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Relationship of anthropometric measurements to thyroid nodules in a Chinese population

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ABSTRACT

Objective: Previous studies have found that overweight and obesity are related to numerous diseases, including thyroid cancer and thyroid volume. This study evaluates the relationship between body size and the presence of thyroid nodules in a Chinese population.

Methods: A total of 6793 adults and 2410 children who underwent thyroid ultrasonography were recruited in this cross-sectional study in Hangzhou, Zhejiang Province, China, from March to October, 2010. Sociodemographic characteristics and potential risk factors of thyroid nodules were collected by questionnaire. Height and weight were measured using standard protocols. Associations of height, weight, body mass index (BMI) and body surface area (BSA) with the presence of thyroid nodules were evaluated using multiple logistic regression models.

Results: After adjustment for potential risk factors, an increased risk of thyroid nodule incidence was associated with height (OR 1.15, 95% CI 1.02 to 1.30), weight (OR 1.40, 95% CI 1.24 to 1.58), BMI (OR 1.26, 95% CI 1.11 to 1.42) and BSA (OR 1.43, 95% CI 1.27 to 1.62) in all adults, but most obviously in women. In children, similar associations were observed between risk of thyroid nodule incidence and weight, BMI and BSA, but not height. BSA was the measurement most significantly associated with thyroid nodules in both adults and children.

Conclusions: This study identified that the presence of thyroid nodules was positively associated with weight, height, BMI and BSA in both women and girls. It suggests that tall, obese individuals have increased susceptibility to thyroid nodules.

Trial registration number: NCT01838629.

Strengths and limitations of this study

- Subjects included adults and children.
- Large sample size.
- Weight and standing height were measured using a standardised protocol by a trained examiner rather than being self-reported.
- The main results are presented after adjustment for many potential confounders, including cigarette smoking and alcohol drinking, two important factors that influence overweight.
- The number and size of thyroid nodules were not recorded, and the thyroid nodules were not classified.

INTRODUCTION

Most thyroid nodules are benign,[1] but 5–6.5% are malignant (carcinomas, cancer (CA)).[2] Because thyroid function is linked to development and growth, height and weight are seen as possible indicators of thyroid nodule risk. Overweight and obesity are major risk factors for a number of chronic diseases, including diabetes, cardiovascular diseases and cancer. They are the fifth leading risk for global deaths. In addition, 7–41% of certain cancer burdens are attributable to overweight and obesity.[3] Data from epidemiological studies demonstrate a direct correlation between body mass index (BMI) and the risk of medical complications and mortality rate.[4 5] The prevalence of overweight and obesity has been increasing in most economically developed countries for several decades, and there is evidence that it is also increasing in economically developing countries.[6 7] The prevalence of obesity has recently been increasing dramatically in China as a developing country. A national survey indicates that the prevalence of overweight and obesity, respectively, are 24.1% and 2.8% in men and 26.1% and 5.0% in women.[8] Meanwhile, previous studies have reported functional and morphological alterations in the thyroid gland in relation to obesity.[9–13] As thyroid hormones increase the basal metabolic rate, low thyroid function, even within the clinically normal range, could decrease metabolic speed and lead to obesity.[13 14] In addition, Bastemir *et al*[12] found that serum levels of thyroid-stimulating hormone correlate positively with the degree of obesity and some of its metabolic consequences in overweight people with normal thyroid function. Furthermore, Guth *et al*[15] reported that BMI correlated positively with thyroid size. Although the vast majority of nodules are benign, risk factors for thyroid nodules in the euthyroid population have not yet been fully elucidated. A previous study on a Chinese population indicated that overweight (OR 1.199, 95% CI 1.078 to 1.333) might be a risk factor for thyroid nodules after adjustment for age and gender.[16] Similarly, Guth *et al*[15] observed that mean thyroid size correlated strongly with body weight. However, Kim *et al*[17] reported that Korean patients with thyroid nodules were shorter and lighter and had a smaller body surface area (BSA) than those without thyroid nodules. In women in particular, being shorter and overweight were identified as independent risk factors for the presence of thyroid nodules.

