	9	9	1 8 (14.9)
Cold intolerance, n (%)	2	0	2 (1.7)
Hypothermia < 36 °C, n (%)	10	11	21 (17.4)
Bradycardia < 60/min, n (%)	6	17	23 (19.0)
Blood biochemistry tests			
Sodium, meq/L	137.0±6.5	133.2±8.9*	134.8±8.1
Hemoglobin, mg/dL	10.4±2.3	11.1±1.9	10.8±2.1
Cholesterol, mg/dL	222.5±90.1	178.9±57.0*	198.4±76.5
Thyroid function tests			
Free T4 (ng/dL)	0.40±0.04	0.53±0.28*	0.47±0.28
TSH (μIU/L)	86.26±81.23	65.91±52.12	74.82±67.80
Days of hospitalization (days)	15	24*	20
Two–year mortality, n (%)	4	24*	28 (23.1)

Values are expressed as mean±standard deviation, number or percentage.
FT4: free thyroxine; TSH: thyroid stimulating hormone.
*Significant difference between Group A and B, $p < 0.05$.

Table 2 Differences in main admission and discharge diagnoses attributing to present illness

	Group A, ≤ 75 year-old (n=53)		Group B, > 75 year-old (n=68)	
	admission	discharge	admission	discharge
Hypothyroidism,n (%)	5 (9.4%)	23 (43.4%)*	2 (2.9%)	24 (35.3%)*
Others than hypothyroidism, n (%)	48 (90.6%)	30(56.6%)*	66 (97.1%)	44 (64.7%)
Heart diseases, n	17	9	30	19
Neuro-mental diseases, n	7	2	13	7
Gastrointestine diseases, n	4	3	11	3*
Renal diseases, n	8	4	4	2
Others, n	12	12	8	13

*Significant difference between admission and discharge, $p < 0.05$.

(26.4%), coronary artery disease (22.3%), congestive heart failure (22.3%), and cerebrovascular disease (18.2%). Nineteen patients (15.7%) had a history of arrhythmia, including atrial fibrillation (n=12), sick sinus syndrome (n=3), second degree atrioventricular block (n=2), third degree atrioventricular block (n=1), and ventricular tachycardia (n=1). Eighty-six patients (71.1%) had coexistent heart diseases including hypertension, coronary artery disease, congestive heart failure, or arrhythmia. Patients in group B had a higher rate of coexistent heart diseases than group A (p=0.027).

The most common electrocardiographic abnormalities noted at admission were non-specific ST-T changes (n=21), low voltage (n=18), myocardial ischemia (n=16), sinus bradycardia (n=15), and atrial fibrillation (n=13). Patients in group A had a higher serum sodium and cholesterol levels compared to group B (p=0.011 and 0.007, respectively).

Differences in admission and discharge diagnoses

The most common division assignments at admission were cardiology (36.4%), nephrology (12.4%), neurology (7.4%), gastroenterology (6.6%), and endocrinology and metabolism (6.6%). The most common suspicious diagnosis at admission was heart diseases (38.8%) including congestive heart failure (n=13), arrhythmia (n=8), pericardial effusion (n=5), coronary artery disease (n=2), shock (n=1), and syncope (n=1) and this was followed by renal diseases (18.2%), neuro-mental diseases (16.5%), gastrointestinal diseases (12.4%) and hypothyroidism (5.8%) (Table 2). The diagnoses at discharge showed some difference when compared to those on admission, with heart diseases decreasing significantly to 23.1% (p=0.012), and neuro-mental diseases decreasing significantly to 7.4% (p=0.046). A significant difference in diagnosis of gastrointestinal diseases at admission and discharge was also observed for group B (p=0.045). The diagnosis rate of hypothyroidism after thyroid screening was analyzed by McNemar $\chi 2$ tests and showed significantly improved in group A (p=0.012) but not group B (p=0.121).

Hypothyroidism was the main discharge diagnosis and this covered 47 of the 121 patients. Among these 47 patients, pericardial effusion (9), hyponatremia (7), hypothyroidism (7), bradycardia (3), ileus (3), consciousness change (3), weakness (3), congestive heart failure (2), coronary artery disease (2), dementia (1), cerebrovascular accident (1), dizziness (1), myopathy (1), edema (1), ventral hernia (1), ampulla of Vater lesion (1) and lung can-

Table 3 The correlation coefficient between clinical parameters and thyroid function tests in patients with primary hypothyroidism

	age	BMI	sodium	hemoglobin	cholesterol
TSH	-0.143	0.230*	-0.004	-0.108	0.281**
FT4	0.118	-0.250*	0.079	0.215*	-0.352**
T3	0.135	-0.088	0.177	0.138	-0.218

BMI: body mass index; FT4: free thyroxine; T3: triiodothyronine; TSH: thyroid stimulating hormone.
*p < 0.05
**p < 0.01

cer (1) were the tentative diagnoses at admission. Seven patients were correctly diagnosed with hypothyroidism at admission, of which four were seen at the outpatient department and presented with malaise, nausea or poor appetite; the other three were seen at the Emergency Department and presented with bradycardia, hyponatremia, and drowsiness.

