Metabolic risk factors for thyroid nodules in different ages

ThePrevalence ofThyroidNodules and theCorrelation between Thyroid Nodules and itsMetabolicRiskFactorsin DifferentAgeGroups

Running titleMetabolic Risk Factors for TN

Highlights

1. Elderly people has higher prevalence of TN;
2. Hypertension, T2DM and smoking may be risk factors for TN in elderly people;
3. Hypertension might be independent risk factors for TN in non-elderly people.

Abstract

Objective: To explore the prevalence of thyroid nodules (TN), along with the correlation between TN and metabolic risk factors in different age groups. Methods: Data from 5599 residents who participated in the epidemiological investigation of TN from Jan to May 2014 were enrolled. The participants were divided into two groups based age: elderly group (≥60 years) and non-elderly group (≥18, but < 60 years). The levels of metabolic indices were measured. Logistic regression analysis (LRA) was performed to assess the association between TN and metabolic risk factors. Results: The prevalence of TN in the elderly group was higher than the non- elderly group (61. 49% *versus* 43. 9%, $P = 0.000$). Patients with TN had higher prevalence of metabolic syndrome (MetS), hypertension, overweight/obese, hyperglycemia, and type 2 diabetes (T2DM) ($P < 0.01$). Moreover, in the non- elderly group, LRA indicated that sex and age (odds ratio (OR) = 1. 820; OR = 1. 037) were independent risk factors for TN, along withT2DM and

smoking (OR = 1. 212; OR = 1. 157) after adjustment for sex and age. Furthermore, in the elderly group, sex was independent risk factor for TN (OR = 1. 366). Besides, hypertension had positive correlations with TN in the two groups (OR = 1. 176ï¼Œ *P* = 0. 031; OR= 1. 353ï¼Œ *P* = 0. 012) after adjustment for sex and age. Conclusion: Elderly people had higher prevalence of TN. Hypertension, T2DM and smoking may be independent risk factors for TN in elderly people, as well as hypertension in non-elderly people.

Key words: Thyroid nodules; Metabolic syndrome; Metabolic Risk Factors;

Introduction

Thyroid nodules (TN), a frequent clinical problem, are one of the most common thyroid diseases. The reported prevalence rate of TN has recently increased dramatically due to the improved imaging modalities, age, female sex, iodine deficiency, and nuclear exposure or other factors [1-6]. Although most people with TN are asymptomatic [7], the disease is clinically important primarily owing to their malignant potential [8]. Therefore, an early detection of the associated risk factors in TN has received much attention in the field of medical science.

The metabolic syndrome (MetS), a cluster of cardiovascular risk factors (e. g. hypertension, glucose and lipid metabolism, obesity, insulin resistance (IR), dyslipidemia), has become a leading health concern in all over the world [9-11]. It is characterized by atherogenic dyslipidemia, insulin resistance and hypertension [12]. In addition, an increasing number of studies have found MetS and its components have significant association with the functional and

morphological alteration in thyroid [13-18]. It is well known that age plays a vital role in both TN and Mets [1, 19]. A recent Chinese study suggested that the elderly population had a high prevalence of TN, and hypertension along with prediabetes and diabetes might be independent risk factors for TN [20].

However, clinical data about the association of MetS and its related components with different age groups are extremely rare. The purpose of study was to explore the prevalence of TN among different age groups and to investigate the correlation between TN and its metabolic risk factors. The results identified by our researches from this study might contribute to a better early detection for TN.

Material and Methods

Participants

The participants were chosen from people surveyed in the epidemiological investigation of thyroid nodules in a Chinese community-based population aged over 18 years. From Jan to May 2014, community resident population (≥6 years, aged ≥18 years, range 18–85 years) who lived in Daxing district, Beijing, China, were enrolled in this survey. The inclusion criteria were aged ≥18 years old. The participants with any of the following characteristics were excluded from this research: pregnancy and lactation, past history of thyroid surgery, treatment history with radioisotopes, medications may have an impact on thyroid function (e. g. thyroxine, anti-thyroid drugs, amiodarone, and iodine), past history of head and neck radiotherapy, incomplete information, history of heart failure or severe neurological or psychological illness (e. g. depression, epilepsy, schizophrenia) that may have an influence

on thyroid function tests, and those people who did not cooperate with physical examination. Totally 6323 volunteers completed the questionnaire. After excluding 724 participants whose demographic information was incomplete and data on thyroid ultrasonography (US) were unfinished, 5599 patients (3569 females and 2030 males) were enrolled in our study. This study was approved by the local Ethics Committee, and informed consents were obtained from all enrolled patients.