Therefore, the association of anthropometric measurements with thyroid nodules is still unclear. Furthermore, previous studies have rarely focused on the relationship of anthropometric measurements with thyroid nodules in Chinese. The aim of our study was to examine the relationship of anthropometric measurements with thyroid nodules in a large sample of a Chinese population.

MATERIALS AND METHODS

Population features

From March to October 2010, this large cross-sectional study was conducted in Hangzhou city, which is one of the largest commercial cities in eastern China. Details of the population have been previously reported.[18]

Subjects and study design

All participants were recruited on the basis of the following strategies. There are eight districts and five counties in greater Hangzhou. First, three sub-districts or towns were selected randomly from each district or county (except Binjiang district), so 36 sub-districts or towns were selected from greater Hangzhou. Then, one community or village was randomly selected from each sub-district or town. Next, 100 households from each community or village were randomly selected. Finally, we selected 3600 households for interview. The family members of the household were chosen based on the following criteria: (1) age at least 6 years; (2) living for more than 5 years at the present residence. Exclusion criteria were: (1) coronary angiography or endoscopic retrograde cholangiopancreatography in the past 6 months; (2) taking amiodarone; (3) abnormal kidney function or serious illness.

The eligible family members of the selected households were assembled at the village or community administration centre. The researchers introduced the study protocol and obtained written informed consent from each. Meanwhile, interviews were scheduled with the participants. The study protocol was approved by the institutional review board of Hangzhou Center of Disease Control and Prevention. This survey was carried out by well-trained personnel (including community clinic physicians, nurses, public health doctors).

Collection of epidemiological data

The participants were interviewed using a structured questionnaire, which covered demographic characteristics and health status, including sex, age, nationality, physical activity, lifestyle, dietary habits, and personal or family history of thyroid disease (including time of diagnosis).

Collection of data on anthropometric measurements and thyroid nodules

Height and weight were measured using standard protocols, without shoes or outerwear. Height was measured to the nearest 0.1 cm on a portable stadiometer with a GMCS-I-type tripod. Weight was measured to the nearest 0.1 kg with the subjects standing motionless on a scale with a balance-beam scale (RGT-140 weighing apparatus; Wuxi). An ultrasound examination of the thyroid was performed to detect thyroid nodules with a Sonoline Versa Pro (Siemens, Munich, Germany) with a 7.5 MHz, 70 mm linear transducer (effective length, 62 mm). A thyroid nodule was defined as a discrete lesion that was distinct from the surrounding thyroid parenchyma and which had a solid portion regardless of having a cystic portion.

Body mass index

The BMI is defined as the weight in kilograms divided by the square of the height in metres. Although the BMI calculation does not take into account factors such as frame size and body tissue composition, BMI categories are generally used to estimate adiposity and assess how much an individual's body weight departs from what is normal or desirable for a person of that height. According to the criteria recommended by the Working Group on Obesity in China,[19] the classification of BMI for adults was as follows: BMI<24, low (normal and underweight); 24≤BMI, high (overweight and obese). For children, the reference BMI was calculated using the reference height and weight of each age group.[20]

Body surface area

BSA is a commonly used index in clinical practice to correct for patient size differences in various physiological measurements and in calculating drug dosage. BSA is a more accurate measure of obesity, including central obesity, as it is a measurement of area and is able to account for the difference between muscle and fat better than BMI secondary to muscle versus fat.[21] Previous studies have observed an association between BSA and thyroid volume and nodules.[17 22] Various formulas have been proposed for estimating BSA from a patient's weight and height, which may result in slightly different values.[23–26] The most commonly used formula in day-to-day clinical practice is the Mosteller formula:

BSA (m^2)=(square root of product of weight (kg)×height (cm))/60.[25] This formula is simplified from one produced by Gehan and George,[23] and has become a common standard because it is easy to memorise and its use requires only a handheld calculator. So the Mosteller formula was used in our study to calculate BSA.