The causes of primary hypothyroidism

Amiodarone-induced hypothyroidism occurred in 14 patients (11.6%). Six patients (5.0%) developed hypothyroidism after radiotherapy for laryngeal or esophageal carcinoma. Twenty-nine of the 73 patients (39.7%) analyzed for anti-TG and/or anti-TPO antibodies had a positive result, resulting in a diagnosis of Hashimoto's hypothyroidism.

Thyroid function tests

Among all 121 patients, the mean TSH level was 74.82±67.80 μIU/mL (range 10.10-470.37 μIU/mL), and the mean free T4 level was 0.47±0.28 ng/dL (range 0.02-1.39 ng/dL). Furthermore, there was a positive correlation between BMI, cholesterol levels and TSH levels and a negative correlation between BMI, cholesterol levels and free T4 levels (Table 3). Twenty-nine patients of group A (54.7%) and thirty-four of group B (50%) were analyzed for T3 and the results were 60.80±32.23 ng/dL and 71.52±45.02 ng/dL, respectively. The T3 mean value for all 63 patients was 66.58±39.72 ng/dL.

Outcomes

The 2–year mortality rate was significantly higher in group B than in group A (p<0.001). Five patients diagnosed with hypothyroidism died while hospitalized, and an additional 21 patients died during the 2–year follow-up period. Most patients died as a result of sepsis (n=16) or cardiovascular events (n=6) including sudden death (n=2), acute myocardial infarction (n=1), ventricular tachycardia (n=1), congestive heart failure with cardiogenic shock (n=1) and dissecting aortic aneurysm (n=1). Age, BMI, T3, serum sodium, hemoglobin and cholesterol levels were predictors of 2–year mortality based on Cox's proportional hazards regression (Table 4). Three models were performed to detect the influence of T3 levels on 2–year mortality. In the model 1 only T3 levels were analyzed. In the model 2 both T3 levels and age were included. In the model 3 those factors with statistical significance obtained in Table 4 were included. After adjustment for all factors, the main factors associated with 2–year mortality in the hospitalized patients with hypothyroidism were ages and hyponatremia (Table 5).

Table 4 The hazards ratio of?various uni-variate on 2-year mortality in the hospitalized patients with hypothyroidism

	Unadjusted		
	Hazard ratio	95% CI	*P*
Age	1.078	1.029-1.129	0.001
Sex(male)	2.181	0.884-5.381	0.090
BMI	0.902	0.825-0.987	0.024
CVD	1.028	0.417-2.535	0.952
TSH	1.000	0.995-1.006	0.980
FT4	0.487	0.119-1.989	0.316
T3	1.011	1.000-1.021	0.044
Sodium	0.948	0.915-0.982	0.003
Hemoglobin	0.798	0.665-0.957	0.015
Cholesterol	0.993	0.987-0.999	0.031

BMI: body mass index; CVD: cardiovascular diseases; FT4: free thyroxine; T3: triiodothyronine; TSH: thyroid stimulating hormone.

DISCUSSION

We enrolled patients with primary hypothyroidism and serum TSH levels above 10 μIU/mL into the analysis, because there is no substantial evidence supporting negative outcomes in patients with subclinical hypothyroidism when the TSH levels are minimally elevated between 4 and 10 μIU/mL.[13] This analysis showed that 94.8% of hospitalized patients with hypothyroidism had primary hypothyroidism, which was similar to the incidence reported in another study.[14] In large population studies of elderly patients, the incidence of hypothyroidism has been found to vary from 1% to as high as 17%, with

Table 5 Three models of Cox regression analysis to assess the influence of several covariates on 2-year mortality in hospitalized patients with hypothyroidism

	Model 1		Model 2		Model 3	
Covariates	Odds ratio (95%C.I.)	p	Odds ratio (95%C.I.)	p	Odds ratio (95%C.I.)	p
T3	1.011 (1.000-1.021)	0.044	1.007 (0.997-1.017)	0.163	1.011 (0.998-1.024)	0.101
Age (>75 vs < 75)			7.001 (1.575-31.110)	0.011	6.736 (1.233-36.805)	0.028
BMI (<18.5 vs ≥ 18.5)					1.204 (0.312-4.653)	0.787
Hyponatremia (yes vs. no)					4.118 (1.107-15.311)	0.035
Anemia (yes vs. no)					0.689 (0.130-3.652)	0.661
Hypercholesterolemia (yes vs. no)					0.974 (0.097-9.797)	0.982