Questionnaires and P hysical examination

All enrolled volunteers were asked to complete standardized questionnaires including personal information and clinical data, such as age, gender, diagnosis and treatment history for thyroid disease and metabolic diseases (e. g. diabetes, hypertension, hyperlipidemia), along with smoking habit. Height, weight and waist circumference (WC) were recorded, then, body mass index (BMI) was calculated by dividing body weight (kg) by squared body height (m^2). Right brachial artery blood pressure was measured three times in the sitting position after 5 min rest with a standard electronic blood pressure monitor (HEM- 906, OMRON Co. Inc., Japan), and the mean was calculated.

Data collection and Investigation

All participants received fasting blood specimen collection (3-4 ml) at the early morning. The samples were left standing at room temperature, and stored at -70 °C refrigerator. An oral glucose tolerance test (OGTT) using 75 g glucose load was performed to participants who did not have diagnosis and

take medicine history for diabetes. Fasting plasma glucose (FPG), postprandial blood glucose (PBG), total cho1esterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured by the medical laboratories of Peoples' Liberation Army General Hospital (PLA-GH) using automatic

biochemical analyzer (7600-020, HITACHI Inc., Tokyo, Japan).

Thyroid US

Imaging of the thyroid gland was conducted on color Doppler ultrasound machines (GE Logiq- e, 7-10 MHz linear probe) or portable color Doppler ultrasound scanner SonoScape S2 Vet ((SonoScape Co. LTD, Shenzhen, China) with multifrequency (7-10 MHz) linear transducer. All the procedure was performed by a single researcher.

Standard of Diagnosis for MetS

The patients were diagnosed with MetS according to the diagnostic criteria of the Chinese Diabetes Association (CDS) [21]. If three or more of the following criteria for ages and sex were met: (1) overweight or obese: BMI ≥ 25ï¼Ž0 kg/m ^{2} ; (2) hyperglycemia (fasting glucose ≥ 6. 1 mmol/L, or 2 h loading plasma glucose (PG) ≥ 7. 8 mmol/L), or impaired glucose tolerance (IGT) or type 2 diabetes; (3) clinic BP ≥140/90mmHg, or those who had been diagnosed as diabetes combination with treatments ; (4) hypertriglyceridemia (TG concentration > 1. 7 mmol/L), or HDL-C < 0. 9mmol/L and 1. 0 mmol/L (male and female, respectively). T2DM was diagnosed according to the criteria of World Health Organization (WHO) in

1999 [22]: a FPG ≥ 7. 0 or 2 h PG ≥ 11. 1 mmol/l, or those who had been diagnosed as diabetes combination with treatments.

Statistical analysis

Categorical variables were analyzed using by χ2 test. Continuous variables, presented as mean ± SD, were compared using Student t test. A logistic regression analyses (LRA) was performed to assess the impact of the prevalence rate of thyroid nodules on MetS in elderly and younger people. All analyses were conducted using statistical package for the social sciences (SPSS) software (version 13. 0; SPSS Inc., Chicago, IL). A P value of < 0. 05 was considered as statistically significant.

Results

General characteristics of patients with TN

General characteristics and levels of metabolic indices of the two groups are shown in Table 1. Totally 5599 patients (3569 females and 2030 males) were divided into elderly group (1558 patients, 984 females and 574 males) andnon-elderly group (4041 patients, 2585 females and 1456 males). Among the 5599 patients, 2732 patients were diagnosed with TN: elderly group 958 patients (318 females and 640 males, 65. 56 ± 4. 75 years); non-elderly group 1774 patients (1227 females and 547 males, 48. 70 ± 8. 16 years). The total prevalence of TN was 48. 79%, whereas the prevalence of TN was 61. 49% and 43. 9% in elderly group and non-elderly group, respectively. There was significantly difference in the two groups ($P = 0.000$). In addition, there were significantly differences in sex, age, BMI, WC, SBP, DBP, TC, LDL,

FPG, PBG, UA, and drinking ($P < 0.05$) on the whole between patients with TN (N = 2732) and patients without TN (N = 2867), however, there were no statistically significant difference in TG, HDL-C, and smoking. Moreover, in the non-elderly group, there was no significant difference in TG and HDL-C ($P = 0.995$, $P = 0.447$), but had statistically significant difference in the rest metabolic indices. Unlike the non-elderly group, apart from TG and HDL-C, there were also no significant differences in age, WC, SBP, DBP, FPG, PBG, UA, smoking.