Definition of variables

For adults, height, weight, BMI and BSA were dichotomised into a high group and a low group. The detailed criteria of each group are shown in online supplementary table S1. For classification of height and weight for adults, we used The Survey Report on National Physical Fitness of Chinese, 2005. In children, the high group included subjects with height or weight equal to or greater than the reference standard for each age group (1 year a group) for the two genders. BMI was classified according to the reference calculated using the reference height and weight of each age group (1 year a group) for the two genders.[20] BSA was classified according to the average value for each gender.

Statistical analysis

Comparison of height, weight and age between patients with and without thyroid nodules was conducted by t test. Comparisons between groups were made using the χ^2 test for qualitative data, including gender, education, marriage, place of residence, cigarette smoking, alcohol drinking, salt appetite, milk consumption, diet patterns and types of salt. Listwise deletion was used to address the missing data in the model.

The adjusted associations of height, weight, BMI and BSA with thyroid nodules were estimated using a logistic regression model stratified by gender. The variables showing a significant difference between the group with and without thyroid nodules were taken as covariates in logistic regression models: age, BMI, educational level, marital status, place of residence, cigarette smoking, alcohol drinking, diet flavour, types of salt, dietary patterns, milk consumption. For adults, age was classified into five classes: 18–29, 30–39, 40–49, 50–59, ≥60. For children, age was classified into four classes: 6–8, 9–11, 12–14, 15–17. To account for the correlation of members in the same household, we calculated robust estimates of variances with a generalised estimating equation using the SAS procedure GENMOD. All analyses were performed with SAS V.9.0. A value of $p<0.05$ was considered significant.

RESULTS

Baseline characteristics of study population

A total of 12 438 individuals were recruited, but 3235 were excluded from analysis because of the absence of anthropometric measurements. Final analyses included 9203 subjects (6793 adults and 2410 children). The average age of the adults was 47.93 years; 62.96% were female, and 4.39%, 66.13%, 26.34% and 3.14% were underweight, normal, overweight and obese, respectively. The sociodemographic characteristics of adult patients with and without thyroid nodules are shown in table 1. Of the 6793 adults, 2228 (32.80%) had thyroid nodules; 71.01% were women. Subjects with thyroid nodules were older, shorter and more likely to be female ($p<0.001$). Moreover, the distributions of education, marital status, place of residence, smoking, drinking, salt appetite, milk consumption and diet patterns showed significant differences between the two groups (table 1).

The sociodemographic characteristics of the paediatric patients with and without thyroid nodules are shown in table 2. Subjects with thyroid nodules were older and more likely to be female ($p<0.05$). The distributions of place of residence, salt appetite and types of salt showed significant differences between the two groups (table 2). Among the children, 47.55% were under the reference BMI and 52.45% were over the reference BMI. In total, 257 (10.66%) children had thyroid nodules; more than half (57.98%) were girls (table 2).

Relationship between anthropometric measurements and thyroid nodules in adults

Relationships between anthropometric measurements (height, weight, BMI, BSA) and thyroid nodules were estimated by gender (table 3). According to the pooled results, height (OR 1.15, 95% CI 1.02 to 1.30), weight (OR 1.40, 95% CI 1.24 to 1.58), BMI (OR 1.26, 95% CI 1.11 to 1.42) and BSA (OR 1.43, 95% CI 1.27 to 1.62) were significantly associated with an increased risk of thyroid nodules. Similar trends were observed in the separate female and male groups, but no significant association was seen in men. The associations with tertiles of exposure (height, weight, BMI, BSA) were very similar to previous findings when subjects diagnosed with thyroid diseases were excluded (see online supplementary table S2).