Anemia: hemoglobin levels less than 12 g/dL in females or less than 14 g/dL in males; BMI: body mass index; hypercholesterolemia: serum cholesterol levels greater than or equal to 240 mg/dL. Hyponatremia: serum sodium concentration less than 135 mmol/L; T3: triiodothyronine.

women being more commonly affected than men.[15-17] The prevalence of hypothyroidism in the elderly in a community of southern Taiwan was 2.51%, of which 34.8% had overt hypothyroidism, with autoimmune disease the major cause.[18] However, we found fewer cases of subclinical hypothyroidism than overt hypothyroidism, which is different to previous reports.[15,18] The reasons for this may be as following. First, this analysis enrolled hospitalized patients rather than a community population. Second, our population consisted of more males than females and males had a lower rate of subclinical hypothyroidism than females. Third, the thyroid function test was not part of the routine screening tests of hospitalized patients. Further studies are needed to clarity whether undetected hypothyroidism contributed to the low rate of subclinical hypothyroidism at this hospital.

The diagnosis of primary hypothyroidism was not always easy, especially when it was concurrent with non-thyroid illnesses, since only 7 of the 121 patients with primary hypothyroidism in this study were correctly diagnosed at admission. Even after thyroid screening, the diagnosis rate of hypothyroidism in group B improved insignificantly. This highlights the challenges present when detecting hypothyroidism in elderly hospitalized patients. There was a high prevalence of thyroid dysfunction in the elderly in-patient population, but the symptoms were too often explained away as part of the normal processes of aging. Therefore, thyroid diseases in the elderly can easily go unrecognized.[19-21] Moreover, interpretation of thyroid function tests is also difficult in older individuals due to age-associated changes in thyroid function, such as slight increase in TSH levels, slight decrease in total T4 and a slight decrease in T3 but with these usually remaining within normal limits. Thyroid function is also alternated secondary to non-thyroid illnesses, recovery from illness, and drugs.[22] This analysis only included hospitalized patients and these individuals were therefore more likely to have concomitant diseases that could mimic or mask the presentation of hypothyroidism. This might have contributed to the low rate of suspicion of hypothyroidism at admission and a high degree of suspicion will allow the correct diagnosis to be made.

Thyroid dysfunction was observed in aged hospitalized patients and was related to the mortality. It has been reported that low serum T3 levels correlate with severity of illness among elderly hospitalized patients,[21] and free T3 level was a powerful predictor of mortality during hospitalization among elderly patients.[5] On the other hand, the Zoetermeer study, which enrolled ambulatory relatively healthy men (age 73-94 years), concluded that a low free T4 related to a decreased risk of 4–year mortality, while serum TSH and T3 were not related to mortality.[23] Elderly subjects have a higher rate of coexistent cardiovascular diseases. Thus, increased mortality might be expected in elderly individuals with hypothyroidism. Hypothyroidism is associated with major cardiovascular risk factors, but the association of hypothyroidism and circulatory mortality is inconsistent.[24] This inconsistency can be partly explained by confounding factors and selection bias.[24] We did not find any association between serum TSH and free T4 levels and 2–year mortality. However, we did find that T3 level was a significant uni-variate of 2–year mortality. Ages and hyponatremia were potential predictors of 2–year mortality after adjustment for all factors. Patients with hyponatremia had an increased risk of death in hospital, especially among patients admitted with cardiovascular disease, metastatic cancer, and those for procedures related to the musculoskeletal system.[25] We only enrolled hospitalized patients with newly diagnosed primary hypothyroidism,

and therefore a different patient selection may also have contributed to the different results. Further well-designed prospective studies are needed to clarify whether ages and hyponatremia are predictors of mortality in hospitalized patients with hypothyroidism.

There are three main limitations to this study. First, this is a single center, retrospective analyses involving a review of medical records retrieved from a Veterans General Hospital in Taiwan. Institution selection bias could have affected the results in term of sex-related differences. Second, thyroid function tests were not routinely use to screen all hospitalized patients, and patients with hypothyroidism might not have been recognized if clinicians did not recognize the non-specific or atypical presentations of hypothyroidism. Third, the typical findings of hypothyroidism such as coarse skin, periorbital puffiness, cold skin, and delayed ankle reflex relaxation could not be obtained via this retrospective chart review. Fourth, T3 was evaluated in only 19 of 26 patients who died and this might have confounded the influence of T3 on mortality.