Comparison of pr e valence of TN Mets and its component s

Comparison of prevalence of TN Mets and its components in the two groups was described in Table 2. As shown in Table, we could see patients with TN had higher prevalence of MetS, hypertension, overweight/obese, hyperglycemia, and diabetes T2DM than non-TN patients ($P < 0.01$). However, in the elderly group, there was only hypertension had statistically significant difference between TN and non-TN ($P = 0.003$). In the non-elderly group, there was significantly difference in MetS ($P = 0.008$), hypertension ($P < 0.001$), hyperglycemia ($P < 0.001$), overweight/obese ($P = 0.007$), and T2DM ($P < 0.001$).

Multivariable risk assessment

LRA of different metabolic components predicting TN was presented in Table 3. In elderly group, we found that female sex was independent risk factor for TN ($B = 0.312$, odds ratio (OR) = 1.366, $P = 0.039$). Besides, hypertension had positive correlations with TN ($B = 0.302$, OR = 1.353, $P = 0.012$) after adjustment for sex and age. Whereas, in non-elderly group, female sex and

age were still independent risk factors for TN (B = 0. 599, OR = 1. 820, P = 0. 000; B = 0. 036; OR = 1. 037, P = 0. 000). Moreover, the results also indicated that hypertension (B = 0. 163, OR = 1. 176, P = 0. 031) as well as smoking and T2DM (B = 0. 146, OR = 1. 157, P = 0. 047; B = 0. 192, OR = 1. 212, P = 0. 030) were all independent risk factors for TN after adjusting for sex and age.

Discussion

In the present study, we collected the data from 5599 residents (age≥18 year) who participated in the epidemiological investigation of TN from Jan to May 2014. The results indicated that elderly people had higher prevalence of TN than non-elderly group. Patients with TN had higher prevalence of MetS, hypertension, overweight/obese, hyperglycemia, and T2DM. Female sex was still independent risk factors for TN either in the elderly group or the non-elderly group. Hypertension, T2DM and smoking may be independent risk factors for TN in elderly people, as well as hypertension in non-elderly people.

A German study found thatthe prevalence of TN was 20. 2% among the participants with age 20-79 years in the previously iodine-deficient region [23]. Another research conducted by Guo *et al.* showed that the prevalence of TN was 46. 6% among aged over 40 years [20]. In addition, previous studies demonstrated that female sex was independent risk factor for TN [1, 20, 24]. In line with the above studies, TN was found in 48. 79% among the aged over 18 years, and 61. 49% and 43. 9% in elderly group and non-elderly group, respectively. The prevalence of TN in our study was slightly

higher than other study owing to two main reasons: all the enrolled participates received sensitive imaging techniques (thyroid US); female sex accounted for a more ratio (3569 females and 2030 males). The results suggested that the prevalence of TN increased progressively with age. Therefore, elderly person especially females sex deserve attention for the examination of TN.

Meanwhile, it had been demonstrated that thyroid function had far-reaching effects on glucose and lipid metabolism, energy metabolism, and blood pressure (BP), as well as strong correlations between thyroid volume and body weight, BMI, WC [16, 25-30]. Besides, Semra *et al.* proved that IR was an independent risk factor for nodule formation in an iodine-deficient environment [15]. In accordance with these studies, in our study, patients with TN had higher levels of BMI, CW, SBP, DBP, TC, LDL, FPG, and PBG than non-TN patients. However, there was no significance in TG and HDL-C in the two groups. Moreover, we also found that patients with TN had higher prevalence of MetS, overweight/obese, hyperglycemia, and T2DM. In addition, hypertension was presented with a strong correlation with TN either in the elderly group or the non-elderly group after adjustment for sex and age. The results indicated that thyroid hormones might be general metabolic controllers coordinating with numerous metabolic processes. It is, therefore, reasonable to stress the value of screening TN for people with the above diseases, especially hypertension.

However, there were limitations in our study. We did not evaluate the thyroid function, such as thyroid stimulating hormone (TSH), and insulin levels in each group. Moreover, we did not divide into more groups based age in the

non-elderly group. Although the limitations, the results identified by our researches might provide better evidences for early detection of TN for people with MetS or bad results of metabolic components.

In conclusion, elderly people and female sex had higher prevalence of TN than non-elderly group. Patients with TN had higher prevalence of MetS, hypertension, overweight/obese, hyperglycemia, and T2DM. Hypertension, T2DM and smoking may be independent risk factors for TN in elderly people, as well as hypertension in non-elderly people. Better control of BP, blood glucose and lifestyles (e. g. smoking, drinking) may play significant roles in preventing andtreating of TN.