Relationship between anthropometric measurements and thyroid nodules in children

Relationships between anthropometric measurements and thyroid nodules were also determined in children (table 4). According to the pooled results, weight (OR 1.37, 95% CI 1.03 to 1.81), BMI (OR 1.38, 95% CI 1.04 to 1.83) and BSA (OR 2.97, 95% CI 1.85 to 4.77) were significantly associated with thyroid nodules. The significant association of BSA with thyroid nodules was observed in both boys (OR 2.57, 95% CI 1.25 to 5.28) and girls (OR 3.36, 95% CI 1.82 to 6.20); BMI and weight were also positively related to thyroid nodules in both genders, but a significant association of BMI was observed in boys and a significant association of weight was observed in girls. No significant association was observed between height and thyroid nodules.

Table 1 Distributions of sociodemographic characteristics among adult patients with and without thyroid nodules

Variable	Nodules (n=2228)	No nodules (n=4565)	p Value
Age, years	53.49±13.80	44.93±13.72	<0.001
Height, cm	160.72±7.25	162.24±7.54	<0.001
Weight, kg	59.30±8.12	59.10±8.33	0.177
BMI, kg/m^2	23.07±2.69	22.52±2.65	<0.001
Gender			
Male	646 (28.99)	1870 (40.96)	<0.001
Female	1582 (71.01)	2695 (59.04)	
Education*			
Primary school	922 (42.10)	1317 (29.15)	<0.001
Junior high school	647 (29.54)	1440 (31.87))	
Senior high school	470 (21.46)	1283 (28.40)	
Junior college and above	151 (6.89)	478 (10.58)	
Marriage			
Single	78 (3.51)	378 (8.29)	<0.001
Married	1980 (88.98)	3981 (87.30)	
Divorce	22 (0.99)	47 (1.03)	
Widowed	139 (6.25)	140 (3.07)	
Other	6 (0.27)	14 (0.31)	
Residence location			
Urban area	1214 (54.49)	2125 (46.55)	<0.001
Rural area	1014 (45.52)	2440 (53.45)	
Cigarette smoking			
Never	1825 (82.65)	3508 (77.46)	<0.001
Ever	69 (3.13)	121 (2.67)	
Current	314 (14.22)	900 (19.87)	
Alcohol drinking			
No	1822 (83.27)	3608 (80.55)	0.027
Yes	366 (16.73)	871 (19.45)	
Salt appetite			
Moderate	1135 (51.24)	2479 (54.52)	0.036
Salty	469 (21.17)	916 (20.15)	
Light	611 (27.58)	1152 (25.34)	
Milk consumption			
Yes	837 (42.02)	1965 (45.55)	0.009
No	1155 (57.98)	2349 (54.45)	
Diet patterns†			
Balanced	1662 (74.73)	3484 (76.32)	0.043
Vegetarian	403 (18.12)	722 (15.82)	
Meat	159 (7.15)	359 (7.89)	
Types of salt‡			
Iodised salt	2082 (94.38)	4385 (96.65)	<0.001
Non-iodised	124 (5.62)	152 (3.35)	

Values are mean±SD or n (%).
*Educational status: primary school group includes illiterate subjects; senior high school group is made up of senior high school and technical secondary school.
†Vegetarian indicates that subjects consistently had a vegetable diet; meat indicates that subjects consistently had a meat diet; moderate indicates that subjects intermittently had a vegetable or meat diet.
‡Iodised salt indicates that subjects consistently consumed iodised salt; non-iodised salt indicates that subjects intermittently consumed iodised salt or consistently consumed non-iodised salt.
BMI, body mass index.

DISCUSSION

This study, performed in a large Chinese population, demonstrated that height, weight, BMI and BSA were positively associated with thyroid nodules in adults and children, but only significantly in female adults and children. More explicitly, in the present study, the significant association between high BSA and thyroid nodules was not obviously influenced by sex, age, place of residence and iodine intake.