In conclusion, hospitalized patients with primary hypothyroidism may present as cardiac or neuromental diseases. Ages and hyponatremia attributed to 2–year mortality in the hospitalized patients with hypothyroidism. Further well-designed prospective studies are needed to clarify fully whether aged patients with primary hypothyroidism have a higher rate of coexistent heart disease, a longer duration of hospitalization, or a higher mortality rate.

REFERENCES

1. Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, Grimley Evans J, Hasan DM, Rodgers H, Tunbridge F, Young ET. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. Clin Endocrinol (Oxf) 1995;43:55-68.
2. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med 2000;160:526-534.
3. Morganti S, Ceda GP, Saccani M, Milli B, Ugolotti D, Prampolini R, Maggio M, Valenti G, Ceresini G. Thyroid disease in the elderly: sex-related differences in clinical expression. J Endocrinol Invest 2005;28:101-104.
4. Barrou Z, Kiffel C, Lidy C. Dysthyroidism in elderly patients. Clinical characteristics. Presse Med 2001;30(39-40 Pt 1):1939-1943.
5. Iglesias P, Muñoz A, Prado F, Guerrero MT, Macías MC, Ridruejo E, Tajada P, Díez JJ. Alterations in thyroid function tests in aged hospitalized patients: prevalence, aetiology and clinical outcome. Clin Endocrinol (Oxf) 2009;70:961-967.
6. Helfand M, Redfern CC. Clinical guideline, part 2. Screening for thyroid disease: an update. American College of Physicians. Ann Intern Med 1998;129:144-158.
7. 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;91:2159-2164.
8. Razvi S, Ingoe L, Keeka G, Oates C, McMillan C, Weaver JU. The beneficial effect of L-thyroxine on cardiovascular risk factors, endothelial function, and quality of life in subclinical hypothyroidism: randomized, crossover trial. J Clin Endocrinol Metab 2007;92:1715-1723.
9. Ordas DM, Labbate LA. Routine screening of thyroid function in patients hospitalized for major depression or dysthymia? Ann Clin Psychiatry 1995;7:161-165.
10. Helfand M, Crapo LM. Screening for thyroid disease. Ann Intern Med. 1990;112:840-849.
11. Van Camp G, Bourdoux PP, Bonnyns MA. Age influence on clinical features in hospitalized thyroid patients: dissimilarity between clinical and laboratory findings in adulthood. A retrospective study. Thyroidology 1992;4:75-82.
12. Cooper DS. Subclinical hypothyroidism. N Engl J Med 2001;345:260-265.
13. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, Franklyn JA, Hershman JM, Burman KD, Denke MA, Gorman C, Cooper RS, Weissman NJ. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA 2004;291:228-238.
14. Pimentel L, Hansen KN. Thyroid disease in the emergency department: a clinical and laboratory review. J Emerg Med 2005;28:201-209.
15. Levy EG. Thyroid disease in the elderly. Med Clin North Am 1991;75:151-167.
16. Parle JV, Franklyn JA, Cross KW, Jones SC, Sheppard MC. Prevalence and follow-up of abnormal thyrotropin (TSH) concentrations in the elderly in the United Kingdom. Clin Endocrinol (Oxf) 1991;34:77-83.
17. Vanderpump MP, Tunbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. Thyroid 2002;12:839-847.

18. Chuang CC, Wang ST, Wang PW, Yu ML. Prevalence study of thyroid dysfunction in the elderly of Taiwan. Gerontology 1998;44:162-167.
19. Simons RJ, Simon JM, Demers LM, Santen RJ. Thyroid dysfunction in elderly hospitalized patients. Effect of age and severity of illness. Arch Intern Med 1990;150:1249-1253.
20. Bonar BD, McColgan B, Smith DF, Darke C, Guttridge MG, Williams H, Smyth PP. Hypothyroidism and aging: the Rosses' survey. Thyroid 2000;10:821-817.
21. Chuo AM, Lim JK. Thyroid dysfunction in elderly patients. Ann Acad Med Singapore 2003;32:96-100.
22. Chiovato L, Mariotti S, Pinchera A. Thyroid diseases in the elderly. Baillieres Clin Endocrinol Metab 1997;11:251-270.
23. van den Beld AW, Visser TJ, Feelders RA, Grobbee DE, Lamberts SW. Thyroid hormone concentrations, disease, physical function, and mortality in elderly men. J Clin Endocrinol Metab 2005;90:6403-6409.
24. Völzke H, Schwahn C, Wallaschofski H, Dörr M. Review: The association of thyroid dysfunction with all-cause and circulatory mortality: is there a causal relationship? J Clin Endocrinol Metab 2007;92:2421-2429.
25. Waikar SS. Mount DB. Curhan GC. Mortality after hospitalization with mild, moderate, and severe hyponatremia. Am J Med 2009;122:857-865.