Thyroid nodules are very common in the general population. The present investigation shows that the prevalence of thyroid nodules was 32.80% in adults and 10.66% in children; but they are found clinically in 4–8% of cases.[27] In our study, being tall and heavy was

Table 2 Distributions of sociodemographic characteristics among paediatric patients with and without thyroid nodules

Variable	Nodules (n=257)	No nodules (n=2153)	p Value
Age, year	12.01±2.73	11.06±3.56	<0.001
Height, cm	150.50±15.84	142.90±19.68	<0.001
Weight, kg	43.83±11.44	38.56±14.39	<0.001
Gender			
Male	108 (42.02)	1083 (50.30)	0.012
Female	149 (57.98)	1070 (49.70)	
Residence location			
Urban area	153 (59.53)	1028 (47.75)	0.0004
Rural area	104 (40.47)	1125 (52.25)	
Diet pattern*			
Balanced	202 (78.91)	1663 (77.46)	0.519
Vegetarian	30 (11.72)	271 (12.62)	
Meat	24 (9.37)	213 (9.92)	
Salt appetite			
Moderate	127 (50.00)	1200 (56.02)	0.042
Salty	61 (24.02)	380 (17.74)	
Light	66 (25.98)	562 (26.24)	
Milk consumption			
Yes	192 (80.67)	1599 (77.73)	0.300
No	46 (19.33)	458 (22.27)	
Types of salt†			
Iodised salt	236 (94.02)	2063 (96.58)	0.042
Non-iodised	15 (5.98)	73 (3.42)	

Values are mean±SD or n (%).
*Vegetarian indicates that subjects consistently had a vegetable diet; meat indicates that subjects consistently had a meat diet; moderate indicates that subjects intermittently had a vegetable or meat diet.
†Iodised salt indicates that subjects consistently consumed iodised salt; non-iodised salt indicates that subjects intermittently consumed iodised salt or consistently consumed non-iodised salt.

significantly associated with thyroid nodules in all adults and women, respectively. However, only the relationship between weight and thyroid nodules was found to be significant in children. To date, few studies have focused on the relationship between anthropometric indexes and thyroid nodules. A previous study[28] showed that thyroid nodules might share similar risk factors with thyroid cancer: iodine deficiency was associated with an increased incidence of thyroid cancer, largely via benign thyroid conditions such as nodules, which were, in turn, strongly associated with thyroid cancer. In addition, body size might be associated with iodine requirement and therefore indirectly related to the presence of thyroid nodules.

Our results are similar to the findings in 88 256 Canadian women in 2012: height was found to be positively associated with the risk of all combined cancers and thyroid cancer, and height was significantly positively associated with risk of thyroid cancer in multivariable models.[29] Further, the European Prospective Investigation into Cancer and Nutrition (EPIC), a large study including half a million subjects, also observed a positive association between height and thyroid cancer in female but not male subjects.[30] Beyond these findings from a European population, a pooled analysis of individual data from 12 case–control studies conducted in eight countries (America, Asia and Europe) suggests that height was moderately related to thyroid cancer risk.[31] In addition, a similar association of height with thyroid nodule risk among Koreans was observed in female but not male subjects.[17] In our findings on a Chinese population, the moderate association of height with thyroid nodules was also observed in female subjects, which is consistent with the results from Korea in Asia and even a European population. However, the association was not significant in children, but we still found an increased OR for greater height (OR 1.30, 95% CI 0.89 to 1.90). This may be due to the small numbers of children studied, and therefore the association between height and thyroid nodules in children needs further investigation.

Furthermore, similarly to height, a meta-analysis of data from eight countries also indicated an association of weight with risk of thyroid cancer in female rather than male subjects.[31] In 2010, Clavel-Chapelon *et al*[32] reported that there was a significant dose–effect relationship between thyroid cancer risk and weight in France. In Asia, a significant association between weight and thyroid nodules in female subjects has been observed in a Korean population.[17] Our data confirm these findings after adjustment for the relevant covariates. Altered thyroid status has profound effects on skeletal development and growth and on adult bone maintenance. The fact that thyroid hormones are associated with regulation

Table 3 Adjusted* logistic regression to identify correlations between body size and thyroid nodules in adults

Variable	Nodules, n (%)	No nodules, n (%)	OR (95% CI)	p Value
Pooled				
Height†				
Low	1334 (59.87)	2576 (56.43)	1.00	
High	894 (40.13)	1989 (43.57)	1.15 (1.02 to 1.30)	0.0245
Weight‡				
Low	1222 (54.85)	2760 (60.46)	1.00	
High	1006 (45.15)	1805 (39.54)	1.40 (1.24 to 1.58)	<0.0001
BMI§				
Low	1438 (64.54)	3351 (73.41)	1.00	
High	790 (35.46)	1214 (26.59)	1.26 (1.11 to 1.42)	0.0003
BSA¶				
Low	1068 (47.94)	2675 (58.60)	1.00	
High	1160 (52.06)	1890 (41.40)	1.43 (1.27 to 1.62)	<0.0001
Female				
Height†				
Low	968 (61.19)	1596 (59.22)	1.00	
High	614 (38.81)	1099 (40.78)	1.24 (1.07 to 1.44)	0.0050
Weight‡				
Low	946 (59.80)	1960 (72.73)	1.00	
high	636 (40.20)	735 (27.27)	1.71 (1.47 to 1.98)	<0.0001
BMI§				
Low	1002 (63.64)	2048 (75.99)	1.00	
High	580 (36.66)	647 (24.01)	1.47 (1.26 to 01.72)	<0.0001
BSA¶				
Low	627 (39.63)	1366 (50.69)	1.00	
High	955 (60.37)	1329 (49.31)	1.53 (1.32 to 1.77)	<0.0001
Male				
Height†				
Low	366 (56.66)	980 (52.41)	1.00	
High	280 (43.34)	890 (47.59)	1.00 (0.82 to 1.24)	0.9699
Weight‡				
Low	276 (42.72)	800 (42.78)	1.00	
High	370 (57.28))	1070 (57.28)	1.00 (0.80 to 1.20)	0.8690
BMI§				
Low	436 (67.49)	1303 (69.68)	1.00	
High	210 (32.51)	567 (30.32)	1.00 (0.81 to 1.23)	0.9892
BSA¶				
Low	441 (68.27)	1309 (70.00)	1.00	
High	205 (31.73)	561 (30.00)	1.21 (0.97 to 1.51)	0.0871

*Adjustment for age, sex, education, marriage, smoking, alcohol drinking, residence location, types of salt, salt appetite, diet patterns, milk consumption.
†Male: high: height≥170 cm, low: height<170 cm; female: high: height≥160 cm, low: height<160 cm.
‡Male: high: weight≥65 kg, low: weight<65 kg; female: high: weight≥60 kg, low: weight<60 kg.
§Low=BMI<24.0; high: BMI≥24.
¶Male: high: BSA≥1.80 m^2, low: BSA<1.80 m^2; female: high: BSA≥1.55 m^2, low: BSA<1.55 m^2.
BMI, body mass index; BSA, body surface area.

of the growth of long bones may be a possible explanation for the association between height and thyroid nodules.[33] Moreover, genetic and environmental factors (eg, diet, nutrition) that are correlated with adult height and weight and also influence thyroid function might be another possible explanation for their association.[31]

Analogously, a significant association between BMI and thyroid nodules was observed in the pooled results for adults. A similar association was observed in women, but not men. In children, significant associations of BMI with thyroid nodules were also observed. Our findings in adults are consistent with results in German[34] and Italian[35] studies and similar to findings from a Korean population.[17] However, results from previous prospective and case–control studies on the association of BMI with thyroid cancer risk have generally been more inconsistent in men than women. In a large Norwegian cohort of more than two million, the risk of thyroid cancer increased moderately with increased BMI in both sexes, but the results were not adjusted for smoking and other potential confounders.[36] After adjustment for key covariates such as cigarette smoking, alcohol drinking, physical

Table 4 Adjusted* logistic regression to identify correlations between body size and thyroid nodules in children

Variables	Nodule, n (%)	No nodules, n (%)	OR (95% CI)	p Value
Pooled				
Height†				
Low	140 (54.47)	1259 (58.48)	1.00	
High	117 (45.53)	894 (41.52)	1.15 (0.87 to 1.53)	0.3347
Weight‡				
Low	118 (45.91)	1175 (54.58)	1.00	
High	139 (54.09)	978 (45.42)	1.37 (1.03 to 1.81)	0.0292
BMI§				
Low	106 (41.25)	1040 (48.30)	1.00	
High	151 (58.75)	1113 (51.70)	1.38 (1.04 to 1.83)	0.0248
BSA¶				
Low	77 (29.96)	1144 (52.22)	1.00	
High	180 (70.04)	1009 (47.78)	2.97 (1.85 to 4.77)	<0.0001
Girls				
Height†				
Low	79 (53.02)	643 (60.09)	1.00	
High	70 (46.98)	427 (39.91)	1.30 (0.89 to 1.90)	0.1719
Weight‡				
Low	63 (42.28)	555 (51.87)	1.00	
High	86 (57.72)	515 (48.13)	1.55 (1.07 to 2.25)	0.0218
BMI§				
Low	63 (42.28)	488 (45.61)	1.00	
High	86 (57.72)	582 (54.39)	1.25 (0.86 to 1.81)	0.2391
BSA¶				
Low	43 (28.86)	556 (51.96)	1.00	
High	106 (71.17)	514 (48.04)	3.36 (1.82 to 6.20)	0.0001
Boys				
Height†				
Low	61 (56.48)	616 (56.88)	1.00	
High	47 (43.52)	467 (43.12)	0.97 (0.63 to 1.49)	0.8870
Weight‡				
Low	55 (50.93)	620 (57.25)	1.00	
High	53 (49.07)	463 (42.75)	1.15 (0.75 to 1.77)	0.5120
BMI§				
Low	43 (39.81)	552 (50.97)	1.00	
High	65 (60.19)	531 (49.03)	1.59 (1.03 to 2.44)	0.0355
BSA¶				
Low	34 (31.48)	588 (54.29)	1.00	
High	74 (68.52)	495 (45.71)	2.57 (1.25 to 5.28)	0.0104

*Adjustment for age, sex, residence location, types of salt, salt appetite, diet patterns, milk consumption.
†High: height or weight≥reference standard; low: height or weight<reference standard.
‡High: height or weight≥reference standard; low: height or weight<reference standard.
§The reference height and weight were used to calculate the BMI reference.
¶Male: high: BSA≥1.26 m^2, low: BSA<1.26 m^2; female: high: BSA≥1.22 m^2, low: BSA<1.22 m^2.
Mean of male BSA=1.26 m^2; mean of female BSA=1.22 m^2.
BMI, body mass index; BSA, body surface area.

activity and medical history of diabetes, the largest prospective study conducted in the USA also found a significant positive association between BMI and thyroid cancer risk in women.[37] Moreover, a systematic review conducted by Peterson *et al*[38] in 2012 (including 37 studies) showed that most of the studies confirmed a positive association of BMI with thyroid cancer in both sexes. The inconsistent results between men and women in previous studies are probably due to smaller numbers of cases in men and the lack of control for important covariates (eg, cigarette smoking, alcohol intake). Current smoking and alcohol intake are associated with BMI.[39–42] Lack of adjustment for smoking status or alcohol drinking may be an important bias in the association between BMI and risk of thyroid nodules. The present study covered adults and children, and the associations of BMI with thyroid nodules were consistent in adults and children after adjustment for important covariates. Based on large samples and reducing important biases, our findings indicate that overweight and obesity are associated with thyroid nodules in both adults and children. The association may be a metabolic consequence of excess adipose tissue. Leptin produced by adipocytes has important influences on central regulation of thyroid function through stimulation of thyrotropin-releasing hormone. This seems to be important for downregulation of thyroid function in states of energy deficits, but the importance for modulation of thyroid function under more physiological conditions is uncertain.[43 44] In addition, thyroid hormones may be a significant determinant of sleeping energy expenditure in subjects without overt thyroid dysfunction.[45] Similarly, differences in thyroid function, within what is considered the normal range, are associated with differences in BMI, caused by longstanding minor alterations in energy expenditure.[13] What is more, obesity is associated with insulin resistance and increased production of insulin and insulin-like growth factors, which in turn have been reported to be associated with thyroid disorders.[2 46 47]

Similarly to thyroid cancer,[2 37] thyroid nodules are more common in women than in men.[48–52] Sex differences in the association between BMI and thyroid cancer have been confirmed in other studies.[31 53 54] Similar results were observed in a Korean study.[17] Patients who were normal or overweight according to BMI subgroup were identified as having a higher frequency of thyroid nodules. However, no significant relationship between body size and thyroid nodules was observed in men. Our findings in adults were consistent with a sex difference in the association of BMI with thyroid nodules. The difference in thyroid nodule incidence between the two genders suggests that growth and progression of thyroid tumours is influenced by sex hormones, particularly oestrogen.[55 56] However, sex differences in the correlation between body size and thyroid nodules were not obvious in children. This may due to the smaller difference in sex hormones in children compared with adults. Few studies have noted a correlation between body size and thyroid nodules in children; our findings in children require further investigation.

BSA is a better indicator of circulating blood volume, oxygen consumption and basal energy expenditure than BMI or weight.[57] In the present study, BSA was significantly associated with thyroid nodules in adults and children. The association was not influenced by sex, age, place of residence and iodine intake. A positive association of thyroid cancer with current BSA was consistently found in adults by Suzuki *et al* in Japan in both sexes after adjustment for the main covariates.[58] In addition, it has been reported that BSA plays a dominant role in thyroid cancer risk and explains the apparent role of BMI in adults.[57] Muscle is more dense than fat, and BMI is not able to differentiate increased weight.[59] BSA is a more accurate measure of obesity, including central obesity, as it is a measurement of area and is able to account for the difference between muscle and fat better than BMI secondary to muscle versus fat.[21] In many ways, the association between BSA and thyroid nodules more strongly confirms the increased risk of thyroid nodules with overweight and obesity than the association between BMI and thyroid nodules.

Considering the potential selection bias introduced by subjects with thyroid problems, we re-evaluated the associations of height, weight, BMI and BSA with thyroid nodules after excluding subjects with diagnosed thyroid disease (see online supplementary tables S3 and S4). Our analyses showed that the associations were very similar to our findings before excluding these subjects. Moreover, we observed similar associations of anthropometric measurements with thyroid nodules when considering quartiles as cut-off points (see online supplementary table S2). Our findings indicate that higher anthropometric measurements are significantly associated with thyroid nodules in Chinese. Further, our study was performed in large populations of adults and children. In addition, weight and standing height were measured using a standardised protocol by a trained examiner rather than being self-reported, reducing the bias of overestimation or underestimation of height and weight.[60 61] Moreover, all participants were screened for thyroid nodules via ultrasonography, reducing the potential for screening bias. In addition, in order to reduce possible bias, we adjusted for most main covariates, including cigarette smoking and alcohol drinking, two important factors that influence overweight.[39–42] In particular, salt type, salt appetite and diet patterns were taken as covariates in the analytical models; the effect of iodine on risk of thyroid nodules was considered. Hence, the associations of anthropometric measurements were robust.

LIMITATIONS OF STUDY

There were several limitations in this study. First, waist and hip circumferences were not measured, which hampered examination of the association of central adiposity with thyroid nodules. Second, the number and mass of the thyroid nodules were not recorded, and the thyroid nodules were not classified. Therefore it was not possible to determine different associations between anthropometric measurements and different kinds of thyroid nodule. Also, the age difference between the subjects with and without thyroid nodules may be a potential bias.

CONCLUSION

We found that thyroid nodule risk increased with weight, height, BMI and BSA, especially in female subjects. Similar trends in relationships between thyroid nodules and weight, BMI and BSA were observed in children. Of the four indicators, BSA was mostly strongly associated with the presence of thyroid nodules. It implies that individuals who are tall and obese have higher susceptibility to thyroid nodules.

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